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ABSTRACTS

Presidential Lecture

PL

Discovery of autoantibodies and their clinical application

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Conflict of interest: Yes

Autoantibodies are the hallmark of systemic autoimmune diseases. More than 100 of autoantibodies have been found in various connective tissue diseases and their target antigens are identified. Most of the autoantigens are important enzymes or regulatory factors that are involved in essential function of genes and cells such as replication, recombination, transcription, splicing and translation. The elucidation of fine structure and function of autoantigens gave important insights not only in pathophysiology of autoimmune diseases but also in basic molecular and cell biology. I graduated Keio University School of Medicine in1978, and started the studies of autoantibodies in connective tissue disease that had been one of the main projects in the rheumatology laboratory supervised by Professor Mitsuo Homma as a postdoctoral student. At that time, I was given the theme of autoantibodies in polymyositis and dermatomyositis (PM/DM) that had been thought to be the disease with no autoantibodies. In this study, the discovery of anti-Ku antibody in myositis overlap syndrome determined my future step of the research. To identify the target autoantigen, I worked in Yale University and learned the method of molecular biology. The Ku antigen was a 70kD and 80kDa heterodimer protein with dsDNA end binding activity, which was demonstrated later as the activating factor of DNA-dependent protein kinase. I also succeeded the molecular cloning of the 80kDa Ku protein (Ku80). Now the name "Ku" has remained, and the Ku protein is thought to be the molecule that plays important roles in multiple cellular functions such as DNA repair and gene recombination. Moreover, the immunoprecipitation method (both RNA and protein), which I learned and modified, has still been a powerful technique to discover novel autoantibodies. Most autoantibodies are closely associated with certain diseases and clinical features, and give us important clinical information for diagnosis, classification, prognosis, clinical course and treatment strategy. In recent years, more and more new autoantibodies have been recognized, some of which I have participated in the discovery and the development of detection systems. In particular, many novel autoantibodies found in PM/DM have clear association with clinical manifestation of patients. Autoantibodies to a series of aminoacyl-tRNA synthetases (anti-ARS antibodies) are associated with a common clinical manifestation, termed anti-synthetase syndrome including myositis, interstitial lung disease (ILD), mechanic's hand, polyarthropathy and Raynaud' phenomenon. Anti-MDA5 antibody is found in patients with clinically amyopathic dermatomyositis (CADM) and strongly associated with acute ILD with poor life prognosis. These two myositis-specific autoantibodies are both associated with ILD, but their clinical significance is totally different. ILD in anti-ARS-positive patients show a good response to the initial glucocorticoid therapy but their long-term prognosis is poor because of frequent recurrences. On the other hand, ILD in anti-MDA5-positive patients is characterized by rapid progression and resistance to the conventional therapy, and shows very poor prognosis within several months. We have experienced improved outcome by introducing an early and intensive immunosuppressive regimen in such patients and concomitant use of plasmapheresis in more intractable cases. Recently, these new myositis-specific autoantibodies have been approved to use in routine laboratory tests. New autoantibodies and detection systems may be expected as useful tools for early diagnosis and treatment strategy of myositis and ILD.

Representative Session

RS

Regulatory T cells and autoimmune disease

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Conflict of interest: None

Regulatory T (Treg) cells, which specifically express the transcription factor Foxp3, are actively engaged in the maintenance of immunological self-tolerance and homeostasis. The majority of them develop in the thymus as a functionally distinct and mature T-cell subpopulation, with their stable Foxp3 expression chiefly maintained by Treg-specific DNA demethylation. It is poorly understood, however, how Treg-specific transcriptional and epigenetic changes are initiated and coordinated to determine the Treg cell lineage in the thymus. Here, with recently demonstrated associations of super-enhancers with cell type-specific gene regulation and lineage determination in various cell types, we first identified Treg cell-specific super-enhancers (Treg-SEs), many of which were associated with the Treg signature genes, such as *Foxp3*, *Ctla4* and *Il2ra*. The establishment of Treg-SEs developmentally began in Treg progenitor cells before *Foxp3* transcription and Treg-specific DNA demethylation, facilitating early induction of the associated genes. It required the genome organizer Satb1, which bound to Treg-SEs before their activation and extended its binding sites within the SEs along Treg cell differentiation. T cell-specific deletion of *Satb1* impaired Treg-SE formation in Treg precursor cells, hindering both Treg-specific DNA demethylation and the transcription of Treg-SE-associated genes including *Foxp3*. The consequent arrest of Treg cell differentiation at the precursor stage resulted in spontaneous development of severe autoimmunity and IgE hyperproduction. Our results thus demonstrate how Satb1-dependent Treg-SE establishment and subsequent transcriptional and epigenetic changes control Treg cell linage specification in the thymus, and how molecular anomaly in this process causes autoimmune and other immunological diseases via affecting Treg cell development.

Symposium

S1-1

Clinical significance of a new inflammatory marker LRG in evaluating disease activity of rheumatoid arthritis

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Conflict of interest: Yes

Acute phase reactants such as CRP and SAA and erythrocyte sedimentation rate (ESR), which are upregulated in response to IL-6, have been used as good inflammatory biomarkers to monitor disease activities of immune disorders including rheumatoid arthritis (RA). Nowadays, however, molecular-targeted anti-rheumatic agents such as tocilizumab that can inhibit IL-6 function are widely used as effective therapies. Because these IL-6-inhibiting agents can shut down the upregulation of acute phase reactants, current biomarkers are unhelpful to evaluate disease activity during such therapy. Moreover, these biomarkers are also not useful to evaluate activities in some immune disorders such as ulcerative colitis (UC) and systemic lupus erythematosus, because these disorders are not necessarily accompanied with IL-6 elevation. To develop a new biomarker, we took advantage of proteomic screening and identified a candidate biomarker leucine rich α2 glycoprotein (LRG) from sera of RA patients. Interestingly, we found that LRG expression is induced not only in liver but also at the site of inflammation, in both IL-6-dependent and -independent manners. Thus, LRG likely has unique properties different from current inflammatory biomarkers. Indeed, our data indicate that LRG is correlated well with the disease activity of inflammatory bowel diseases including UC. We already have applied an LRG quantification kit for the manufacturing approval to use LRG as a biomarker of UC. We also plan to develop LRG as a biomarker of RA during IL-6-inhibiting therapy such as tocilizumab. Moreover, interestingly, our data indicate that LRG functions as an enhancer of TGF-β signaling and mice lacking LRG are resistant to experimental inflammatory diseases such as DSS-induced colitis and collagen-induced arthritis. In this talk, I will report clinical significance of a biomarker LRG in evaluating RA disease activity during tocilizumab therapy. I will also report a pro-inflammatory role of LRG in the pathology of RA.

S1-2

Microbiota in rheumatoid arthritis

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Conflict of interest: None

It has recently been demonstrated that intestinal microbiota contributes to not only production of nutrients but also development of adaptive immunity and resistance to infection. Furthermore, alteration of microbiota composition, called dysbiosis, has been shown in several disorders. Some of these disorders are triggered by dysbiosis itself. Rheumatoid arthritis (RA) is caused by genetic predisposition, but several environmental factors also contribute to the RA manifestation. Some of mouse models of arthritis do not develop joint inflammation in germ-free condition, indicating that intestinal microbiota is involved in the pathogenesis of arthritis. We analyzed whether microbiota contributes to the RA pathogenesis. We analyzed fecal microbiota composition in healthy controls (HC) and early RA patients, who were diagnosed as RA within two years. We found that some of early RA patients showed altered composition of microbiota, in which Prevotella copri was markedly increased. We then analyzed whether dysbiosis found in some early RA patients was involved in the RA pathogenesis using a mouse model of arthritis, SKG mouse model. SKG mice, which were orally treated with combination of antibiotics, did not develop joint inflammation, indicating that intestinal microbiota is implicated in the arthritis development. Therefore, we made germ-free SKG mice, and colonized them with HC-type fecal microbiota (HC-SKG) and RA-type fecal microbiota (RA-SKG). RA-SKG mice developed more severe arthritis than HC-SKG mice did. These findings indicate that dysbiosis observed in some of early RA patients contributes to development of joint inflammation.

S1-3

Multi-lectin assay detecting glycosylation alteration related with rheumatoid arthritis disease activity

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Conflict of interest: None

The entire complement of glycans on the cell, i.e., cell glycome, is defined by the glyco-synthesis machinery regulated by the expression pattern of more than 100 glycogenes. The glycome depends on the extent of cell differentiation and the state of the cells such as the origin of a tissue, its developmental stage, and the presence of malignancy. Therefore, the cell glycome analysis leads to knowing the cell. Glycan-binding substances such as lectins have been used to characterize specific histological types of diseased cells in pathology. Multi-dimensional staining by lectins is expected to find out a novel glycome shift during disease progression, which triggers discovery of disease-specific biomarkers. Lectin microarray is a unique multi-assay system based on the protein chip technology. Owing to its simplicity and highest sensitivity, this system has been used as a tool for differential glycan analysis of intact glycoproteins in clinical samples including tissue, primary cell, and serum. One of the good practical applications is finding out disease-related *N*-/*O*-glycosylation alterations on tissue specimens; thereby we have applied the specific information in tissue glycome to the uppermost stream of glycobiomarker development. As another application, a method was constructed for focused differential glycan profiling of an endogenous glycoprotein assisted by a specific antibody, which is ideal for glycobiomarker verification and construction of assay. In this symposium, I will introduce the concept and one example for the microarray-based multi-lectin analysis toward development of a glycobiomarker for estimating rheumatoid arthritis disease activity.

S1-4

Chemokine blockade for rheumatic diseases

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Conflict of interest: Yes

Chemokine induces directional cellular migration. About 50 chemokines and 20 chemokine receptors have been identified. In the rheumatic diseases and inflammatory diseases, chemokine might contribute accumulation of inflammatory cells into the inflamed tissue. In addition, chemokine could also induce angiogenesis, stimulation of monocyte/macrophage, T cell, B cell and fibroblast, and osteoclastogenesis. Expressions of chemokine and chemokine receptor in the affected region have intensively analyzed and the effects of chemokine blockade on animal models of the diseases were evaluated. It has been reported that in the rheumatoid arthritis, a large number of chemokines were expressed in the synovial tissue. Blockade of some of the chemokines was effective for the arthritis of animal models. Clinical trials of monoclonal antibodies against CCL2 and the receptor, CCR2, and synthetic compounds of CCR5 inhibitor for rheumatoid arthritis were conducted, but they were not effective. However, oral CCR1 inhibitor was effective in the phase II clinical trial and anti-CXCL10 (IP-10) monoclonal antibody was also effective in the phase II trial. Moreover, anti-CX3CL1 (fractalkine) monoclonal antibody was found safe and well tolerated, and demonstrated clinical efficacy in patients with rheumatoid arthritis in the phase I/II trial. In systemic lupus erythematosus and polymyositis/dermatomyositis, expressions of chemokine and chemokine receptor were also analyzed. Effects of the chemokine inhibition on the animal models were also demonstrated. Chemokine blockade is a promising novel treatment strategy for rheumatic and inflammatory diseases.

S1-5

Recent Progress and perspective of JAK inhibitors for the treatment of rheumatoid arthritis

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Conflict of interest: Yes

Considerable advances in the treatment of rheumatoid arthritis (RA) have been made by the combined use of methotrexate (MTX) and biological DMARDs. Clinical remission becomes an achievable goal in many patients and rapid and appropriate induction of remission is prerequisite to halt joint destruction. However, biological DMARDs require intravenous or subcutaneous injection and some patients fail to respond to these drugs or lose their primary response. Currently, Janus kinase (JAK) inhibitors have been developed as a new class of DMARD that inhibits the non-receptor tyrosine kinase family JAK involved in intracellular signaling of various cytokines and growth factors. Several JAK inhibitors have been developed as new therapies for patients with RA as oral synthetic DMARDs. A JAK inhibitor, tofacitinib, has already been approved in many countries. Results of phase III clinical trials using a JAK1/2 inhibitor, baricitinib, have shown feasible efficacy and tolerable safety. Both drugs are effective in patients who showed inadequate response to biological DMARDs as well as synthetic DMARDs. In addition, clinical phase III trials using filgotinib and upadacitinib, selective JAK1 inhibitors, are underway. Because JAK inhibitors inhibit multiple cytokines and signaling pathways, further studies are needed to determine their risk-benefit ratio and selection of the most appropriate patients for such therapy. These issues will need to be watched closely as further data emerge from long-term extension studies of RA cohorts. Thus, determination of risk factors for infection and carcinogenicity is one of the top priorities for rheumatologists.

S1-6

Efficacy and safety of denosumab, directing against RANKL in RA treatment

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Conflict of interest: Yes

Joint destruction is an indispensable process, resulting in the irreversible functional disability in Rheumatoid Arthritis. In particular, bone erosion is a main part of joint destruction and molecular mechanism underlying the osteoclast differentiation has been well recognized. While denosumab, fully human monoclonal antibody directing against RANKL is now widely used in clinical practice for the treatment of osteoporosis, clinical trials of denosumab in RA has also been conducted. Following initial phase 2 trial in US, late phase 2 trials comparing denosumab 60mg every 2 months, 3 months, 6 months, and placebo in active RA for one year (DRIVE trials), and phase 3 trials (DESIRABLE) demonstrated significant benefit in inhibiting progression of bone erosions. In this symposium, the role of denosumab in RA treatment will be discussed by reviewing the recent data regarding efficacy and safety of denosumab.

S2-1

Sarcopenia in Asia: consensus report of the Asian Working Group for Sarcopenia

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Conflict of interest: None

Sarcopenia, a well-known geriatric syndrome, has gained extensive attentions in research and in clinical practice in recent years. However, due to the differences in ethnicity, cultural, social and anthropometric backgrounds, clinical characteristics and clinical implications regarding to sarcopenia in Asian people may differ greatly from Caucasians. In 2014. Asian Working Group for Sarcopenia (AWGS) has proposed the Asian consensus for sarcopenia diagnosis based on available publications. The AWGS criteria basically followed the European consensus, but determine different cut-offs for diagnosis based on previous papers from Asian countries. After the introduction of AWGS criteria, more than 200 papers related to sarcopenia have been published from Asian countries, However, a great number of challenges still exist. First, the higher adiposity of Asian people than Caucasians made the diagnosis of sarcopenia in Asian people more difficult. On the other hand, the declining rates of muscle mass, strength and physical performance in Asian populations were slower. Lastly, the muscle mass of young ladies in most Asian countries may be lower than older ladies in their own countries, which may be related to cohort effect. More studies are needed to clarify the clinical impact of sarcopenia in the future.

S2-2

Frailty and sarcopenia: 2017 update

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Conflict of interest: Yes

Sarcopenia is characterized by loss of muscle strength and muscle mass, leading to falls and adverse health outcomes, while frailty is associated with vulnerability to adverse health outcomes such as disability, need for long-term care, hospitalization, loss of independence, and mortality. For sarcopenia several diagnostic algorithms have been proposed including ours, the Asian Working Group for Sarcopenia criteria and the consensus has been formed to define sarcopenia as the combination of loss of muscle strength/physical function and muscle mass. Sarcopenia is an important health care issue in patients with rheumatoid arthritis along with many other diseases such as COPD, heart failure, renal failure and cancer, although most of the health care professionals do not understand how to diagnose and treat sarcopenia. That is why we are now working on the clinical guidelines for sarcopenia based on systematic review. Most of the diagnostic criteria for sarcopenia require walking speed and grip strength for the assessment of physical function. However, it is sometimes difficult to measure walking speed at the doctor's office. Therefore, we tried to find measurements which have a significant association with walking speed and can be performed at the doctor's office so that primary care physicians to make a diagnosis of sarcopenia. In this study we tried to determine the association of one leg standing and the five-chair stand test with walking speed. In community-dwelling older people, we found that the cutoff for one leg standing to predict sarcopenia is 3 sec or less and that for five chair stands is 10 sec or less. Thus we conclude that one leg standing and the five-chair stand test can be used for the assessment of sarcopenia in place of walking speed in daily practice. In terms of frailty, a consensus has not been completely formed thus far and many diagnostic scales are available worldwide. Among many diagnostic criteria, the cardiovascular health study criteria have been extensively used for research for the last 10 years. Additionally we need to define cognitive frailty and social frailty in addition to physical frailty. The current status will be discussed.

S2-3

Epidemiology of the locomotive syndrome: 2017 update

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Conflict of interest: None

Locomotive organ disorders are major causes of disability and require support. Given the increasing proportion of elderly individuals in the Japanese population, a comprehensive and evidence-based prevention strategy for musculoskeletal diseases is urgently required. The Japanese Orthopaedic Association (JOA) proposed the term 'locomotive syndrome' to designate a condition requiring nursing care or the risk of developing such a condition, following a decline in mobility resulting from

one or more disorders of the locomotive organs, which include the bones, joints, muscles, and nerves. In addition, the JOA proposed the following three tests as candidate indices to assess the risk of developing the locomotive syndrome: the two-step test, stand-up test, and 25-question geriatric locomotive function scale, and determined the clinical decision limits of these indices for assessing the risk of locomotive syndrome. However, little information is available regarding the epidemiology of the locomotive syndrome and/or locomotive organ disorders, and the interactions between them. The Research on Osteoarthritis/Osteoporosis Against Disability (ROAD) study, which started in 2005-7, is a prospective cohort study that aims to elucidate the environmental and genetic background for musculoskeletal diseases. It was designed to examine the extent to which risk factors for these diseases are related to clinical features, laboratory and radiographic findings, bone mass and geometry, lifestyle, nutritional factors, anthropometric and neuromuscular measures, and fall propensity. In the present symposium, we present epidemiological indices such as the prevalence and co-existence of locomotive organ disorders including osteoarthritis of the knee, lumbar spine, and hip, osteoporosis, and sarcopenia, using the latest data of the ROAD study. Further, we describe mutual associations among locomotive organ disorders. Finally, we show the prevalence of the locomotive syndrome using tests proposed by the JOA for assessing the risk of developing it.

S2-4

Sarcopenia in rheumatoid arthritis patients

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Conflict of interest: Yes

Sarcopenia is characterized by loss of muscle strength and muscle mass, leading to falls and adverse health outcomes. Patients with rheumatoid arthritis (RA) may have a higher risk for sarcopenia due to chronic inflammation, reduced physical ability, and concomitant treatments such as glucocorticoids. We comprehensively analyzed the state of sarcopenia in 388 female RA patients. We measured muscle mass, muscle strength, and walking speed and defined sarcopenia based on the diagnostic algorithm of the Asian Working Group for Sarcopenia. The prevalence of sarcopenia in RA patients was extremely high (37.1% of all and 51.0% of over age 65) compared with the age-matched general populations (5.0~13.0% of over age 65). The prevalence of 'low muscle mass' which can be defined only by muscle mass was also high (49.0%) in RA patients, excluding the possibility that the high prevalence of sarcopenia in RA patients is due to the false positive effect by the evaluation of hand grip strength related to pain or deformity of joints. RA patients with sarcopenia had approximately 2.0-fold higher risk of falls, 11.5-fold higher risk of fractures. Longer disease duration, advanced stage of RA, and mal-nutrition positively correlated with sarcopenia, while the use of biological DMARDs negatively associated with sarcopenia. Thus, sarcopenia is a serious complication that degrades ADL and QOL of RA patients. Use of biological DMARDs but not glucocorticoids may have the potential to reduce the prevalence of sarcopenia and improve the disease outcome of RA.

S2-5

Cachexia and Rheumatoid Arthritis

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Conflict of interest: None

Cachexia is negative prognosticator for patients' quality of life, morbidity and mortality. It is most commonly associated with cancer, chronic heart failure and HIV/AIDS. However, cachexia is present in most subchronic and chronic diseases including rheumatoid arthritis and it is characterized by >5% weight loss over a period of 12 months, or a low BMI plus additional biochemical abnormalities. A major contributor to cachexia is inflammation and its associated cytokines (most prominently TNF alpha, IL-1, IL-6) that induce the loss of muscle protein through an activation of FoxO and NfkB transcription factors leading to a strong induction of atrogens including MAFbx and MuRF1, which are considered rate-limiting E3-ligases in the up-regulation of proteasomal protein degradation. Further mechanisms of cachexia include intracellular blunting of the anabolic insulin/IGF-1 signaling, increased autophagy and cell death. Moreover, myostatin – the negative regulator of muscle growth – is up-regulated under cachectic conditions, including in rheumatoid arthritis. Currently, there are no approved drugs to treat cachexia and treatment options so far are limited to nutritional support and exercise training. Unfortunately some drugs targeting the underlying diseases and/or inflammation such as glucocorticoids may actually increase the loss of muscle mass. In conclusion, cachexia is a multifactorial syndrome that leads to a bad prognosis for the patients and has no currently approved drugs to treat it. Therefore, more research in the field is imperative.

S3-1

New treatment strategies for systemic sclerosis

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Conflict of interest: None

Systemic sclerosis (SSc) is a connective tissue disease comprising three different pathogenesis: Dermal and visceral fibrosis, peripheral circulatory disorders, and autoimmunopathy. Efforts to surmount these pathogeneses are active, though progress is not as substantial in areas such as rheumatoid arthritis. Treatment is either disease-modifying treatment or supportive treatment for established lesions. The former had required diagnostic criteria for pursuit of early treatment when lesions are reversible, and the 2013 ACR/EULAR criteria established the needed framework, leading to current clinical trial of treatment for fibrotic lesions with agents such as tocilizumab and nintedanib. [A1] Autologous hematopoietic stem cell transplantation has also been attempted, but prudence is required due to frequent transplant-related deaths. Under supportive treatment for SSc, progress has been made against pulmonary arterial hypertension (PAH). Potent effective PAH-specific drugs have been developed and adopted widely for PH in SSc (PH-SSc). However, subsequent reports have stated that their benefit is inferior to that in idiopathic PAH, a reminder of the complexity of PH-SSc. With optimization of indication, efficacy of up-front combination of PAH-specific drugs has also been reported. PAH-specific drugs also have a reverse remodeling effect on pulmonary vascular lesions and effectiveness against fingertip ulcers and may hold potential for disease-modifying treatment of vascular lesions in SSc. We anticipate that more widespread early disease-modifying treatments in appropriate period will lead to improvement for more SSc patients. However, curative, breakthrough, disease-modifying treatments will not be immediate. Supportive treatment is also highly important, and future treatment strategies allowing seamless pursuit of both therapeutic aims will be crucial.

S3-2

New therapeutic strategies for intractable vasculitides

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Conflict of interest: None

The nomenclature of vasculitides was reviewed during the Chapel Hill Consensus Conferences (CHCC 2012) 18 years after an earlier revision in 1994, and has since become conventional in congress presentations and in many scientific journals. The Japanese translations of this nomenclature were unified by the Research Committee on Intractable Vasculitides of the Ministry of Health, Labour and Welfare in 2016. The new translations are expected to become widely used in Japan soon. The two main types of large vessel vasculitis, Takayasu arteritis (TA) and giant cell arteritis (GCA) are categorized in the CHCC 2012 nomenclature. The mainstay of therapy for these arteritides has been steroids and immunosuppressants such as methotrexate, but biologics have recently come into use. The efficacy of tocilizumab (TCZ) was demonstrated in a recent randomized, double-blind, placebo-controlled trial of TCZ for the induction and maintenance of remission in TA and GCA. Rituximab (RTX) has been available in Japan for treating ANCA-associated vasculitis (AAV), a

major form of small vessel vasculitis. Numerous reports have shown that RTX is comparable to cyclophosphamide (CY) as induction or maintenance therapy for AAV. Also, the guidelines published by the Research Committee on Intractable Vasculitides in February 2017 recommend the use of RTX as a substitute for CY in some patients. Various clinical trials are ongoing, and the committee has launched a new cohort study in which all patients administered RTX are registered. This is expected to provide a new body of evidence from Japan. The report of the 18th International Vasculitis and ANCA workshop to be held in Tokyo in March 2017 will be presented.

S3-3

Issues and opportunities for the patients with special type Behçet's disease

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Conflict of interest: Yes

Clinical phenotype of Behçet's disease (BD) in Japan is changing. Retrospective analysis of nearly 600 BD cases in Yokohama City University and related hospitals during the past 30 years revealed continuous reduction of patients with complete type, genital ulcers, and HLA-B51 positivity[1]. Complete type was found in 38.4% of BD patients diagnosed before 2000, while 17.8% after 2008. As for GI type, significant increment was observed (11.5% before 2000, and 16.5% after 2008). Similar change in clinical manifestations is also reported from Korea, suggesting alteration of yet unknown environmental factors in these geographic areas. Possibly due to such change, rate of untypical cases with severe manifestation are growing, challenging our diagnosis and treatment strategies. There are not enough evidence exist on treatment of neuro, GI, and vascular BD. In Mediterranean area where BD patients are commonly found, vascular BD is relatively common, while GI type is rare. Components in EULAR recommendations for the management of Behçet disease have several statements not suitable to BD patients in Japan. Guidelines released from Behçet's disease research committee, the Ministry of Health, Labor and Welfare of Japan is useful in daily practice, though there are several limitations. Recent approval of anti-TNF for the treatment of special type BD is promising, but further collaborative studies are necessary to establish its efficacy in our BD patients. Because the disease is rare and severe, not many facilities are well-prepared to treat these patients and therefore some patients are visiting hospitals away from their residence. I will discuss on current issues, clinical patterns, and recent treatment strategies on special type BD. Reference. 1. Kirino et al, Continuous evolution of clinical phenotype in 578 Japanese patients with Behçet's disease: a retrospective observational study.

S3-4

Progress in diagnosis and treatment for neuropsychiatric systemic lupus erhythematosus

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Conflict of interest: None

Systemic lupus erhythematosus (SLE) is typical systemic autoimmune disease resulting in disturbance for multiple organs. Among the manifestations caused by SLE, neuropsychiatric SLE (NPSLE), which also called CNS (central nerves system) lupus, is one of the important manifestation on management for patients with SLE, as NPLSE is frequently associated with severe diseases. Classification criteria in 1999 proposed by American College of Rheumatology (ACR) is widely used for diagnosis of NPSLE, however, the items involved in the criteria are various and not specific manifestation for SLE. Moreover, NPSLE is often difficult to diagnose as many other factors not related to SLE such as viral infection and drug induced psychosis should be excluded. Although MRI analysis and laboratory test such as IL-6 measurement in serum or cerebral spinal fluid are commonly used for diagnostic tools for NPSLE, the findings of these examination are not highly specific for NPLSE. Therefore, useful specific surrogate marker for diagnosis of NPLSE is expected to be established. Recently, autoantibodies to neurogenic antigen such as anti-N-Methyl-D-Aspartate Receptor Subunits NR2A/B antibody or components of complement such as C5a have been reported to be recognized in serum or SCF of SLE patients. These autoantibodies are expected to be a candidate for useful diagnostic marker of NPSLE and many researcher are interested in progression of research regarding these autoantibodies. In treatment of NPSLE, combination corticosteroid and intravenous cyclophosphamide (IVCY) is proposed as standard treatment for NPSLE by Japanese Ministry of Health, Labor and Welfare, however, some patients are refract to this therapy. Therefore, efficacy in alternative treatment for the refract NPSLE patient such as biologics (rituximab or other biologics) and other immunosuppressant shall be expected to be verified.

S3-5

New Treatment Strategies of Lupus Nephritis

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Conflict of interest: Yes

Based on the results of several RCTs in 2000s, guidelines or recommendations for lupus nephritis were published in 2012, such as from ACR. In these guidelines or recommendations, MMF or IVCY are recommended for the induction therapy of active Class III/IV lupus nephritis, and MMF or azathioprine for the maintenance therapy. To develop better induction therapy, efficacy of addition of biologics or other immunosuppressants to MMF, or sometimes to IVCY, has been examined. However, most biologics, including rituximab and abatacept, failed to overcome the standard therapy. In case of immunosuppressants, the combination therapy with MMF and calcineurin inhibitor showed better results in some studies. Followed by the single-center small RCT in 2008, the multi-center RCT was conducted in China, in which efficacy of the MMF and tacrolimus (TAC) was examined compared to IVCY for Class III to V lupus nephritis. The results of the study showed that the combination therapy achieved a significant higher incident of complete remission than IVCY, which was published in 2015. In addition, just recently, results of AURA-LV study were reported in ACR 2016, in that effects of a combination therapy with MMF and voclosporin, an analogue of cyclosporine A, were examined. This study met the primary endpoints, demonstrating statistically significantly greater complete remission at 24 weeks than MMF alone. In Japan, by the approval of MMF for the treatment of lupus nephritis in 2015, the worldwide standard therapy has become easier to perform. In addition, TAC has been more used in Japan than abroad, because its was approval in 2007. In this symposium, the recent advances of treatment of lupus nephritis both abroad and in Japan will be summarized, together with some clinical data in our institute.

S3-6

A Strategy to Develop New Therapeutic Agents for Systemic lupus erythematosus

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Conflict of interest: Yes

Lupus nephritis, an organ dysfunction that develops in approximately half of patients with systemic lupus erythematosus (SLE), is a common pathological condition that affects prognosis and its complete remission is difficult. It is the most important lesion targeted for the treatment of SLE. Recent advances in drug development technology have led to development of many drugs for numerous autoimmune diseases, including rheumatoid arthritis, and the drugs have been replacing existing therapeutic strategies. However, patients with SLE are not necessarily receiving the benefits of such new drugs. In fact, many clinical studies have ended in failure. Innovations that are not described in existing treatment protocols are required from the stage of designing a study protocol on the basis of the features of drugs. When clinical studies on SLE, which presents with various lesions, are conducted, the important points are setting of therapeutic targets, regimens of combination therapy, methods of assess-

ment, and guarantee of safety. For studies on lupus nephritis, setting of therapeutic targets is also important at first. To investigate optimal targets of candidate drugs, it should be taken into consideration that their therapeutic effects are affected by race, histological type of nephritis, severity of nephritis, etc. For treatment contents, the concomitant use of steroids is important. Many clinical studies show that bolus administration of steroids substantially affects assessment of activity of new drugs used as concomitant drugs. Because their efficacy varies depending on the methods, timing, and targets of assessment, it is necessary to examine whether new drugs can be evaluated by simple assessment mainly based on urine protein and creatinine levels. Furthermore, the use of new drugs requires sufficient safety assessment, and it is important to consider treatment for adverse events even during a clinical study. In this article, we describe the points actually taken into consideration to develop the protocol and the problems with the actual outcomes in an investigator-initiated clinical study on bortezomib, a new drug for SLE, as an example.

S4-1

Overview

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Conflict of interest: None

In the classification of idiopathic interstitial pneumonias (IPs) in 2013, 6 major disease type are defined. 2 types of them are chronic fibrosing IP, and are consist of usual interstitial pneumonia (UIP) and nonspecific interstitial pneumonia (NSIP). Another 2 types of them are acute/subacute IP, and are consist of diffuse alveolar damage (DAD) and organizing pneumonia (OP). Last 2 types of them are smoking-ralated IP, and are consist of desquamative interstitial pneumonia (DIP) and respiratory brhonchiolitis with interstitial lung disease (RB-ILD). Various IPs associated with collagen vascular diseases (CVD-IPs) were classified according to this classification. But ther are some points inappropriate for this application of idiopathic IPs classification to CVD-IPs. Firstly, regarding idiopathic IPs, the difference in prognisis between UIP and NSIP is apparent, but regarding CVD-IPs the difference is not clear. Secondly, in NSIP of CVDs, there are differences in response to therapy and prognosis according underlying CVDs. Some NSIP patients of DM/PM had rapid progressing nature and bad prognosis. So there are many problems in the application of classification of idiopathic IPs to CVD-IPs. We need new concept for classification of CVD-IPs considering underlying CVDs. Regarding treatement of CVD-IPs, we will soon get new option of anti-fibrotic agents besides immunosuppressive agents. We need to construct new framework of treatement. In this presentation, I will talk about the above points.

S4-2

Pulmonary fibrosis in microscopic polyangiitis

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Conflict of interest: None

Microscopic polyangiitis (MPA), belongs to ANCA-associated vasculitis, reveals systemic vasculitis involving such as lungs, kidneys, skin and nervous system. Interstitial pneumonia is one of the dominant symptoms of MPA, not only pulmonary hemorrhage as pulmonary capillaritis. Some of the patients with MPA initially showed interstitial pneumonia before the other organs involvement. Nationwide study by Research Committee of Intractable Vasculitis Syndrome of MHLW reported that 47% of MPA had interstitial pneumonia. Chronic, elderly-onset and valuable respiratory symptoms such as no complaints, slight dry cough and dyspnea. Decreased DLco (diffusing capacity for carbon monoxide, carbon monoxide diffusing capacity) is one of the early signs of interstitial pneumonia. Reticular or small ring shadows on chest X-ray films and reticular, honey come and infiltrative shadows on lung CT are shown. These findings are clinically classified into idiopathic pulmonary fibrosis (IPF). Pathological findings of the interstitial pneumonia in MPA shows usual interstitial pneumonia (UIP) and shows similar pattern of interstitial pneumonia occurs in other rheumatic diseases, such as dermatomyositis and systemic sclerosis. It is not well known that the relationship among interstitial pneumonia, ANCA and vasculitis. Also, there are no fixed guidelines for the treatment of interstitial pneumonia especially occurred at early stage in MPA. I will discuss these basic and clinical problems of interstitial pneumonia in MPA in this symposium.

S4-3

Interstitial pneumonia (IP) associated with rheumatoid arthritis (RA)

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Conflict of interest: Yes

In RA patients, we encounter frequently 4 types of IPs. Among them 2 types of IPs are chronic fibrosing types cconsist of usual interstitial pneumonia (UIP) and nonspecific interstitial pneumonia (NSIP). Other 2 types of them are acute/subacute IP consist of diffuse alveolar damage (DAD) and organizing pneumonia (OP). DAD and OP of RA have prognosis similar to idiopathic DAD and OP. Frequency of RA-UIP is similar to that of RA-NSIP. In RA-UIP, we often find airway centered lesion unlike in idiopathic UIP. RA-UIP has bad prognosis like idiopathic UIP unlike UIP of other CVDs than RA. Major causes of deaths of RA-UIP are acute excerbation of IP and lung cancer and pulmonary infection. There is no established treatement strategy for chronic fibrosing IP of RA. In our department, we successfully use tacrolimus for chronic fibrosing IP of RA. We will soon get new option of anti-fibrotic agents besides immunosuppressive agents for tretement of RA-IP. In RA patients with IPs, there are restrictions of usage of anti-rheumatic drugs. In this presentation, I will talk about the above points.

S4-4

Updated treatment strategy for systemic sclerosis-associated interstitial lung disease

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Conflict of interest: Yes

Interstitial lung disease (ILD) is the leading cause of disease-related morbidity and mortality in patients with systemic sclerosis (SSc). There is substantial variability in the disease course of SSc-ILD; some patients show progressive decline in lung function, leading to end-stage lung disease and subsequent death, whereas others exhibit pulmonary function that remains stable for many years. Factors associated with ILD progression and poor prognosis have been extensively examined, and disease extent by high-resolution computed tomography (HRCT) >20% or forced vital capacity predicted <70% is found to predict poor ILD outcomes. However, these features are typically observed in the advanced and irreversible stages of ILD. Since functional impairment is hardly reversible once normal tissue architecture has been replaced by fibrotic scarring tissue, it is critical to identify patients in the early stages of progressive ILD, prior to appearance of functional impairment, and to initiate treatment as early as possible. SSc-ILD is currently treated mainly with oral or intravenous cyclophosphamide (CYC), but this drug has a significant risk for severe side effects, including carcinogenesis and impaired fertility. Recent randomized comparative trials have shown that mycophenolate mofetil exerts efficacy similar to CYC and safety profiles better than CYC, and long-term efficacy of autologous hematopoietic stem cell transplantation is superior to that of intravenous CYC. In addition, clinical trials of tocilizumab, rituximab, and nintedanib are ongoing globally. Even though these new classes of the treatment option would be available in future, it is essential to accurately predict the future progression of ILD and mortality to select patients who may benefit from the treatment.

S4-5

Interstitial lung disease with anti-ARS antibody

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Conflict of interest: None

A variety of myositis-specific autoantibodies (MSAs) can be detected in polymyositis/dermatomyositis (PM/DM) and each of them is closely associated with characteristic clinical features. Especially, two of them have strong relation to interstitial lung disease (ILD) with PM/DM (PM/DM-ILD), anti-aminoacyl-tRNA synthetase (ARS) and anti- melanoma differentiation-associated gene 5 (MDA5) antibody. About 70-85% of PM/DM-ILD patients are positive for either of them, and more than 90% of PM/DM Japanese patients with either of them have concomitant ILD. Because clinical course and prognosis are different between anti-ARS- and anti-MDA5-positive patients, they are important markers not only for diagnosis but also for classification of PM/DM-ILD. To date, 8 anti-ARS antibodies have been reported, anti-Jo-1, PL-7, PL-12, EJ, OJ and KS antibody. All of them have association with anti-synthetase syndrome; myositis, ILD, arthritis, Raynaud's phenomenon, fever and mechanic's hand. ILD with anti-ARS antibody is usually chronic and often repeats relapse though it shows preferable response to initial treatment with glucocorticoid. However, some differences in clinical manifestation and prognosis among patients expressing different ARS antibodies. A part of anti-ARS-positive patients show ILD without myositis. Even in such cases initial glucocorticoid therapy seems to be effective, but often needs immunosuppressants for recurrence. Because the prognosis of anti-ARS-positive ILD patients are better than that of idiopathic pulmonary fibrosis, it is important to screen anti-ARS antibody in idiopathic interstitial pneumonia patients. In Japan, enzyme-linked immunosorbent assays (ELISA) for anti-ARS antibody became to be available in daily practice from January 2014. There are seldom patients who are positive for anti-ARS by ELISA but negative by immunoprecipitation. Clinical features of such patients will be showed in this symposium.

S4-6

Clinical characteristics of interstitial lung disease associated with anti-MDA5 autoantibody positive dermatomyositis

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Conflict of interest: None

Polymyositis/Dermatomyositis (PM/DM) is one of idiopathic inflammatory myopathy characterized by proximal muscle weakness and myalgia. PM/DM is often occurred with interstitial lung disease (ILD) and clinical course, response to treatment and prognosis of complicating ILD is well known to be extremely diverse. Correct evaluation and selection of appropriate treatment of ILD is important because ILD is one of important factor that influences the prognosis of PM/DM. Autoantibodies found in patients with PM/DM are well known to be useful for the classification of ILD. Anti-aminoacyl transfer RNA synthetase (ARS) antibody and anti-CADM-140/MDA5 antibody is well known as major antibodies that are closely associated with ILD accompanied by PM/DM DM. Anti-MDA5 antibody is closely associated with acute or sub-acute type of ILD that is refractory and has poor prognosis despite of intensive treatment with high-dose glucocorticoid and immunosuppressive agents (rapidly progressive interstitial lung disease: RP-ILD). In this symposium, clinical characteristics, laboratory and imaging findings, recommended therapy and prognosis of ILD associated with anti-MDA5 autoantibody positive DM are reviewed.

S5-1

New knowledge about IgG4-related dacryoadenitis and sialadenitis

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Conflict of interest: None

According to recent cohort studies of each country, it has become clear that the major organ lesions of IgG4-related diseases (IgG4-RD) are lacrimal and salivary glands and pancreas. Dacryoadenitis and sialadenitis brings not only changes in facial appearance but also decrease of tears and saliva. We recently have experienced a case of involving lesions in other organs in the natural course of IgG4-related dacryoadenitis and sialadenitis (IgG4-DS). It is considered to be a transition from Mikulicz's type to systemic type. Here, I would like to outline the clinical features, diagnosis and treatment for IgG4-DS including latest topics. We have established a patient registration system for IgG4-RD, SMART registry. As of the end of 2016, 192 cases were registered, and the data size was 895.4 patient-years. Almost all patients had IgG4-DS. The sex ratio was 1.1:1, in favor of the male, and the average age was 65.6 years old. The frequency of the complication of other organ involvements was 59.4%. The most common organ lesion was pancreas (22.9%). The success rate of clinical remission induction by glucocorticoid therapy was 100%. However, the steroid-free remission rate was only 4.7%, and in many cases maintenance treatment had been carried out. By monitoring the levels of serum IgG4, the annual relapse rate was suppressed to 3.3%. Immunosuppressants were used for 7.9% of the IgG4-DS patients. The SMART registry has clarified the clinical features of IgG4-DS. With regard to the diagnosis, either diagnostic criteria for IgG4-related Mikulicz's disease or the comprehensive diagnostic criteria for IgG4-RD are used. However, biomarkers that reflect the activity of this disease have not been found yet and treatment algorithm has not been verified. Further the long-term prognosis is not unclear. I would like to discuss on unmet medical needs in everyday clinical practice at this point.

S5-2

IgG4-related kidney disease -up to date-

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Conflict of interest: None

In IgG4-related disease, various renal lesions including tubulointerstitial nephritis (TIN), glomerular disease, renal pyelitis and perivasculitis are observed. The term "IgG4-related kidney disease"(IgG4-RKD) has been proposed as a comprehensive term for the primary renal lesions associated with IgG4-related disease. Among them, TIN with abundant IgG4-positive plasma cells, characteristic fibrosis and often tubular basement membrane immune complex deposits, is the most dominant feature and referred to as IgG4-related TIN, which may cause acute or chronic renal dysfunction without obvious urinary abnormalities. A diagnostic algorithm for IgG4-RKD proposed by the Japanese Society of Nephrology is useful for finding renal lesions in IgG4-related disease, in which high levels of serum total IgG and IgG4, and high levels of serum IgE and hypocomplementemia are initial check points for patients with some forms of kidney damage, and thereafter renal radiological and histological findings are evaluated. Recently, the high frequency of hypocomplementemia in patients with kidney disease was reconfirmed in the studies of Japan and North America in IgG4-related disease. The most common glomerular lesion related to IgG4-related disease is membranous glomerulonephritis, and may or may not be associated with TIN. Corticosteroid therapy usually leads to a rapid improvement in terms of renal function, radiology and serology in patients with IgG4-RKD. However, renal function does not recover completely and renal atrophy develop in patients with advanced renal damage. Therefore, early diagnosis and treatment are necessary. In glucocorticoid monotherapy for IgG4-RKD, a moderate dose is sufficient for induction, and recovery of renal function can be maintained for a long period on low-dose maintenance, although relapse can occur even in patients receiving maintenance therapy.

S5-3

Differential diagnosis of IgG4-related respiratory disease

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Conflict of interest: None

It is sometimes difficult to differentiate IgG4-related respiratory disease (IgG4-RRD) from other diseases including multicentric Castleman's disease, sarcoidosis, and collagen vascular diseases. The respiratory working group supported by Intractable Diseases Health and Labor Sciences Research Grants proposed diagnostic criteria for IgG4-RRD in 2015. The criteria include:(I) Presence of chest CT abnormality. (II) Se-

rum IgG4 level exceeding 135 mg/dl. (III) Histology of intra-thoracic organs. (IV) Other organ involvement. To clarify the clinical features of IgG4-RRD and delineate differential points from mimickers, the working group collected the data of IgG4-RRD and non-IgG4-related respiratory diseases. The proposed provisional criteria are useful for clarifying the entity of IgG4-RRD when clinical manifestations are similar. However, diagnosis of cases with lung-limited lesions is still problematical. Further research is needed to confirm the validity of the criteria.

S5-4

IgG4-related periaortitis/retroperitoneal fibrosis and hydronephrosis

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Conflict of interest: None

Periaortitis/retroperitoneal fibrosis (PA/RF) is one of the major organ manifestations of IgG4-related disease (IgG4-RD). Radiographically, periaortitis represents predominant periaortic, concentric, and thickened or mass-like lesions of vascular wall, and retroperitoneal fibrosis represents pseudotumor or plaque-like lesions in the peri-ureteral regions or the pelvis. These lesions share the pathological features including lymphoplasmacytic infiltration, storiform fibrosis, and obliterative phlebitis with IgG4-related other organ lesions. The clinical features of patients with IgG4-related PA/RF are also similar to those of patients with IgG4-RD affecting other organs. The general features of these patients include advanced age, male predominance, allergic predisposition, elevated serum IgG4 levels, and good response to glucocorticoid (GC) therapy. In addition, the specific features of them include luminal dilatation of the affected perivascular lesions and hydronephrosis, both of which can cause life-threatening conditions or organ insufficiency. Since subjective symptoms including pain and fever, and serum CRP elevation are relatively rare in these patients, physicians should pay attention to latent existence and progression of periaortic/retroperitoneal lesions and their serious complications. An optimal therapeutic strategy including indications for treatment and the treatment regimen has not been well established in IgG4-related PA/RF. Although response to initial GC therapy is good, tapering or discontinuation of GC often results in a high risk of disease relapse. In addition, the efficacy and appropriate timing of steroid-sparing immunosuppressive agents have not been established. Moreover, careful observation after the GC initiation is mandatory when the affected aorta/artery shows luminal dilatation because there is a risk of exacerbation of the luminal dilatation or rupture of the affected aorta/artery as an unintended consequence of treatment.

S5-5

Innate immunity associated with IgG4-related disease

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Conflict of interest: None

IgG4-related disease (IgG4-RD) is a newly proposed disease entity that is characterized by massive infiltration of IgG4-expressing plasmacytes and by marked elevation of serum levels of IgG4. Although adaptive immunity leading to the enhancement of IgG4 Ab responses are considered to play a pivotal role in the development, recent studies provide evidence that excessive innate immune responses are involved in IgG4-RD. To analyze the innate immune responses associated with IgG4-RD, we established cell-culture systems that are composed of B cells and antigen-presenting cells (APCs) from healthy controls and IgG4-RD patients, respectively. We found that peripheral blood APCs from IgG4-RD patients enhanced IgG4 Ab production by healthy control B cells upon stimulation with TLR or NLR ligands. Such T cell-independent IgG4 Ab production depended upon BAFF produced by APCs, which suggests that excessive innate immune responses underlie the immuno-pathogenesis of IgG4-RD. We then turned our attention to the activation of plasmacytoid dendritic cells (pDCs) since type I IFN signaling pathways are involved in the expression of BAFF. Indeed, pDCs isolated from IgG4-RD patients produced higher levels of both IFN-alpha and BAFF than those from healthy controls. B cells from healthy controls produced a large amount of IgG4 upon co-culture with pDCs from IgG4-RD, but not from healthy controls. Compatible with the results of these human studies, an experimental model of murine autoimmune pancreatitis (AIP) was characterized by massive accumulation of pDCs into the pancreas and by enhanced type I IFN responses. Interestingly, infiltration of pDCs producing IFN-alpha and IL-33 was seen in the pancreas of IgG4-RD patients, but not chronic pancreatitis patients. Depletion of pDCs by 120G8Ab, blockade of type I IFN signaling pathways by type I IFN receptor Ab, or blockade of IL-33 signaling pathways by ST2 Ab reduced both inflammatory and fibrogenic responses in murine AIP. Taken together, our recent data highlight the importance of pDCs-mediated IFN-alpha-BAFF and IFN-alpha-IL-33 pathways in the immuno-pathogenesis of human IgG4-RD and murine AIP.

S5-6

Approach to establish Diagnostic Criteria for IgG4-RD by Japan and US

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Conflict of interest: None

1) Unification of nomenclature and establishment of general concept: IgG4-related disease (IgG4-RD) is the new disease concept proposed by Japanese investigators in this century. Two groups for IgG4-RD, Umehara team and Okazaki team were organized in 2009 by The Ministry of Health, Labour and Welfare Japan. Two groups unified a name of disease as “IgG4 related disease (IgG4-RD)”. They also established general concept of this entity, “IgG4-RD is the new condition with elevated serum IgG4 and prominent IgG4-positive plasma cell infiltration, and may occur, either synchronously or metachronously, in a variety of organs.” **2) Establishment of Comprehensive Diagnostic criteria:** IgG4-RD includes various clinical conditions. For the diagnose of IgG4-RD, Comprehensive Diagnostic (CD) criteria for IgG4-RD has been established, which consists with three items, 1) organ involvement, 2) elevated serum IgG4 more than 135mg/dl, and 3) increased IgG4-positive cells more than 10/HPF and IgG4/IgG ratio more than 40%. **3) Organ-specific criteria:** Two IgG4 groups were integrated into all Japan IgG4 team (chairman: T. Chiba, Kyoto University) in 2012. For the case without definite diagnosis, organ-specific criteria for IgG4-RD such as AIP, cholangitis, kidney disease, respiratory disease and ophthalmic disease have been established. **4) IgG4-RD international symposium:** International symposiums of IgG4-RD were held in 2011 years (Boston) and 2014 years (Hawaii) by Prof. Stone, Harvard University. Naming of IgG4-RD associated conditions were proposed and pathological diagnostic criteria was published. **5) International Classification Criteria:** The third international symposium will be held in Hawaii, 2019. Prior to the symposium, experts gathered in Boston as the classification criterion committee. 500 cases of IgG4-RD and IgG4-Mimicker were collected from all over the world. Based on the analysis, international IgG4-RD classification criteria will be published.

S6-1

Radicular pain due to spinal disorders

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Conflict of interest: None

The prevalence of chronic pain was 13-23% in japan. Pain occurred most frequently in the low back pain, neck pain, and shoulder pain. Low back pain is caused by neurogenic, tumor, infection, or internal organic

diseases. Neurogenic low back pain is about 10% and lumbar disc herniation (LDH) and lumbar spinal stenosis (LSS) are included. These diseases are focused on in this presentation. It is known that chemical factors, as well as a mechanical factor, are associated with inducing pain in patients with LDH. Various chemical substances, such as tumor necrosis factor-alpha, serotonin, are expressed in DRG in LDH model which was developed to simulate the clinical findings of LDH. This presentation introduces the target substances to induce pain and their possibility for improving pain related behavior. LSS has various symptoms, such as neurogenic intermittent claudication (NIC), associated with leg pain or numbness. NIC can be divided into three types, nerve root type, cauda equina type and mixed type. There are several hypotheses for mechanism of NIC. Reduction of blood flow in nerve after compression might be one of the causes of NIC. Chronic compression of cauda equina causes the decrease of walking duration, expression of ischemic marker, and delay of nerve conduction velocity. In addition, the dysfunction of endothelial cells might lead to a contraction of blood vessels induced by serotonin in chronic compressed cauda equina. There are various targets of pharmacological treatment. It is important to consider both the target substances and timing of pharmacological administration of optimal results. Clinical and basic investigations are needed.

S6-2

Discogenic low back pain

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Conflict of interest: None

Intervertebral disk (IVD) pathology is thought to be one significant contributor to non-specific low back pain (LBP). Several authors had been reported the presence of nerve fibers in the deep layers of the annulus fibrosus of IVDs (Deep Nerve Ingrowth) and the up-regulation of inflammatory mediators in IVDs would be the pathomechanism of discogenic LBP. In this study, we elucidated the details pathomechanism of discogenic LBP using various animal models of IVD degeneration including injury or/and dynamic compression, and secreted protein acidic rich in cysteine (which is associated with IVD degeneration) knockout mice. As a result, we observed as follows, 1) Deep Nerve Ingrowth: Increased innervation of degenerated IVDs and herniated IVDs by sensory nerve fibers in SPARC-KO mice and sensory nerve ingrowth from injured anulus fibrosus in IVD injury model. 2) IVD injury induced the transient increase in inflammatory mediators including TNF alpha, IL-6, and NGF. IVD injury and dynamic compression induced the persistent increase in inflammatory mediators. 3) IVD injury and dynamic compression induced long-term up-regulation of pain-related molecules in the sensory nervous system. 4) Macrophages in the injured IVDs produced inflammatory cytokines, but not growth factors. Inflammatory cytokines promoted the production of NGF, VEGF, mPGES1 (The synthetase of Prostaglandin (PG)), and COX-2 in IVD resident cells. Based on these studies, “Deep nerve ingrowth”, “Mechanical Stress” and “Inflammation” might contribute to discogenic LBP. Regarding the treatment for discogenic LBP, we previously reported good results of anterior interbody fusion surgery for discogenic LBP patients with “Deep nerve ingrowth” and “Mechanical Stress”. At the point of treatment for “Inflammation”, we conducted clinical trial which are evaluated the efficacy for single intradiscal injection of Etanercept or Tocilizumab for chronic discogenic LBP, and concluded TNF alpha or IL-6 inhibition provided short-term relief of discogenic LBP. For the long-term effect, further study would be needed to inhibit multiple inflammatory cytokines or to develop any other targets for discogenic LBP.

S6-3

Pain originating from facet joint: focus on lumbar facet joint pain

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Conflict of interest: None

[Introduction] While the incidence of neck and lower back pain in rheumatoid arthritis (RA) patients varies according to reports, it is estimated to be approximately 30%–50%. Problems involving the facet joints are the most typical causes of pain originating in the spine; therefore, understanding facet joint pathology is very important. In the present report, general pathology, diagnosis, and treatment of facet joint pain will be discussed, with emphasis on the lumbar vertebrae. [Pathology] Facet joints are synovial joints and their articular capsules are known to have nerve endings, such as mechanoreceptors and nociceptors. Some reported pathological conditions of intervertebral joint pain include 1) pain caused by mechanical deformation stimulating nociceptors in the synovial joints (so-called intervertebral sprains); 2) arthritic deformation; 3) synovial joint or membrane inflammation; and 4) post-traumatic articular microfractures. [Diagnosis] Kemp sign, one-point indication, and focal tenderness of the paraspinal muscles are the physical examinations that have the highest sensitivity and specificity for detecting lumbar facet joint pain. There are no specific imaging signs in arthrosis; therefore, facet blocks are used in actual clinical diagnosis. However, it is worth noting that blocks result in many false positives; therefore, blocks over several sessions are recommended to arrive at a proper diagnosis. [Treatment] In cases that are resistant to conservative treatment in which the effects of facet blocks are brief, electrical denervation of the medial branch of the dorsal ramus is indicated. To increase the levels of safety and reliability for this electrical denervation technique, compound muscle action potentials of the multifidus muscles are recorded while the medial branch of the dorsal ramus is electrically stimulated and favorable treatment results have been reported.

S6-4

Neuro-muscular mechanism of myofascial pain

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Conflict of interest: None

Many people are suffering from various kinds of myofascial pain, but their causes and mechanisms are not well understood. Myofascial pain syndrome is characterized with existence of the taut band (hardening in the muscle) and referred pain in the distant area while pressing the sensitive spot in the taut band. As for the experimental model delayed onset muscle soreness (DOMS) has been used because DOMS shows similar changes. In this presentation we will show our recent findings on the neuro-muscular mechanism of DOMS. DOMS is an unpleasant sensation after unaccustomed strenuous exercise, and its most characteristic symptoms are tenderness and movement related pain in the exercised muscle, which are a type of mechanical hyperalgesia. DOMS is easily induced by lengthening contraction (LC). Microinjuries of muscle fibers and subsequent inflammation is currently accepted mechanism for DOMS. However, we observed that rats develop DOMS after a bout of LC without apparent muscle injuries and inflammation. LC bout application for 14 days is revealed to be a chronic model. During LC bradykinin-like substance (arg-bradykinin, in case of rats) is released from the endothelial cells, and it activates B2 bradykinin receptors on the muscle cells, thereby stimulates upregulation of nerve growth factor (NGF) in muscle/satellite cells. In addition, cyclooxygenase-2 is upregulated in the muscle, and its product (prostaglandin E2) upregulates glial cell line-derived neurotrophic factor (GDNF) in the muscle/satellite cells. These neurotrophic factors sensitize muscle thin-fiber receptors. There are also interaction between NGF and GDNF at the primary afferent level. The most important finding of our study is that muscle/satellite cells upregulate production of NGF and GDNF as a result of their activities. Upregulation of NGF and GDNF in the muscle may also be implicated in other forms of muscle pain, this is to be studied. Fascial thin-fiber receptors will be briefly introduced.

S6-5

Joint pain

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ty

Conflict of interest: None

【Introduction】Many patients suffer from impaired ADL/QOL due to joint pain. The most common disease causing joint pain is osteoarthritis. 【Joint structure】The joint structure includes joint cartilage, subchondral bone, synovium, ligament, joint capsule, meniscus, and acetabular lip, and any tissue can be said to cause joint pain. 【Pain qualities】It was believed that osteoarthritis pain was nociceptive pain. However, upon investigation with a screening tool, it was suggested that a neuropathic element is included in slightly more than 20% of osteoarthritis cases. This means that careful attention is required when selecting drugs. 【Adjacent joint damage】Because leg joint damage causes pain, disturbance of excursion, and leg length discrepancy, adjacent joints compensate for function. In the long term, the compensation joints become damaged. Adjacent joint damage is common in hip-joint disease, with coxitis knee and hip-spine syndrome well known. 【Treatment of joint pain】Recently, many drugs available for arthralgia have come on the market. Moreover, the importance of exercise therapy has increased. However, we should refrain from aimlessly continuing conservative treatment. We should seek the opinions of specialists to propose the appropriate invasive therapy. We should not miss out on the opportunity for joint preservation surgery. Hip replacement surgery is an excellent treatment. However, as persistent postoperative pain has been reported in many articles, it is necessary to thoroughly conduct preoperative and perioperative pain control. 【Rheumatoid arthritis treatment and arthralgia】 Due to advancements in therapeutic drugs for rheumatoid arthritis, pathologic control has drastically improved. However, because there are few self-repair functions in the joints, it is believed that opportunities to examine osteoarthritis patients in which rheumatoid arthritis has remitted will increase. Moreover, the indications for joint preservation surgery in remitted patients may also be a subject for future discussion.

S6-6

Skeletal pain based on pathogenesis of osteoporosis

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Conflict of interest: None

Background Several studies have indicated that osteoporosis patients also experience idiopathic skeletal pain independent of those fractures or deformity. We have demonstrated that the pathological changes leading to increased bone resorption by osteoclast activation are related to the induction of pain, and anti-bone resorption agent treatment improved the pain. However, it is still unknown those mechanism. In the present study, we assessed skeletal pain in ovariectomized (OVX) mice, a model of postmenopausal osteoporosis, to elucidate the mechanisms leading to osteoporosis-related bone pain. Methods We evaluated skeletal pain in OVX mice by through an examination of pain-like behavior as well as immunohistochemical findings. Serum level of tartrate-resistant acid phosphatase 5b (TRAP5b), a marker of osteoclast activity, was measured. We assessed the effects of bisphosphonate, a potent osteoclast inhibitor, on those parameters. In addition, we examined the effect of antagonists to transient receptor potential vanilloid type 1 (TRPV1) and acid-sensing ion channel (ASIC) 3, as acid-sensing nociceptors; and P2X2/3, as an ATP-ligand nociceptor, on pain-like behavior. Results The OVX mice showed a decrease in the pain threshold value, and bisphosphonate caused an increase in the pain threshold value. TRAP 5b was significantly negatively correlated with the pain threshold value. Furthermore, we found that antagonists to TRPV1, ASIC3 and P2X2/3 improved pain-like behavior in OVX mice. Discussion These results indicated that the skeletal pain accompanying osteoporosis is possibly associated with the acidic microenvironment and increased ATP level caused by osteoclast activation under a high bone turnover state. We speculated that those nociceptors have some roles in mechanisms that the skeletal pain occured in association with pathological conditions of osteoporosis.

S7-1

The role of male as a supervisor or husband in the career development of female physicians

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Conflict of interest: None

In 2015, the Japanese House of Councillors voted to pass the law for increasing gender equality in the workplace. The principal objects of the law are to promote and improve gender equality in employment and in the workplace; and to support employers to remove barriers to the full and equal participation of women in the workforce, in recognition of the disadvantaged position of women in relation to employment matters. This gender equality policy was contextualised mainly as a women's issue. However, there has been an increasing acknowledgement of the crucial role of men in building gender equality as equal partners with women. In particular, more attention should be paid to the role of men as a supervisor to achieve gender equality in the workplace. The work environment should aim for health care workers participating JCR not to leave work through life events including pregnancy, delivery and child care. Differential actions should be taken in each workplace to achieve the goal. Needless to say, the supervisor in each workplace holds the key to the gender equality. In this session female healthcare workers of JCR introduce how they developed their careers. At the same time, the male key persons of them (e.g. supervisors and husbands) explain how they took action for the gender equality.

S7-2

What should we do in order to maintain work-life balance in surgical specialty?

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Conflict of interest: None

Recently, the number of women entering the field of surgery is increasing and the proportion of women surgeons among newly registered surgical board holders is now more than 20%. Various studies have pointed out that women physicians with children have many disadvantages with respect to career development because of the gender-related demands of labor at home. In order to assess the working styles of men and women surgeons in Japan, in July 2014, the Japan Surgical Society (JSS) recruited all members (n = 29,861) via the internet to participate in a nationwide survey of surgeons. The items investigated in this descriptive study included demographic information and working styles obtained based on a self-administered questionnaire. In total, 6,211 surgeons answered (response rate of 20.8%; 5,586 men and 625 women). The largest age stratum was 40–49 years for men and 30–39 years for women. Overall, respondents listed clarification of the labor contract, including salary and work hours, as the highest priority for improvement. Women surgeons with children were more likely to be part-time employees, work fewer hours, and take fewer house calls/on-calls compared with their men counterparts. As a result, a significant difference in working style was observed between men and women surgeons in Japan because of the conservative gender stereotype. In addition to consolidate the systems of childcare, it is necessary to overcome latent gender bias in order to improve current inappropriate conditions and achieve gender-free work-life balance.

S7-3

Initiatives of the Japanese Society of Nephrology —From gender equality to career support

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Conflict of interest: None

The Japanese Society of Nephrology (JSN), which aims to facilitate the maintenance of expertise and self-study of physicians, provide a place

for research, and contribute to Society, established the Gender Equality Committee in November 2006 with the goal of promoting both men and women to be active, and celebrated its 10th anniversary last year. Last year, we also organized a committee commemorating the 10th anniversary at the Eastern Regional Meeting. The first thing the committee did was establish the mission, goals, and measures regarding the activities of the Society following approval by the Board of Directors, announce them on the website. Now, even though 10 years have passed, that mission and goals have not faded, and we are steadily realizing each and every one. Specific measures include the following: 1) Performed Gender Equality Participation Committee initiatives as Society-led programs for general and regional meetings without fail; 2) Established nursery facilities at the general and regional meetings without fail; 3) Established a Gender Equality Participation Committee booth at general and regional meetings; 4) Amended the Society regulations to stipulate the length of service necessary for acquiring a specialist qualification according to the number of working days of the week; 5) Twice administered questionnaires from the committee to members; 6) Ensured a balance in male-female ratio, location, and workplace of committee members, and ensured that not only the committee members but also observers and advisors remain flexibly active; 7) Enhanced the home page; 8) Recommended symposists and moderators for the meetings. At the start of activities, the awareness of members did not increase, and there were many male and female members of JSN who seemed to regard the Society as an extension of support for female physicians at the hospital level, but the board of directors has been actively working on placing a certain number of women in decision-making institutions, and I feel that we have achieved success in this regard. I would like to introduce the progress and achievements of the gender equality activities of JSN over the past 10 years as well as discuss future issues.

S8-1

Pathogenic roles of ACPA in RA

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S8-2

A biological functions of autoantibodies in patients with systemic sclerosis

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Conflict of interest: Yes

Systemic sclerosis shows three major characters of tissue fibrosis, vasculopathy, and autoimmunity. Most of patients have anti-nuclear antibody, including anti-topoisomerase I antibody, anti-centromere antibody, anti-RNA polymerase III antibody, and so on. These anti-nuclear antibodies are strongly specific for patients with systemic sclerosis. Due to its specificity, a new classification criterion contained those specific anti-nuclear antibodies. However, from a lot of studies until now, those anti-nuclear antibodies could not exert a biological function. On the other hand, several autoantibodies have been found against cell-membrane receptors which were distinct from anti-nuclear antibodies. In 2006, anti-platelet-derived growth factor receptor antibody was discovered in patients with systemic sclerosis. This autoantibody exhibited a biological properties which directly stimulated tissue fibroblasts and might be involved in tissue fibrosis. In 2009, we investigated the association of anti-muscarinic-3 acetylcholine receptor antibody with severe gastrointestinal tract dysmotility. This autoantibody might contribute to pseudoobstruction in patients with systemic sclerosis. Recently, autoantibodies against endothelin receptor and angiotensin receptor were found in patients with pulmonary arterial hypertension and systemic sclerosis. The biological functions of these autoantibodies could be involved in vasculopathy in patients with systemic sclerosis.

S8-3

Clinical significance of autoantibodies in neuropsychiatric systemic lupus erythematosus

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Conflict of interest: None

Neuropsychiatric (NP) involvement is one of the refractory disorders in patients with systemic lupus erythematosus (SLE). The frequency of neuropsychiatric SLE (NPSLE) is reported to be various (12-75%), probably because NPSLE diagnosis is sometimes difficult. Although the pathological mechanisms of NPSLE is not well known, autoantibodies (auto Abs), inflammatory mediators (e.g., IL-6 and IFN-α), and vasculopathy might be involved in the NPSLE pathogenesis. Auto Abs against *N*-methyl-D-aspartate (NMDA) receptor subunit 2 (NR2), which cross-react with anti-DNA Abs, are frequently observed in cerebrospinal fluids (CSF) especially in patients with diffuse NPSLE. In animal models, induction of anti-NR2 Abs in sera alone did not result in CNS damage. Blood brain barrier (BBB) injury by LPS, however, can induce CNS damage because anti-NR2 Abs pass through BBB into CNS and bind hippocampal neuronal cells (Kowal C, *et al, Immunity*, 2004; 21: 179-88). In our NPSLE cohort, anti-NR2 Ab titer correlated with BBB permeability (albumin quotient, *Q*alb), but not serum anti-NR2 titers. Also, anti-NR2 ab presence is associated with an increased level of IL-6 in CSF. Taken together, anti-NR2 may be pathogenic for NPSLE. To date, we have studied anti-U1RNP Abs in CSF in NPSLE because anti-U1RNP Abs are frequently observed in sera from a certain subset of NPSLE (e.g., aseptic meningitis). Actually, the presence of CSF-anti-U1RNP Abs is closely associated with the elevated levels of IFN-α and MCP-1 and one of the possible biomarkers in NPSLE (*Lupus,* 2014;23:635-42). Interestingly, anti-U1RNP Ab itself did not increase IL-6 level in CSF, but did increase IL-6 levels in the presence of anti-NR2 Abs. In this symposium, auto Abs in patients with NPSLE are reviewed and the associations between auto Abs and inflammatory mediators will be discussed.

S8-4

Association between Myositis-Specific Autoantibodies and Pathophysiology in Inflammatory Myopathies

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Conflict of interest: None

Polymyositis/dermatomyositis (myositis) is one of the autoimmune diseases, basically affects the muscles, skin and other parts of the body such as joints, lungs and heart. Myositis-specific autoantibodies (MSAs) are revealed in most of myositis patients as follows: anti-ARS, anti-MDA5, anti-TIF1-γ, anti-Mi-2, anti-SAE, anti-NXP2/MJ and so on. Measurement of MSAs is useful to predict clinical features, courses and prognosis and determine short-term and long-term therapeutic strategy for myositis. This tool has provided benefits for improvements of physical dysfunction and prognosis in patients with myositis. On the other hand, it remains unclarified whether MSAs are directly linked to pathogenicity in myositis. According to a previous report, immune complexes containing anti-Jo-1 and necrotic cell material induced production of interferon-α in peripheral blood mononuclear cells. In addition, it has been reported that titers of MSAs such as anti-Jo-1, anti-MDA5 and anti-SRP are significantly correlated with disease activity/severity in myositis. Intriguingly, degradation fragment of Jo-1 which is a histidyl-tRNA synthetase has an ability of being chemotactic for monocytes and lymphocytes via CC chemokine receptor 5. Autoanigens which each MSA recognized are over-expressed in regenerating muscle fibers. These abundant autoantigens for MSAs might also induce inflammation through innate immunity and lead much more production of MSAs via acquired immunity. This relationship between autoantigens and autoantibodies could develop and exacerbate pathophysiology in myositis. In this section, the association of MSA with pathogenicity in myositis will be discussed.

S8-5

Anti-neutrophil cytoplasmic antibody (ANCA) and neutrophil extracellular traps (NETs)

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Conflict of interest: None

ANCA is an anti-neutrophil cytoplasmic antibody, which major antigen is myeloperoxidase (MPO) or proteinase 3 (PR3). ANCA is implicated in the pathogenesis of ANCA-associated vasculitis (AAV). AAV includes 3 primary vasculitides; namely, microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA), and eosinophilic granulomatosis with polyangiitis (EGPA), and secondary vasculitides, such as propilthiouracil (PTU)-induced AAV. Neutrophils primed by pro-inflammatory cytokines express MPO and PR3 on the cell surface. ANCA binds to the antigen and simultaneously bridges the antigen and bystander Fcg receptor on the cell, which activates the neutrophil. Consequently, the activated neutrophil releases reactive oxygen species and lytic enzymes, and then contributes to the development of small vessel vasculitis. This ANCA-cytokine sequence has been regarded as a pivotal theory for understanding the pathogenesis of AAV. Recent studies have revealed that neutrophil extracellular traps (NETs) extruded from activated neutrophils are also implicated in the vascular endothelial cell injury. In addition, some breakthrough suggested the involvement of NETs in the mechanism of ANCA production. NETs are composed of chromatin fibers extruded from activated neutrophils and decorated with antimicrobial proteins, such as MPO. Although NETs play an essential role in the innate immune system, excessive formation and/or persistence of NETs can cause some adverse events. Thus, NETs are strictly regulated *in vivo*. The most important NET degradation factor is DNase I in the serum. On the other hand, approximately 30% of patients administered with an anti-thyroid drug, PTU, produce MPO-ANCA. It has been shown that the generation of DNase I-resistant NETs induced by PTU could break the tolerance to MPO, resulting in the production of MPO-ANCA. Actually, DNase I activity in the sera of AAV patients was significantly lower than healthy controls. The collective findings suggest the involvement of NETs-ANCA vicious cycle in the pathogenesis of AAV.

S8-6

Thrombotic/hemorrhagic diseases caused by autoantibodies

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Conflict of interest: Yes

Patients with systemic autoimmune diseases are prone to thromboembolism associated with the presence of antiphospholipid antibodies (aPLs), thrombotic thrombocytopenic purpura (TTP) associated with ADAMTS-13 inhibitor, or atypical hemolytic uremic syndrome (aHUS) in the presence of factor H inhibitor. On the other hand, anti- FVIII autoantibodies cause acquired hemophilia. Antiphospholipid syndrome (APS) is one of the most frequent acquired thrombophilia caused by aPLs. aPLs target b2-glycoprotein I, prothrombin and other phospholipid binding proteins. Recently, complement activation has been implicated in the pathogenesis of APS. Acquired TMA (thrombotic microangiopathy) comprise TTP, HUS and aHUS. TMA is relatively frequent in patients with systemic autoimmune diseases represented by SLE and scleroderma. Many of TMA patients with systemic autoimmune diseases are negative for ADAMTS-13 inhibitors, thus classified as aHUS-like TMA, but factor H inhibitor is not frequently detected either. Because patients with inhibitor respond well to treatment including plasma exchange, lower prevalence of inhibitors may be one of the reasons for resistance to therapies and poorer prognosis of TMA in those with systemic autoimmune diseases. Acquired hemophilia is a bleeding disorder in the presence of anti-coagulation factor antibodies represented by anti-FVIII antibody. Acquired hemophilia is occasionally accompanied by autoimmune disease such as rheumatoid arthritis and SLE. In this symposium, we would like to discuss the contributions of autoantibodies to thrombotic/hemorrhagic disorders in the clinical practice of rheumatic diseases.

S9-1

MHC class II-associated neo-self antigens as a new target for autoimmune diseases

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Conflict of interest: None

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. 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 strong correlation has been observed between autoantibody binding to misfolded proteins associated with MHC class II molecules and the autoimmune disease susceptibility conferred by each MHC class II allele. These observations suggest that misfolded proteins rescued from protein degradation by MHC class II molecules function as a “neo-self” antigens that might induce abnormal immune response in autoimmune diseases.

S9-2

Pathological implications of semaphorins in autoimmune diseases

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Conflict of interest: None

Semaphorins were originally identified as repulsive and collapsing neural guidance factors during neuronal development. The semaphorin family consists of more than 20 proteins, and cumulative findings have demonstrated that these proteins have multiple roles, including organogenesis, angiogenesis, tumor metastasis, bone metabolism, retina homeostasis, and regulating immune responses. Sema4D, the first semaphorin protein that was determined to have immunoregulatory functions, promotes humoral immune responses via the activation of B cells and DCs. Sema4A is involved in T cell activation and differentiation. Sema7A is involved in inflammatory responses via T cell–macrophage interactions. These proteins constitute a family of immunoregulatory molecules that we refer to as immune semaphorins. From a clinical point of view, semaphorins have been implicated in various human autoimmune disorders; for example, Sema3A and Sema4A in atopic dermatitis, Sema4A, Sema4D, and Sema7A in multiple sclerosis, and Sema4D in rheumatoid arthritis. In addition, we have recently suggested Sema4D inhibits neutrophil activation and is implicated in pathogenesis of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). Serum levels of soluble Sema4D were elevated in AAV patients and were correlated with disease activity scores. In neutrophils from AAV patients, cell-surface expression of Sema4D was significantly down-regulated. Moreover, cell-surface Sema4D on neutrophils bound to plexin-B2 on endothelial cells, and this interaction suppressed neutrophil activation, including oxidative burst and resultant neutrophil extracellular traps formation. This regulatory function of Sema4D–plexin-B2 axis implicates the potential of Sema4D as a disease activity marker and a therapeutic target for AAV. In this talk, I will review current understanding of immune semaphorins, and discuss their involvement in the pathogenesis of autoimmune diseases. Reference Kumanogoh A, Kikutani H. Immunological functions of the neuropilins and plexins as receptors for semaphorins. Nat Rev Immunol. 2013;13 (11):802–814.

S9-3

The link between neutrophil migration and synovial inflammation in arthritis – The regulatory mechanisms by TIARP-

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Conflict of interest: Yes

Neutrophils are abundantly localized in arthritic joint fluid. Its chemotactic role in tissue homing are not clear, probably mainly due to the chemokines and its receptors, and adhesion molecule. TNFa-induced adipose-related protein (TIARP) is a six-transmembrane protein expressed on macrophages, neutrophils and synoviocytes, and we reported that mice deficient in TIARP (TIARP$^{-/-}$) spontaneously develop arthritis. However, the effects of TIARP on neutrophils and fibroblast-like synoviocytes (FLS) have not been elucidated. We analyzed the roles of TIARP in K/BxN serum transfer model using TIARP$^{-/-}$ mice. Arthritis in TIARP$^{-/-}$ mice transferred with K/BxN serum was significantly exacerbated compared with WT mice, due to the enhanced migration of neutrophils in joints confirmed by using cell analysis, cell-depletion antibodies and chimera mice. We characterized the differences in neutrophils between wild-type (WT) and TIARP$^{-/-}$ mice by DNA microarray. Overexpression of CXCR2 (chemokine receptors) and LFA-1 (integrin) was noted in TIARP$^{-/-}$ neutrophils. Neutrophils of TIARP$^{-/-}$ mice showed strong migration activity, which was markedly facilitated by CXCL2 *in vitro* and *in vivo*. Moreover, enhanced production of CXCL2 and IL-6 and cell proliferation was noted in TIARP$^{-/-}$ TNFa-stimulated FLS. Blockade of IL-6R significantly attenuated serum-transferred TIARP$^{-/-}$ arthritis with diminished neutrophil recruitment in joints. Our findings suggested that TIARP independently down-regulated CXCL2 and IL-6 production by FLS, and the expression of chemokine receptors (CXCR2) and LFA-1 in neutrophils, with resultant reduction of neutrophil migration into arthritic joints.

S9-4

Identification of Rheumatoid Arthritis-Associated Fibroblast Subsets by Single Cell Analysis

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Conflict of interest: Yes

Fibroblasts are key mediators of matrix remodeling and inflammation. In rheumatoid arthritis (RA), synovial fibroblasts expand and secrete proteinases and proinflammatory cytokines to damage the synovial tissues in the RA joints. They are also believed to function as stromal cells that recruit and regulate immune cells. Considering these diverse roles of fibroblasts, we hypothesized that fibroblasts may consist of several distinct cellular subsets with distinct functions. This would be analogous to other immune cells including lymphocytes and macrophages, which have functionally distinct subsets. Altered proportions and function of fibroblast subsets might be responsible for the disease pathogenesis. However, little is known about fibroblast heterogeneity, and how that heterogeneity mediates disease pathology. We employed an integrative strategy, including bulk transcriptomics on targeted subpopulations and unbiased single-cell transcriptomics, to analyze fibroblasts from synovial tissues. We identified 7 phenotypic fibroblast subpopulations with distinct expression patterns of surface proteins. These 7 subpopulations could be collapsed into 3 subsets based on transcriptomics data. One phenotypic subset expressing PDPN, THY1, but lacking CD34 was expanded in RA relative to osteoarthritis. Most of the cells in the expanded subset were also expressing CDH11. The 3 subsets expressed different cytokines and matrix metalloproteinases, responded differently to TNF stimulation, potentiated differential osteoclastogenesis, and localized in different regions of synovial microanatomy. We anticipate that applying our strategies for the studies of diseases in which fibroblasts play crucial role would lead to the discoveries of pathogenic subsets of fibroblasts, which will eventually lead to the improvement of therapies in the complexed diseases.

S9-5

Contribution of intestinal microbiota to the pathogenesis of autoimmune disorders

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Conflict of interest: None

Innovation of "next generation sequencer" enabled us to analyze intestinal microbiota. Then, intestinal microbiota has been revealed to mediate not only production of nutrients but also development of adaptive immunity and resistance to infection. Furthermore, alteration of microbiota composition, called dysbiosis, has been shown in several disorders. Many reports demonstrated that inflammatory bowel diseases (IBD), such as Crohn's diseases and ulcerative colitis, which are caused by excessive intestinal mucosal immune responses, are accompanied by dysbiosis. Mouse models of intestinal inflammation demonstrated that intestinal microbiota contributes to the development of IBD. Thus, intestinal microbiota is implicated in the IBD pathogenesis. In addition to IBD, several immune disorders in non-gut tissues have recently been shown associated with abnormality of intestinal microbiota. For example, mouse models of rheumatoid arthritis (RA: joint inflammation) and multiple sclerosis (MS: brain inflammation) do not show inflammatory changes in the absence of intestinal microbiota, indicating the involvement of intestinal microbiota in these immune disorders. Indeed, dysbiosis is shown in patients with RA and MS. Our studies also showed dysbiosis in some of early RA patients, who were diagnosed as RA within two years. Furthermore, a study using a mouse model of arthritis colonized with human microbiota demonstrated that dysbiosis observed in RA patients contributes to the RA development. I would like to discuss with you the involvement of intestinal microbiota in the pathogenesis of immune disorders, particularly IBD and RA.

S9-6

Comprehensive transcriptome and gene polymorphism analysis of immune cell subsets from autoimmune diseases

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Conflict of interest: Yes

It is critically important to identify the immunological features that are associated with autoimmune diseases. The understanding of immunopathology will contribute to the classification of diseases and development of novel treatments. Recent technological progress enabled us to perform detailed analysis of large-scale data from human lymphocytes. We combined immunophenotyping, subset-specific trancriptome analysis, and single nucleotide polymorphisms (SNPs), and attempted to identify disease-related network using gene module-based analysis (WGCNA) and expression quantitative trait locus (eQTL) analysis. We analyzed transcriptome from 21-immune cells subsets and gene polymorphisms from 30 healthy volunteers, 50 SLE, and 30 RA patients. One striking finding from this project was that cell metabolism signal as well as type interferon signal was an important feature that discriminates healty status and lupus. Moreover, SLE patients were classified into high-humoral immunity and low humoral immunity groups based on type I interferon and cell metabolism signals. On the other hand, RA patients showed modification of cell metabolism signal in a different way from SLE patients. Clustering of individuals based on type I interferon and cell metabolism signals exhibited a significant correlation with response to biologics. Furthermore, eQTL analysis that examine linkage between gene expression and gene polymorphisms revealed an association between disease susceptible locus for SLE/RA and cell metabolism signal for SLE/RA, respectively. These results suggested that the modification in cell metabolism signal is one of the causal factors associated with genetic background in autoimmune diseases. Cell metabolism signal may also be useful in the classification of autoimmune diseases. Therefore, compre-

hensive analysis for functional genomics could provide information for the understanding of pathogenesis and the development of novel therapeutic strategies.

S10-1

Spondyloarthritis as a systemic disease

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Conflict of interest: None

Spondyloarthritis (SpA) is a family of disorders that has common clinical features, such as axial spondylitis, peripheral arthritis, enthesitis, uveitis, cutaneous psoriasis, inflammatory enteric lesion, and association of HLA-B27 gene. Recently, axial and peripheral SpA have been classified by their predominant symptom. Ankylosing spondylitis (AS), psoriatic arthritis (PsA), reactive arthritis (ReA), SpA with inflammatory bowel diseases (IBD), are included in SpA. The clinical features can overlap. AS mainly affects young males with onset of inflammatory low back pain characterized by improvement with exercise but not with rest. Most of those patients commonly visit orthopedists at first. It is not unusual to take more than 10 years for diagnosis. Approximately one third of AS patients develop anterior uveitis during the disease course, and inflammatory enteric lesions are observed in 50%, IBD in 5-10%, and psoriatic skin lesions in 10% of the patients. Psoriatic disease includes skin, nail, axial joints, peripheral joints, digits, and enthesis involvement, and cardiovascular events and metabolic syndrome likely to occur in these patients. About 10% of PsA precedes to the skin disease, and the skin lesions can be missed. In PsA, diagnostic delay may result in joint destruction and dysfunction. ReA is an amicrobial arthritis developing after bacterial infections caused by particular bacteria, including enteritis with Salmonella, Shigella, and Yersinia, and urethritis with Chlamydia. Dactylitis, enthesitis, cutaneous eruptions and eye involvements, including conjunctivitis and uveitis, are frequently recognized. Furthermore, post-streptococcal reactive arthritis has been thought to be another type of ReA. Since symptoms and signs of SpA are wide-ranging, SpA should be managed in collaboration among multiple specialists.

S10-2

Psoriatic arthritis (PsA) - Psoriasis and differential diagnosis

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Pathogenic roles of ACPA in RA

Psoriasis is a common chronic inflammatory and complex immune-mediated disease. The IL-23/Il-17 pathway is deeply involved in the development of psoriasis. Mentally as well as physically quality of life diminish in psoriasis patients. PsA is a form of inflammatory arthritis that may occur in up to 20 percent of patients with psoriasis in Japan. Psoriasis has also been associated with cardiovascular disease, uveitis and other systemic diseases. Arthritis appears after the onset of skin lesions in the majority of patients with PsA. A significant proportion of patients with PsA may develop destructive and potentially disabling disease. Early evaluation of disease activity and treatment are much benefit to patients. There is a weak relationship between the severity of skin disease and arthritic involvement, although some studies have suggested that PsA occurs more commonly among patients with severe psoriasis. There are five clinical subtypes of psoriasis. Psoriasis vulgaris, the most common type of psoriasis, most commonly presents with red papules and well-demarcated erythematous plaques topped by silvery scales. The scalp, extensor elbows, knees, and sacral region are common locations for psoriasis vulgaris. Characteristic features of psoriasis may affect the nail, including nail pits, onycholysis, nail bed hyperkeratosis and splinter hemorrhages. Nail lesions occur in 80 to 90 percent of patients with PsA. The psoriatic nail involvement is more common in those with DIP joint arthritis. A diagnosis of psoriasis can be made by history and physical examination in the majority of cases. A full skin examination that includes of the scalp nails, and anogenital skin should be performed in patients with suspected psoriasis. Other characteristics supportive of psoriasis include evidence of the Koebner phenomenon and the Auspitz sign. Differential diagnosis of psoriasis is nummular eczema, seborrheic dermatitis, fungal infection of the nails and cutaneous T cell lymphoma. Occasionally, a skin biopsy is essential to rule out other conditions including cutaneous T cell lymphoma.

S10-3

Clinical Practice of Uveitis

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Conflict of interest: None

There are a lot of systemic disorders with ocular symptoms or complications. In particular, the uvea, which consists of the iris, ciliary body and choroid, is rich in blood vessels and therefore easily influenced by systemic inflammation. Particularly, some kinds of arthritis such as rheumatic arthritis, juvenile arthritis, ankylosing spondylitis, reactive arthritis, psoriasis arthropica and inflammatory bowel diseases, etc. cause recurrent uveitis. However, proper diagnosis and treatment of these refractory uveitides is sometimes very difficult. In addition to well-established steroid and immunosuppressant drugs, newly-developed biological agents such as anti-TNF antibodies are used. This combination requires careful consideration and intelligent management of the patient's treatment. In this lecture, I would like to introduce the clinical practice of uveitis and consider the importance of cooperation among doctors with different specialties.

S10-4

Prevalence and imaging findings of inflammatory bowel disease related spondyloarthritis in Japan

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Conflict of interest: None

Inflammatory bowel disease (IBD) and Spondyloarthritis (SpA) are chronic auto-inflammatory disease that partially share the common pathogenesis. Prevalence of axial SpA has been reported the strong relationship with HLA B-27, and in Japan, axial SpA has been rare disease. The objective of this study was to investigate the prevalence of SpA in Japanese patients with IBD. We performed the questionnaire survey of back pain and peripheral joint symptoms those suggest SpA symptom in Crohn's disease (CD) patients. Image reading of sacroiliac joint with CT or MRI was performed. Four hundred and sixty patients with CD (344 Men, 116 women) were evaluated. The mean age at the survey was 38.0 years with mean disease duration of 10.9 years. Four hundred and one patients (87.2%) were treated with biological drugs. There were 25 CD patients with back pain (5.4%) and 107 CD patients with peripheral joint symptoms (23.3%). CT or MRI were available in 90 patients. In 21 patients, there were imaging changes in sacroiliac joint. Especially, imaging changes in sacroiliac joint were highly recognized in patients with back pain (7/10, 70%). The results in this study showed the one-third of CD patients have SpA symptoms in Japan, and axial SpA with imaging changes was recognized in 7 patients. This study was cross-sectional study and it was difficult to investigate the relationship between disease duration, therapy and joints symptoms, however, the importance of joint symptoms observation by rheumatologist was suggested. In near future, the close cooperation between gastroenterologists and rheumatologists for SpA symptoms in IBD patients should be developed.

S10-5

Clinical manifests and pathogenesis of tonsil-associated diseases

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Conflict of interest: None

Tonsil-associated dieases (Tonsillar focal diseases) are defined as

clinical disorders in the distant organ from tonsil that are caused by tonsil without any symptoms of tonsil itself. Palmoplantar pustulosis (PPP), SCCH (PAO, SAPHO syndrome) and IgA nephropathy (IgAN) are known as typical tonsillar focal diseases. In this symposium, clinical outcome of tonsillectomy and the etiological evidences for the diseases are reviewed.

S10-6

Inflammatory back pain of spondyloarthritis

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Conflict of interest: Yes

Spondyloarthritis (SpA), comprehensive disease concept including ankylosing spondylitis (AS) or psoriatic arthritis (PsA), exhibits various resembling symptoms and response to medicines. SpA is roughly classified into axial SpA which is mainly involved sacroiliac joint or spine like AS, or peripheral SpA which is involved peripheral joints like PsA. Because PsA sometimes shows axial involvement, we should not think that these two are totally different, but they are overlapped. SpA presents various symptoms, such as arthritis of spine and limbs, enthesitis like Achilles' tendonitis, dactylitis, skin symptom like psoriasis, inflammatory bowel diseases such as Crohn disease or ulcerative colitis, uveitis, precedence infection like urethritis by the chlamydia. Since it is well known that association with HLA-B27 is high, it is very important to ask the family history. The existence of the inflammatory back pain (IBP), which develops by 45 years old and continues more than three months, is a key to doubt axial SpA. The typical IBP gets worse by rest, however it gets better by exercise. Axial SpA shows good response to NSAIDs, and the variety of symptom is sometimes relieved naturally without medication. Treatment using NSAIDs occasionally as mere mechanical back pain, might result in ankylosis of spine. It is hard to distinguish axial SpA from mere lumbar pain or herniation of lumbar disc. It is important to confirm whether the inflammation is seen or not in sacroiliac joint or spine by MRI.

S11-1

Nationwide prospective cohort study of Remission Induction Therapy in Japanese Patients with ANCA-associated Vasculitides (RemIT-JAV)

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Conflict of interest: Yes

It was difficult to compare the patient characteristics between Japanese and western clinical studies because classification criteria or assessment tool were differ among these studies. Japanese physicians wondered if evidences based on western clinical studies could be applied to their AAV patients. As a result of empirical adjustment by physicians, limited immunosuppressant use was found in the database of microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA) of the Ministry of Health, Labour and Welfare (MHLW). On the other hand, evidences for usefulness of concomitant immunosuppressant were also not enough in the world. Based on these rationales, a nationwide prospective cohort study of Remission Induction Therapy in Japanese Patients with ANCA-associated Vasculitides (RemIT-JAV) was performed from April 2009 in 22 tertiary care institutions belong to the Research Committee on Intractable Vasculitides of MHLW. Up to now, we revealed; 1) MPO-ANCA positive MPA was the most common form in Japan, 2) one-half of GPA patients were MPO-ANCA positive according to the European Medicines Agency (EMA) classification algorithm, 3) interstitial lung disease was an important clinical manifestation, 4) the MHLW definite criteria had a similar sensitivity and specifcity for eosinophilic granulomatosis with polyangiitis (EGPA) but showed a lower sensitivity and specificity for GPA and a lower sensitivity for MPA in comparison with the EMA algorithm, 5) majority of Japanese patients with MPA and GPA received treatment with limited CY use, and showed high remission and relapse-free survival rates but low GC remission rates, 6) age (>65 years), male sex, severe form, initial PSL dosage (>0.8 mg/kg/day), and smoking habit were predictors of serious infections. I hope to be able to discuss about Japanese clinical practice of AAV based on these results of RemIT-JAV study.

S11-2

Genetics of ANCA-associated vasculitis

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Conflict of interest: None

The epidemiology of ANCA-associated vasculitis (AAV) is substantially different among populations. While granulomatosis with polyangiitis (GPA) is dominant in European populations, microscopic polyangiitis (MPA) accounts for the majority of AAV in the Japanese population. With respect to the ANCA specificity, PR3-ANCA is predominant in the European population, and MPO-ANCA in the Japanese. Difference in the genetic background between populations may be involved in such epidemiological difference. Because of the low prevalence of AAV, a nationwide multicenter collaborative study is being performed on AAV genetics for more than a decade. With increasing sample size, genetic features of Japanese AAV are beginning to emerge. Thus far, two genome-wide association studies (GWAS) on AAV have been published on European populations, and both reported the strongest association of *MHC class II* region with AAV. In the Japanese population, *HLA-DRB1*09:01* was identified to be the risk allele for MPA and MPO-AAV, while *DRB1*13:02* was identified to be the protective allele. With respect to PR3-AAV, *DRB1*04:01* showed a tendency towards association, as previously reported in the European populations. Interestingly, *DRB1*09:01* is highly prevalent in the Japanese, while it is extremely rare in the European populations, while *DPB1*04:01* is common in the European populations but rather rare in the Japanese. Thus, such differences in the genetic background between populations may partly account for the differences in the prevalence in AAV subsets (Kawasaki et al., PLOS ONE 2016). With respect to non-*HLA* genes, the only gene which satisfies the genome-wide significance level is *SERPINA1*(alpha 1-antitrypsin) in GPA/PR3-AAV. The candidate gene analyses thus far suggested association of *IRF5* SNP with MPO-AAV (Kawasaki et al., Genes Immun 2013), as well as of *TNFSF4* and *ETS1* SNPs with PR3-AAV in the Japanese. In this symposium, I will discuss the findings of AAV genetics in the Japanese.

S11-3

International epidemiologic study of the vasculitis, mainly, ANCA-associated vasculitis

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Conflict of interest: None

Geographical differences in the epidemiology of the vasculitis, such as Takayasu arteritis, giant cell arteritis, and Kawasaki arteritis, have been observed. As for small vessel vasculitis, the prevalence of microscopic polyangiitis (MPA) is more common in Japanese patients, but PR3-ANCA positive, granulomatosis with polyangiitis (GPA) in European and US patients. However, the existing schemes, such as ACR classification, CHCC definition and Japanese diagnostic criteria were made in the 1990s and either was used for each study. In this way, the absence of classification standard of the vasculitis has been considered as one of the problems of the international study of the vasculitis. At present, the Diagnostic and Classification Criteria for Vasculitis (DCVAS) study, a multi-

national observational study, is in progress to develop and validate diagnostic criteria and to improve and validate classification criteria for primary systemic vasculitis. To clarify the epidemiologic differences between Japanese and European patients with ANCA-associated vasculitis (AAV), we conducted a population-based survey of AAV in Miyazaki Prefecture, Japan and Norfolk, UK, between 2005 and 2009 on the basis of the sub-classification of EMEA algorithm. There was no major difference in AAV incidence between Japan and the UK, but this prospective study found MPA and MPO-ANCA to be more common in Japan, and GPA and PR3-ANCA in the UK. Recently, an international study has been performed to investigate whether there were differences in phenotype and outcome in MPA and GPA between well-characterized patient cohorts in UK and Japan. Phenotypes in MPA patients were different, but the survival and renal survival were similar. Japanese patients with GPA were less PR3-ANCA positivity and more frequent respiratory involvement than UK patients. The relapse free survival rate was higher in Japan than UK. Under the same classification standard, the international epidemiologic and clinical study of various vasculitis is expected to progress in future.

S11-4

Genetic etiology and its application to treatments of Takayasu arteritis

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Conflict of interest: None

Takayasu arteritis is a rare disease affecting about 6,000 patients in Japan, belonging to large vessel vasculitides. It causes inflammatory, stenotic or dilating lesions on the aorta and its primary branches. Elevation of plasma IL-6, IL-12 and TNF-α levels has been reported, implicating their involvements in the pathophysiology. Takayasu arteritis lacks specific symptoms, leading to difficulties of diagnosis. Glucocorticoids are the standard agents that show the most solid effects. However, Takayasu arteritis typically shows a relapsing course. Although immunosuppressants have been used, the disease is sometimes resistant to them. Because an advanced disease will cause blindness, cerebral infarction or aortic aneurysms, more effective treatments are required. There are two ways of genetic studies for immunologic diseases: analyses of variable molecules such as HLA, and genome-wide association studies (GWAS). The authors reported a new haplotype, HLA-B*67, besides B*52 whose association with onset of Takayasu arteritis has been established. Additionally, the authors performed a GWAS and reported that single nucleotide polymorphisms (SNPs) in the regions of *IL12B* and *MLX* genes were associated with the onset. *IL12B* encodes IL-12/23 p40, a shared subunit of IL-12 and IL-23, which promote differentiation and maturation of NK and helper T cells. The classification of Takayasu arteritis and giant cell arteritis is a problem. The two differ in aspects of geographical distribution, frequently-affected arteries, and comorbidities (ulcerative colitis vs. polymyalgia rheumatica). The epidemiological difference can be explained by that of associated HLAs. The treatments by inhibiting cytokines have been tried. Nakaoka et al. performed a randomized placebo-controlled trial with tocilizumab, an IL-6 receptor inhibitor, and found a tendency of preventing effects on relapses ($p = 0.0596$) (ACR2016). The authors reported a pilot study with ustekinumab, an IL-12/23 p40 inhibitor (Terao, Scand J Rheum, 2015). Because the treatments have been improved, the importance of early diagnosis has been more recognized. Education to general clinicians is needed.

S12-1

Rheumatology – to a brighter future in the next decade?

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Conflict of interest: Yes

The successes of the past do not necessarily predict a brighter future – but lessons learned on this journey if acknowledged and appreciated, certainly should drive progress I will use the example of "soft tissue rheumatism" to discuss how a revised approach to common problems in the spectrum of rheumatic musculoskeletal diseases, using the wealth of cellular and molecular biology methodologies now available to us, can alter paradigms and thereby suggest a rather new approach to treatment. I will draw on data from several recent studies that have challenged the conventional models of tendon disorders and that now proffer completely new treatment possibilities that could transform these conditions in the next decade.

S12-2

Rheumatology in 2027: What shall we do now?

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Conflict of interest: None

Recent years have witnessed tremendous progress in our ability to diagnose and treat patients with a number of systemic inflammatory, autoimmune rheumatologic conditions. These include rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), psoriatic arthritis (PsA), ankylosing spondylitis (AS), and vasculitis. Improvements have been achieved in clinical signs and symptoms, improvement in functional status and quality of life, and prevention of disease associate damage. Improvements have been so substantial over the past few decades that active and spirited discussions concerning how to best define remission across many rheumatologic diseases have become more common. What does the future hold for rheumatology? Despite the great successes that have been achieved, there are several areas where improvements could be made, and hopefully will be made in the next decade. First, utilizing either newer agents or novel treatment paradigms, all patients should achieve the goal of remission. Secondly, we need to personalize our treatments for individual patients, to begin the goal of "precision medicine". Finally, as we continue to learn more about the immunopathogenesis of rheumatologic diseases, can we advance to the point where disease progression can be predicted at the earliest stage, and perhaps prevented? While ambitious, these goals may be within our reach in the next decade.

S12-3

Novel strategies in the treatment of rheumatoid arthritis

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Conflict of interest: Yes

The management of rheumatoid arthritis (RA) is primarily based on the use of disease-modifying antirheumatic drugs (DMARDs). Considering the rapidly evolving field of new therapeutic reagents available for RA, these include the synthetic DMARDs (sDMARDs) with conventional chemical agents such as methotrexate (MTX; csDMARDs) and targeted agents against Janus kinases (JAK) (tsDMARDs), while biological DMARDS (bDMARDs) are subcategorized as originator (boDMARDs) or biosimilar (bsDMARDS). With so many therapeutic options available, treatment decisions remain challenging. To this end, the European League Against Rheumatism (EULAR) recently updated their recommendations for the management of RA based on treatment targets, disease risk assessment, safety aspects and contraindications. MTX is recognized as efficacious and should remain part of the first treatment strategy in patients with active RA, either as monotherapy and usually in temporary combination with glucocorticoids. For low-risk patients who do not respond to their first treatment, another csDMARD strategy (plus glucocorticoids) is preferred, while in patients at high risk of having a poor outcome (high disease activity state, autoantibody positivity, early presence of joint damage) the addition of a bDMARD (current practice) or a tsDMARD (JAK-inhibitor) is recommended. In patients responding insufficiently to MTX and/or other csDMARD strategies, with or without glucocorticoids, bDMARDs (approved tumor necrosis factor [TNF] inhibitors, such as adalimumab, certolizumab pegol, etanercept, golimumab and infliximab; abatacept or tocilizumab; and, under certain circumstances, rituximab) or tsDMARDs (JAK-inhibitors) should be commenced. Biosimilar TNF inhibitors were also included under the proviso they are approved in the USA and/or Europe, which in the European Union (EU)

is the case for infliximab and etanercept. Importantly, based on a lack of clinical evidence to show that using bDMARDs as monotherapy is superior to MTX alone and usually optimal therapeutic response is achieved with the combination of MTX and biologics, the guidelines recommend that all bDMARDs be used preferentially in combination with MTX, unless MTX is not tolerated or contraindicated. Recently, in Europe the European Medicines Agency has granted market authorization to the JAK-inhibitors baricitinib and has expressed a positive opinion for tofacitinib so that these agents will be available soon in the EU to treat RA. This lecture will embark on the recently updated EULAR recommendations on the management of early arthritis and rheumatoid arthritis and will address novel strategies based on the treat to target approach. References 1. Smolen JS, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 Update. Ann Rheum Dis., in press 2. Combe B, et al. 2016 update of the EULAR recommendations for the management of early arthritis. Ann Rheum Dis. 2016 Dec 15. pii: annrheumdis-2016-210602. doi: 10.1136/annrheumdis-2016-210602.

S12-4

From Japanese experiences with advanced aging

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Conflict of interest: Yes

Rheumatoid Arthritis (RA) is characterized by persistent synovitis with autoimmune features, ultimately leading to irreversible joint damage without appropriate treatment. RA affects 0.5-1.0% of the population with the middle age and female predominance. The total population in the globe is expected to increase up to 8.14 billion (2025) from 7.49 billion (2017/1/23) with population growth rate about 1% every year. 60% of the increased population is originating from Asian countries. In addition, average life expectancy in some Asian countries such as Japan is increasing up to 86 years in female and 80 years old in man. Given perspectives for the global population trend, we should consider the perspectives for RA in 2027. In Japan as one of the most advanced aging country, we should seriously pay attention to the concerns on the diagnosis, evaluation, and treatment for RA patients. For example, the lower dose of tolerable MTX and higher MTX poly-glutamate concentrations in RBC, higher response rate of biological agents and Jak inhibitors, higher rate of opportunistic infections such as pneumocystis pneumonia are reported in Japan, compared to western industrialized countries. Although the differences between western countries and Japan would be, of course, genetic and environmental factors, we should consider the aging and related confounding factors. In this regard, I would like to focus on the several Japanese studies and discuss the topics in Japan.

S13-1

Revisiting the 2010 ACR/EULAR classification criteria for rheumatoid arthritis

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Conflict of interest: Yes

Presently, the most commonly used classification criteria for rheumatoid arthritis (RA) is the 2010 ACR/EULAR classification criteria. Until it was adopted, 1987 ACR classification criteria, which were created based on the data from patients with average disease duration of 7.7 years, had been widely used. At the time of their development, the "pyramid approach" was the accepted paradigm for the treatment of RA. However, since the benefits of early aggressive therapy have been confirmed to improve prognosis, new criteria became required for studies on early patients. The novel criteria were developed without the features of long-standing disease such as erosions or nodules, which are changed to a highly RA-specific anti-CCP antibody. Moreover, in order to predict persistent arthritis at an early stage, the number of swollen-painful joints are included. Symmetry and morning stiffness are no longer included. Although it has been verified that the 2010 criteria are suitable for early patient classification, several problems have also been pointed out. For instance, some ACPA-negative patients who are satisfied with the 1987 criteria are now not classified. ACPA-positive RA may have less inflamed joints than patients with ACPA-negative RA fulfilling the 2010 criteria. Furthermore, if the 2010 criteria are used as an inclusion criteria, these trials may include more patients with ACPA-positive RA than expected. On the other hand, as is the case with ACPA-positive RA, the benefits of early treatment for ACPA-negative RA have been confirmed. Therefore, novel tools are needed to identify patients with ACPA-negative RA early. In recent years, the existence of "window of opportunity" in the RA treatment has come to be known. A more detailed classification of the early stages of RA would be useful as well in order to further expand that window. Based on the research on genetic and environmental factors and biomarkers, a classification from a new perspective is also desired.

S13-2

Classification criteria of systemic lupus erythematosus

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Conflict of interest: None

Systemic lupus erythematosus (SLE) is a representative systemic autoimmune disease that has various types of manifestations in multiple organs. For the purpose of research and surveillance, classification criteria for SLE have been developed. The most widely used criteria for SLE were developed by the American College of Rheumatology (ACR) in 1982, revised in 1997 (ACR-97). Many research groups have attempted to refine the ACR criteria, but they failed to generalize. The Systemic Lupus International Collaborating Clinics (SLICC) is an international group of rheumatologists and methodologists dedicating to the clinical research of lupus. By analyzing the limitations of the ACR-97, SLICC presented a new set of classification criteria in 2012 on the basis of an evaluation of mass number of the international SLE patient cohort (SLICC-12). There are previous reports that have validated the functions of the SLICC-12 comparing with ACR-97. In Japan, the multi-center study was performed supported by the grants from the Research on Measures for Intractable Diseases, The Ministry of Health Labour and Welfare. In these validation studies, diagnoses by the expert rheumatologists were defined as the golden-standard. In most of the studies, SLICC-12 showed rather higher sensitivity and similar or lower specificity compared with ACR-97. Thus, SLICC-12 has less risk of overlooking the SLE patients, however, it may be inferior to ACR-97 on extracting the homogenous patients, which is virtually the primary objective of the classification criteria. The SLICC-12 was developed to ameliorate issues with the ACR-97, and is successful to some instance, propounding new aspects of the disease.

S13-3

Classification and criteria for systemic sclerosis and overlap syndrome

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Conflict of interest: None

Systemic sclerosis (SSc) is one of the typical connective tissue diseases in which fibrosis and vasculopathy lead to a complex pattern of organ-based complications. Since the clinical manifestations and the prognosis of SSc are variable, it's been hard to make a diagnosis of SSc in its early stage. The standard classification criteria for SSc were the 1980 `Preliminary criteria for the classification of systemic sclerosis (scleroderma)' by the American Rheumatology Association. Because of the insufficient sensitivity of the 1980 criteria, some new criteria including SSc-specific autoantibodies and nailfold capillary changes have been proposed. In 2013, the American College of Rheumatology and the European League Against Rheumatism proposed the new criteria including disease manifestations of the three hallmarks of SSc: fibrosis of the skin and/or internal organs, production of certain autoantibodies, and vasculopathy. The new criteria included the items of puffy fingers, Raynaud's phenomenon, abnormal nailfold capillaries, and typical autoantibodies, which are

seen in early or mild cases of SSc. The study concluded that sensitivity and specificity of the new criteria was better than the previous classification schemes. However, further studies are needed to validate the new criteria because it still depends on experts' opinion to apply to individual subjects. Vasculopathy including Raynaud's phenomenon and autoantibodies associated with specific clinical manifestations are characters of connective tissue diseases including SSc. Presence of antibodies to U1RNP in patients with mixed connective tissue disease, systemic lupus erythematosus (SLE), and SSc/SLE overlap syndrome may lead high frequencies of puffy fingers and pulmonary hypertension. Antibodies to PM-Scl may associate with fair prognosis of patients with SSc/polymyositis overlap syndrome. Antibodies to Ku are detected in patients with SSc/polymyositis and SLE/polymyositis overlap syndrome.

S13-4

Diagnostic criteria for mixed connective tissue disease

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Conflict of interest: None

Mixed connective tissue disease (MCTD) is a concept proposed by Sharp et al. in 1972 as a disease that comprises a combination of some features of systemic lupus erythematosus (SLE), systemic sclerosis (SSc), and polymyositis (PM). The MCTD criteria in Japan were established by the MCTD Research Committee of the Ministry of Health, Labour and Welfare. Based on the 1984 and 1988 criteria, patients who were positive for anti-U1 ribonucleoprotein (anti-U1RNP) antibody with features of SLE, SSc, and/or PM could be diagnosed as MCTD. In the revised criteria in 1996, pulmonary hypertension (PH) was added and prudence was required in the diagnosis of MCTD in patients with disease-marker antibodies for SLE, SSc, and PM. In the 2005 revised criteria, the term "common findings" was changed to "core findings"; in addition, PH was included and the criterion that required attention to specific autoantibodies was deleted. These revisions were based on the results of a prospective study that compared patients positive for anti-U1RNP antibody only and those with coexisting antibodies. This study found few differences between the two groups with regard to clinical features, according to the presence or absence of other coexisting antibodies. In Japan, although a diagnosis of MCTD entails keeping in mind the concept proposed by Sharp et al., the presence of anti-U1RNP antibody is also valuable. It is important to note that the presence of overlapping features alone cannot explain syndromes, such as PH, chronic swelling of the fingers and dorsum of the hands, and aseptic meningitis. Therefore, MCTD should be distinguished from an overlap syndrome.

S14-1

The change of forefoot deformities in patints with rheumatoid arthritis after starting tight control

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Conflict of interest: None

Various forefoot deformities in patients with rheumatoid arthritis (RA) lead to gait disturbance due to painful plantar callosities, and which might cause surgical treatment. In recent years, surgical procedure for rheumatoid forefoot deformities have changed from arthrodesis and resection arthroplasty to joint-preserving procedure. Because there is no definite criteria, we often indicate joint-preserving procedure even in the case with joint destruction of forefoot, and which indicates that joint destruction of forefoot may not affect on clinical symptom. On the other hand, the cases of rheumatoid forefoot deformity without joint destruction and pain until appearance of painful plantar callosity make us know the mechanism of progression without synovitis. Although we use mTSS to assess the structural damage on radiographs in general, this scoring method cannot detect the change of forefoot deformities without joint subluxation. So, it is not certain whether the forefoot deformities progress in early RA. Radiographic forefoot deformities are evaluated using hallux valgus angle (HV), 1st to 2nd metatarsal angle (M1M2) and 2nd to 5th metatarsal angle (M2M5), and we defined the sum of these angles as total forefoot deformity score (TFDS) to maximize the slight progression of forefeet. We investigated yearly progression of mTSS and TFDS in early RA started MTX-based tight control in daily clinical practice. The mean follow up period was 2.0 years, and in that period, 56.8% of the patients achieved SDAI remission. Clinically relevant radiographic progression (CRRP) which was heigher than smallest detectable change were detected in 4.6% in foot mTSS and 26.1% in TFDS, and predictor of CRRP of TFDS was steroid use. Forefoot deformities of several RA patients progressed gradually after starting MTX-based tight control. These changes cannot be evaluated by existing assessment system like mTSS and predict a long term prognosis of rheumatoid forefoot, so we should take these clinical course of rheumatoid forefoot deformities into account as a treatment outcome.

S14-2

Systemic influence of ankle synovitis: What we can see through *NinJa* database

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Conflict of interest: None

Comprehensive indices such as DAS28[1] are now being utilized in daily practice of rheumatoid arthritis (RA). However, these indices do not evaluate foot joints. Can we do without examination of the foot in clinical practice in RA? Here we overlook how foot disease including ankle synovitis effect systemically on patients with rheumatoid arthritis through fruit of **NinJa** database. Kanazawa et al analyzed distribution of affected joints[2]. Ankle is the 4th most frequent joint of synovitis. Its synovitis is less in patients with earlier disease and more in later. Shimada et al studied impact of each synovitis on CRP and ESR from viewpoint of number and size of swollen joint. This study illustrated increments of CRP and ESR per synovitis in a single medium-sized joint including ankle (0.24 mg/dL and 5.0 mm/1hr, respectively) with linear regression[3]. Tokunaga et al revealed high odds ratio of foot disease about patient pain VAS > 1, which is a factor that hinder satisfying Boolean remisson criteria[4]. Ono et al examined influence of each joint disease on mHAQ, illustrating that foot disease has a great odds ratio about mHAQ > 0.25, which is comparable with those of elbow, hip and knee, secondary to shoulder[5]. In addition, Nishiyama et al classified HAQ-DI into two factors; a reversible factor related to activity and an irreversible one related to joint destruction. Disease in large joints in lower extremities including ankle[6] has greatest correlation with the latter[7]. We have reviewed above the long-term and multifacet influence of foot disease upon patients with RA which **NinJa** has elucidated. These fruits carry a strong feeling of importance of ankle synovitis evaluation in clinical practice of RA.

S14-3

Musculoskeletal ultrasonography of ankle joint in rheumatoid arthritis patients

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Conflict of interest: Yes

Ankle involvement is relatively common in RA patients. A previous report showed that about 20% of RA patients had symptoms at the start of the disease and 50% complained of current ankle symptoms. However

precise clinical examination (CE) for ankle joint is difficult because of its complex anatomical structure as well as various patients' factors such as obesity and edema. Moreover, it is the problem that since ankle is not included in routine clinical assessment for the 28 joints to calculate DAS28, there is a possibility that patients with continuous inflammation in ankle joints would be classified in clinical remission. Ultrasonography (US) is now being an essential method for assessing disease activity in daily clinical practice, having several advantages as non-invasive and real-time evaluation. Previous studies showed US is more sensitive than CE for the detection of inflamed pathology. Several previous studies had applied US examination for ankle joints to show the utility of US for detecting ankle pathology. We also conducted US examination for RA patients to clarify the utility of US for evaluating ankle joints. In this study, US, CE and patient's visual analog scale for pain (pVAS) of each bilateral ankle of 60 RA patients (60.9 ± 15.2 years, 50 female) were assessed. Positive US findings were found in 26.7% of the ankles from 35.0% of the patients. The concordance rate of CE and US were moderate (0.57), while sensitivity and specificity of US were 0.71 and 0.89. Multivariate analysis revealed that ankle US, but not CE, was independently associated with ankle pVAS. Therefore, we concluded that US examination is useful to illustrate RA ankle involvement, especially for patients who complain ankle pain but lack CE findings.

S14-4

Conservative and surgical treatments for rheumatoid forefoot deformities

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Conflict of interest: None

Although the introduction of powerful anti-rheumatic drugs has dramatically improved the treatment of rheumatoid arthritis (RA), many patients still experience progressive joint destruction. Painful forefoot deformities are prevalent in 80-90% of patients with RA, many of whom undergo surgery to treat them. Various methods for treating rheumatoid forefoot deformities are chosen according to the severity of the deformities. In this presentation, the severity of rheumatoid forefoot deformities was classified according to the involvement of the hallux valgus and lesser toes, the flexibilities of the deformities, the presence of calluses, and the severity of the joint destructions. For deformities of the mild severity, rheumatologists should explain the patients about the importance of the anti-rheumatic drugs for the prevention of the joint destructions. For deformities of the moderate severity, therapeutic exercise such as towel gathering and Hohmann's exercise, and plantar orthotics are recommended. In particularly, plantar orthotics can be very effective for rheumatoid forefoot deformities with the moderate severity. If the physicians can simulate the deformities by making the metatarsal pads and arch supports with their fingers to reduce deformities, it may better predict the efficacy of plantar orthotics. Surgical treatments are indicated for serious and severe cases. Joint-preserving surgeries are indicated for the serious cases and Joint-sacrificing surgeries are performed for the severe cases. Although the various types of metatarsal osteotomies are performed in joint-preserving surgeries, the best osteotomy has not been identified. It rather depends on the surgeon's preference. Joint-sacrificing surgeries include resection arthroplasty, arthrodesis, and prosthetic joint replacement. Good long-term outcomes for all these methods have been reported. Although the joint-preserving surgery can be occasionally performed for severe cases because of development of the surgical techniques, the outcomes of that may be inferior to that of the joint-sacrificing surgery. Therefore, surgeons should carefully select a procedure for severe cases.

S14-5

Comprehensive assessment and treatment against rheumatoid foot disorder

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Conflict of interest: None

Even with the progress in the medical treatment of rheumatoid arthritis (RA) using methotrexate (MTX) and/or biologics, there are still unfortunate cases with progressive severe foot deformity and destruction. Foot disorders lead to functional disability of whole lower extremities. Hindfoot pain was controlled by conservative treatment (arch support and/or injection of steroids), when alignment is good. However, if alignment has been getting worse, surgical intervention is often required. Surgeries must be performed under tightly controlled conditions. Thus, advances in medical treatment for RA have contributed greatly to RA-related surgeries, because either of these established surgeries provides good outcomes in RA cases. Mid-hindfoot deformity should be kept in mind as they have the ability to cause recurrence of dorsal dislocation/subluxation of the lesser toe MTP joint, and recurrence of hallux valgus (HV) deformity. Furthermore, leaving the hindfoot deformity is also leaving the contracture of Achilles tendon and gastrocnemius, followed by the dysfunction of extension failure of the knee joint and dysfunction of quadriceps muscles. On the other hand, correction of the hindfoot deformity could cause the improvement of HV deformity and ankle joint deformity/pain. Taken together, comprehensive assessment and treatment against whole parts of the foot is required in rheumatoid foot disorders to achieve the functional improvement of whole lower extremities.

S15-1

Clinical practice guidelines for the management of adults with antineutrophil cytoplasmic antibody-associated vasculitis

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Conflict of interest: Yes

Objective: Several academic organizations have published clinical practice guidelines for antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). We evaluated methodology and recommendations of 'The clinical practice guidelines for the management of adults with AAV 2017'(the CPG of AAV 2017) which was published from the Research Committee on Intractable Vasculitides, the Ministry of Health, Labour and Welfare of Japan in January 2017. Methods: In part 1 of the CPG of AAV 2017, clinical questions (CQs) and recommendations were prepared using Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. In part 2 of the book, basic and clinical aspects of AAV were reviewed by experts of AAV in Japan. Results: Three CQs were included in part 1: remission induction treatment of AAV in CQ1, plasma exchange for remission induction treatment of AAV in CQ2, and maintenance treatment of AAV in CQ3. In all CQs, certainty/quality of evidence was low or very low, and strength of recommendation was weak. Discussion: We carefully followed the basic rules of the GRADE system: systematic review (SR) team and guideline panels are mutually independent, and the latter should include not only specialists but also various stakeholders of the management of a target disease. There were only one or two studies available for SR in each sub CQ, indicating difficulty of SR in rare diseases. Main contents of the recommendations of the CPG of AAV 2017 were similar to those published from EULAR/ERA-EDTA in 2016. During the process of the development of the CPG of AAV 2017, important clinical issues without enough evidence were identified. Planning and implementation of observational studies or clinical trials to answer these questions are future challenges to be addressed. Conclusion: Development of clinical practice guidelines for rare diseases are time-consuming and by no means easy. However, developing clinical practice guideline using international standard method will make the process transparent and increase its quality. Clinicians are encouraged to understand outlines of GRADE system and be able to interpret relevant data which were used to prepare clinical practice guidelines before they start using them.

S15-2

Clinical guideline of Adult Still's Disease

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Conflict of interest: Yes

Since the "Intractable Diseases Law" was made, the national system treating the diseases has changed dramatically. One of the biggest changes is the number of national registered intractable diseases, which increases from fifty-six to 306. Adult Still's disease is no exception. In order to quality control the medical care of the disorder, the Clinical Practice Guideline of adult Still's disease, which was not published worldwide, was required to be published. The research group on autoimmune diseases (the group leader; Takayuki Sumita, professor of Tsukuba University) of "Health and Labor Sciences Research Grant" prepared the publication. The recommendations on 27 clinical questions were made through the systematic review process by members of the editorial group. The guideline is still in preparation and will become public on the JCR meeting.

S15-3

Reccommendations for treatment of polymyositis and dermatomyositis

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Conflict of interest: Yes

Patients with polymyositis (PM) and dermatomyositis (DM) are seen by rheumatologists, neurologists, and dermatologists. Juvenile patients are seen by pediatricians. Although classificasion criteria for these diseases have been set by research teams of the Japanese Ministry of Health, Labour and Welfare, specific treatments could be different depending on the physicians. To build up the comsensus among the physians, the Ministry appointed multidiscipline experts to form a team that investigate and discuss the optimal treatment. The team endeavored to make a treatment guidline that depended on Minds 2007, and should be accepted widely by a broard range of physicians. The final product was approved by the Japan College of Rheumatology, Japanese Society of Neurology and Japanese Society of Dermatogy and issued late 1995. It is the first treatment guidline ever pubished in the world that is approved officially by scientific societies. Since the detailed Clinical Questions will be published in the literature in English, recommendations for intial treatment of the PM/DM patients will be discussed in the session. If the patient has skin manifestations alone, topical treatment with glucocorticoids and/or tacrolimus is recommended. If the patient has rapidly progressive interstitial pneumonitis or associated risk factors, high-dose GC and concomitant use of immunosupressants are recommended. High-dose GC or intermediate-dose GC together with immunosupressants are recomeended for other cases who have muscle manifestations. Pulse GC treatment can be added in severe cases. If the treatments prove to be effective, GC should be tapered. In the case of the initial treatment failure or relapse during GC tapering, immunosuppresants should be added or changed. Intravenous immunoglobulins are recommended for acute efficacy in intial treatment or treatment of refractory cases. The current guidline does not include classification criteria, which is under development by international efforts. The future guildline should include classification of PM/DM and also subsets of PM/DM as well as treatment guildline optimized for the subsets.

S15-4

Guideline for SLE

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Conflict of interest: Yes

Amongst the lupus organ involvements, lupus nephritis (LN) is one of the most common and important manifestations, affecting the mortality and morbidity in patients with systemic lupus erythematosus (SLE). Outside the Asian region, treatment guidelines for LN have recently been issued by American College of Rheumatology and European Renal Association-European Dialysis and Transplant Association. A number of immunosuppressants has been used for the treatment of systemic lupus erythematosus in daily practice, and they contribute to improve the prognosis of the affected patients. In those guidelines, Mycophenolate mofetil (MMF) is recommended for the initial and maintenance treatment. Despite the fact that MMF has not been officially approved for treating LN neither in USA nor in EU, MMF has been used in clinical practice worldwide. In order to clarify the real-world use of MMF as a treatment for LN in Japan, Japan College of Rheumatology surveyed the use of MMF in daily clinical practice. Last year, as a result, MMF was approved for treating LN in Japan. Considering the background, solid data on the efficacy and safety of MMF for the treatment of LN has not been available. Cyclophosphamide (CY) and tacrolimus (TAC) are potent immunosuppressants, frequently used for serious organ involvements in SLE patients. Apart from LN, most serious diseases in SLE, such as neuropsychiatric lupus, thrombotic microangiopathy, are treated by CY. In those guidelines for LN, CY was listed as the first choice for active class III/IV LN in parallel with MMF. We should consider advantages/ disadvantages for both drugs. TAC has been approved for LN in a maintenance phase of the treatment in Japan. In clinical practice, however, TAC is often considered as a potent supporter for MMF or CY in the induction phase for cases with insufficient response for MMF or CY. JCR and the working team sponsored by the ministry of Health, Labour and Warfare are preparing a guideline for the management of SLE in Japan.

S15-5

Guideline for diagnosis and treatment of Sjögren's syndrome

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Conflict of interest: Yes

[Background and Objective] In the Research Team for Autoimmune Diseases, The Research Program for Intractable Disease of the Ministry of Health, Labor and Welfare (MHLW), guidelines for four autoimmune diseases (SS, SLE, PM/DM, SS) have been created for 3 years (2014~2016) in order to establish the standard diagnosis and treatment (medical care). In this symposium, we focused on guideline for diagnosis and treatment of SS. [Methods and Members] We generated guideline for diagnosis and treatment of SS at the point by several evidence and systematic reveiw, using Minds 2014. Committee is coposed of 17 main persons. SR has been done by 31 members (17 and associated 14 persons). [Results] 1) 38 clinical questions (CQ) has been selected. 2) We decided each keywords for CQ and systematically reviewed evidence from PubMed, Ichushi, and Cochrane from January, 2000 to May, 2015. 3) We created SR reports and determined the strength of the recommendation for SR reports from the votes by 17 members. 4) We collected public comments on guideline for SS through Japan College of Rheumatology (JCR) and Japanese Society for Sjögren's Syndrome (JSSS) in December, 2016. 5) Revised version of guideline for diagnosis and treatment of SS was determined as the final version. We are planning to publish the guideline for diagnosis and treatment of SS 2017 in March, 2017. 6) The guideline for diagnosis and treatment of SS 2017 has been proposed to obtain the approval of JCR and JSSS in Jan, 2017. [Conclusion] We created and published guideline for diagnosis and treatment of SS 2017.

S15-6

Attempt to establish the guideline for non-specialists of RA managements based on RA management guideline 2014

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Conflict of interest: Yes

Aim: To establish the draft guideline for non-specialists of RA (rheumatoid arthritis) management based on RA management guideline 2014. Methods: As a part of the project of MHLW study group (Miyasaka team), we have classified the 37 recommendations in the guideline 2014 into 6 recommendations as affordable to non-specialists and 11 recommendations specialized to the RA specialists. Next, we have asked non-specialists whether this classifications are acceptable and feasible or not, by scoring 9 (agree) to 1 (not agree). Results: A total 131 non-specialists answered the questionnaire. Average age was 41.7±9.7, 108 doctors work in the hospital and 18 work in clinic, and including 53 orthopedists, 59 internists, 12 general medicine doctors, and 3 residents. 100 had experience to treat RA patients, and 31 did not. By analyzing the median of the scores, most of this classification were well acceptable and feasible to non-specialists. Especially, it was clearly demonstrated that biologics use should be conducted by specialists but not by non-specialists. Discussion: Guideline for the management of RA in 2014 has received high valuation by the review of Minds. However, this guideline was establish to assist the practice of RA specialists, and is not directly applicable to the daily practice of non-specialists. Thus, we should consider what recommendation is affordable to non-specialists and also what is not feasible to non-specialists. Although those 131 doctors who answered in this study may not be the representative of all non-specialists in Japan, they include wide variety of specialties, thus, it is reasonable to analyze. Thus, the attempt to utilize the recommendations of guideline for specialists to those for non-specialists is efficacious, and may be applicable to other guidelines as well.

S16-1

Treatment and management of childhood and adolescent systemic lupus erythematosus

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Conflict of interest: Yes

Systemic lupus erythematosus (SLE) is the second most common childhood rheumatic disorder. In Japan, there are 1,500 patients with SLE aged less than 15 years. Childhood SLE is more likely to be progressive and complicated by lupus nephritis (LN) than adult SLE. Until early 1980, the five year survival was about 56% in children with SLE. Thereafter, intravenous cyclophosphamide improved their 10 year survival rate to 99%. However, one third of these patients still develop chronic sequelae such as necrosis of the femoral head, end stage renal disease, and recurrent CNS lupus. Unfortunately, a lack of well-designed clinical trials regarding treatment of childhood SLE/LN has resulted in all major guidelines recommending the same treatment for children and adults. However, a serious adverse effect of corticosteroids in children is growth impairment. Therefore, immunosuppressive agents plus steroid therapy are encouraged for quick achievement of remission and reduction of steroid dosage for prevention of relapse. Intravenous cyclophosphamide is still the most effective therapy for induction of remission of severe childhood SLE/LN; however, mycophenolate mofetil is an emerging alternative. Because oral cyclophosphamide has been used since the 1970's for children with idiopathic nephrotic syndrome such as minimal change disease, the safe cumulative dose of cyclophosphamide has been well established. However, it is better to reduce the dosage or refrain from using it. Tacrolimus used alone or in combination is other emerging option and is becoming an essential drug in patients with complex disease. Because SLE is a lifelong chronic disease, robust maintenance of remission is essential for prevention of cardiovascular complications, osteoporosis, and infertility. Additionally, medical staff must support adolescent patients in good adherence, psychosocial development, a smooth transition to adulthood and a bright future.

S16-2

The current status of health care transition in Japan

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Conflict of interest: None

[Background] The transition of adult patients with childhood-onset chronic diseases (APCCD) from the pediatric to adult healthcare system has recently received attention. In Japan, APCCD were referred to as "carryover patients," who were often considered as a burden to the pediatric practice. In 2013, the Japan Pediatric Society summarized their statements and proposed that they address APCCD as "transitional period patients." [The problems of transitional period patients] The problems associated with transitional period patients are because of pediatricians not being equipped to be the primary care provider for adult diseases. Also, the knowledge of prognosis and psychosocial problems of transitional period patients are not widespread among adult-health care providers. These patients often lack social experiences because of their childhood disease and have difficulties in adapting to social life. After commencing work, they are rarely allowed to attend health check-ups, which is necessary for managing their condition. [The psychosocial problem of transitional period patients] The psychosocial problems of transitional period patients were divided into two types: one type is derived from their disease, such as pain or fear of death, and the other is due to an uncomfortable relationship with their parents or maladjustment with their society. Although the protection of children by their parents is important for young children, it is also important for adolescents to achieve independence. Pediatricians should instruct their patients to lead a lifestyle according to the appropriate management of the disease and compliance of medicine usage. [The problem of health care transition] In the future, it is necessary to spread specialized knowledge, to develop a healthcare network between pediatricians and adult-health care providers, and to prepare a transition manual. We hope that adult-health care providers will demonstrate increased interest in health-care transition.

S16-3

Management of women with systemic lupus erythematosus in preconception and during pregnancy

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Conflict of interest: None

Systemic lupus erythematosus (SLE) occurs more frequently in reproductive age women. However, "pregnancy" has been considered as a risky challenge for SLE women and their doctors as SLE is risk factor of obstetric complications or flare is often seen during pregnancy or postpartum. However, due to recent progress in SLE practice and obstetric / neonatal therapeutic techniques, it is not so difficult for SLE women to maintain a stable condition during pregnancy and to obtain healthy children. This symposium outlines the following three points which are considered important when considering treatment and management of SLE women in preconception and during pregnancy. The first point is pre-conception care. Previous studies were documented risk factors for adverse pregnancy outcomes. 1) high disease activity during pregnancy, 2) cases with severe renal dysfunction, pulmonary hypertension, and central nervous system disorder. They were considered to be high risk for disease flare during pregnancy and adverse pregnancy outcomes. Therefore, every SLE women who desire to be bear children should be kept under the good control before pregnancy as much as possible. In addition, SS-A antibody and anti-phospholipid antibody should be checked. The second is "control of the original disease during pregnancy". As mentioned above,

high disease activity during pregnancy increases the risk of pregnancy complications. It is necessary that appropriate medication should be started as soon as possible, when the signs of flare are recognized during pregnancy. Finally, the postpartum follow-up is important. It has been reported that SLE women with previous Maternal-Placental Syndrome (hypertensive disease in pregnancy, fetal loss, small for gestational age and placental abruption) is risk factor for future cardiovascular events. In the future, "postpartum management" could be necessary for SLE women to be lead to a healthy middle-age.

S16-4

Treatment with immunosuppressive drugs during pregnancy and lactation

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Conflict of interest: None

Systemic lupus erythematosus (SLE) is frequently observed in women of childbearing potential. Since it is difficult to predict the timing of pregnancy, a primary physician need to treat such populations considering potential pregnancy. Medications for the treatment of SLE include corticosteroids, immunosuppressants (cyclophosphamide, mycophenolic acid, azathioprine, cyclosporine, tacrolimus and mizoribine), hydroxychloroquine, antihypertensive agents, and anticoagulant agents. Tacrolimus, azathioprine and cyclosporine are contraindicated in pregnant women and potentially pregnant women based on their labels. Since some SLE medications have a concern for safety in pregnant women, treatment with such medications are sometimes discontinued and replaced with increased dosage of steroids in clinical practice. Indeed, safety information for pregnant women are extremely limited in the drug label. To resolve this issue that even clinically beneficial and required medications which regarded as safe in pregnant women based on epidemiological database are still unavailable to Japanese patients, because of "pregnancy contraindication" on the label, a new project of the Health, Labour and Welfare Ministry has started. The objective of this new project is to integrate and evaluate the drug safety information for pregnant women aggregated by The Japan Drug Information Institute in Pregnancy, and promote appropriate use of useful medication in pregnant women through updating drug label. For nursing of women receiving SLE therapy, primary physicians need to select an appropriate therapeutic strategy considering benefit of breastfeeding, type and characteristic of each SLE medication, which requires adequate knowledge of internal medicine.

S17-1

Mechanism of cartilage destruction in RA patients and its repair/regeneration

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Conflict of interest: None

A variety of biologicals improve the outcome from rheumatoid arthritis (RA) therapy; however, remission rate is low, indicating many patients with RA remain to be still resistant to therapy. A problem is that a side effect is developed by targeting common cytokines, such as IL-6 or TNF-a. Further, it's difficult to repair or regenerate damaged joint. Thus there exist these problems faced by lots of unmet needs. In particular, although cartilage destruction contributes to decreased ADL or resistance to therapy, it remains unclear about mechanism of cartilage destruction via activation of fibroblast-like synoviocytes (FLSs). Endogenous mesenchymal stem cells (MSCs) have poor ability to repair damaged tissues due to their dysfunction. Thus there exists no efficient therapy to regenerate destroyed cartilage tissue. In order to clarify mechanism of cartilage destruction and overcome it, we try to figure out why RA pathological conditions are caused. We further deal with therapeutic application by using mesenchymal cells. In this symposium I'll talk about up-to-date data on 1) epigenetic regulation involved in cartilage destruction by FLSs and 2) effective therapeutic application with MSCs in cartilage regeneration. We found that IL-6/STAT3/Ror1 pathway through increased trimethylation levels of H3K9 in Ror1 promoter is critical for induced expression of MMP-13 that plays role in cartilage destruction. This indicates that regulation of epigenome mechanism may contribute to suppression of cartilage destruction. We further found that IL-6R-treated MSCs on PLGA (poly lactic-co-glycolic acid) may differentiate into chondrocytes, and lead to efficient repair/regeneration of cartilage tissue. In conclusion, FLSs activation may play a role in cartilage destruction via epigenetic modification. We further put forward that epigenome regulation or cell technology applied as therapeutic tool might help to overcome cartilage destruction in the treatment of RA for the next generation.

S17-2

Mechanism of bone destruction in rheumatoid arthritis (RA)

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Conflict of interest: None

Introduction: Osteoclasts (Oc) play an important role in bone destruction in RA. Inflammatory cytokines and molecules expressed on Oc induce differentiation and activation of Oc. We review our findings updating the recent findings. 1. Oc precursors are detected in RA tibia BM (1991). Authentic Oc are detected in RA synovium (1994). 2. Both IL-6 and sIL-6R in RA SF induce Oc-genesis via IL-6 transsignalling (1994). 3. RANKL and RANK 1) sRANKL levels and the ratio of sRANKL/OPG in RA SF are elevated (2001). 2) Human T cells express RANKL and induce Oc-genesis. T cells expressing RANKL are detected in RA synovium (2001). 3) Human Th1 cells express RANKL and induce Oc-genesis. These Th1 cells increased in PB of RA patients (2005). 4) Oc-genesis levels in each normal volunteer are significantly correlated with RANK levels on peripheral monocytes. (Nanke et al. 2016). 4. IL-17 1) Memory Th cells in RA synovium produce IL-17 and IL-17 levels are elevated in RA SF. IL-17 incudes Oc-genesis in the co-culture system. (1999). Many other groups have reported that IL-17 plays an important role in the early stage of RA. IL-17-IL23 axis play an important role in the pathogenesis of RA (Yago et al. 2007). 2) In the early onset and untreated RA patients, peripheral CD161+Th1 are elevated (2016a) and levels of IFNg-producing Th17 cells are inversely correlated with ACPA levels (2016b). 3) Novel antibody therapies:Miossec's group reported that aIL-17Ab were used in RA patients whose peripheral concentrations of bioactive IL-17 were high. Schetts' group reported that bispecific antibodies against both IL-17 and TNFa were effective for RA therapy. 4) IL-35 inhibits human Oc-genesis (Yago et al. 2017 in press). 5. TCTA peptide expressed on monocytes induce human Oc-genesis via the fusion process (2009). 6. VDAC is expressed on the membrane of human monocytes and osteoclasts. Antibodies against VDAC inhibits human Oc-genesis (2012). Conclusions. Two ways should be performed for anti-IL-17 therapy of RA: 1) the use of bispecific antibodies against both IL-17 and TNFa; 2) the patients should be selected, for example, those with high peripheral level of bioactive IL-17.

S17-3

Adaptive immune system and bone destruction in RA

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Conflict of interest: None

Rheumatoid arthritis (RA), one of the most common autoimmune diseases, is characterized by inflammation and bone destruction in the joints. Abnormal activation of the immune system leads to RANKL-dependent osteoclast differentiation, which ultimately results in bone destruction in RA. An animal model of RA revealed that a newly identified pathogenic T cell subset exacerbated inflammation and bone destruction in arthritis. Using RANKL conditional knock-out mice, it was demonstrated that synovial fibroblasts are the major RANKL-expressing cells in

arthritis. The pathogenic T cell subset generated in the presence of IL-6 produced by synovial fibroblasts induced osteoclastogenesis potently by upregulating RANKL on synovial fibroblasts, indicating that a synergy between T and synovial fibroblast plays a primary role in the bone destruction. Recently, it was shown that immunecomplexes directly induce osteoclastogenesis via Fcgamma receptors on osteoclast precursor cells in arthritis. Increasing numbers of immune-regulating factors have been identified as new bone-regulating factors, which may be attractive therapeutic targets for bone destruction in RA. The mechanism by which adaptive immunity contributes to the RA pathogenesis will help understand the etiology of RA and develop therapeutic approach against it. I will provide an overview of the mechanism of bone destruction in RA, focusing on the contribution of the adaptive immune system.

S17-4

Intravital imaging of bone and joint destructions in vivo

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Conflict of interest: Yes

Recent development of diverse biological agents has been revolutionizing the clinical practices for treating RA. Nevertheless the actual modes of mechanism have been still elusive how each biologics act on specific target cell types and exert their respectively characteristic pharmacological effects. The presenter has so far originally established the system for visualizing inside of living bone tissues and joints by exploiting intravital two-photon microscopy, and elucidated cellular mechanisms on bone destructions by osteoclasts. Here I introduce the recent data showing the practical mode of actions of different biologics on inflammatory bone destruction in vivo, and, based on these fundamental data, discuss the future perspective on biological treatment of RA.

S17-5

Mechanisms underlying cartilage degeneration in osteoarthritis

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Conflict of interest: None

Osteoarthritis (OA) is the most prevalent joint disease causing chronic disability worldwide in the elderly people. Since experimental mouse models with surgically induced instability in the knee joints were established, many studies have revealed the molecules or signalling pathways responsible for OA. We have shown that hypoxia-inducible factor 2 alpha (HIF-2α) comprehensively regulates OA development through transcriptional induction of various catabolic factors, and that NF-κB signalling upregulates HIF-2α. Meanwhile, obesity, traumatic joint instability and hard work are known as risk factors of OA, indicating that excessive mechanical loading is one of the triggers. I introduce molecular mechanisms underlying OA development by excessive mechanical loading and the NF-κB-HIF-2α axis.

S18-1

The present conditions of infectious diseases that should be overcome in rheumatic diseases

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Conflict of interest: None

There has been a great progress in the treatment of rheumatic diseases in its agents and strategies in this decade. New agents such as methotrexate, calcineurin inhibitor, several class of biologics including tumor necrosis factor inhibitors, target specific disease modifying antirheumatic drug tofacitinib for rheumatoid arthritis, cyclophosphamide pulse therapy and multi-targeted therapy with tacrolimus and mycophenolate mofetil for systemic lupus erythematosus, additionally approved rituximab for microscopic polyangiitis and granulomatosis with polyangiitis had been recommended. These agents and treatment strategy must be helpful to induce remission and maintain of remission or low disease activity preferably reducing unfavorable infectious side effects of corticosteroids. The screening and monitoring procedures how to reduce infection which may impair organ function and quality of life and mortality also progressed. In spite of the progression, there still exists difficulties in controlling infections. In this symposium, 5 topics of infections are listed; infections in respiratory tract which is the most frequent site, intractable chronic infection with non-tuberculosis mycobacterium, perioperative infection, Hepatitis B infection and the way of management to conquest infections in the field of rheumatic diseases. This symposium should be helpful in treating patients with rheumatic diseases.

S18-2

Prevention and Treatment of Pulmonary Infections in Connective Tissue Diseases

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Conflict of interest: Yes

CTD including rheumatoid arthritis are systemic autoimmune diseases characterized by the presence of autoantibodies and auto-reactive lymphocytes, systemic inflammation, and consequently serious organ damage. Pulmonary diseases in CTD are pivotal conditions affected the prognosis and quality of life. These conditions include interstitial lung diseases (ILD), infections, drug-induced diseases and accidental complications. Pulmonary infections are important and their management is required. CTD patients are susceptible to pulmonary infections because of ILD and dysregulated immune system by immunosuppressive drugs and CTD. Targeted drugs including biologics are widely used with favorable response, but infections, especially pulmonary infections, are serious adverse events. We need considerable attention in bacterial and opportunistic infections. Living guidance and early detection are important to prevent the infections. Vaccinations for Streptococcal pneumonia and influenza infection are recommended. We performed living guidance such as mask wearing in the crowd, hand-washing, mouth care, control of sinusitis and diabetes, an appropriate amount intake of the alcohol, and the smoking cessation. The screening tests are also important before initiating immunosuppressive therapy. We need to check the past and family history of tuberculosis (TB) and the presence of infections, and perform physical and laboratory examinations, and chest X-ray and HRCT. Flow chart of the initial correspondence for fever, a cough and dyspnea in the installation guide line for biologics is helpful to diagnose pulmonary infections. We need to consider the other possible causes such as TB, non-TB mycosis, pneumocystis pneumonia, aspergillosis, drug-related pneumonia, and ILD than bacterial infections. There are some cases to turn worse rapidly. Thus, medical intensive care in cooperation with rheumatologists and pulmonologists is pivotal in treating pulmonary infections in CTD patients.

S18-3

Biological therapy for rheumatoid arthritis patients complicated with pulmonary nontuberculous mycobacterial infection. Importance of airway disease as an extra-articular manifestation of RA

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Conflict of interest: None

Biological treatment with respiratory tract disease recognized an extra-articular manifestation of RA, in particularly complicated with pulmonary NTM. NTM disease can spread from bronchial or bronchiolar abnormality. The evaluation of respiratory tract (airway) disease with RA is important because of infectious risk of biological treatment. We analyzed 33 RA patients (mean age 70 years, RA duration 12 years) complicated with bronchiectasis and bronchiolitis. High positive ACAP and RF was shown 91%(466 U/ml) and 100%(441 U/ml), respectively. MTX was co-administered 82%(10mg/w), and biologics were treated during 52 months with on-off using by adverse events. Low disease activity or re-

mission of RA was achieved in 90% by recent biologics (15 ABT, 7 GLM, 4 TCZ), and prednisolone dose could be decreased or discontinued. Biologics were stopped 10 patients such as 3 pneumonia, 4 exacerbation of MAC, however 6 were re-administered. Pulmonary MAC (7 M.avium, 2 M.intra) was bacteriologically determined revealed CT findings with 8 nodular bronchiectatic, 1 fibrocavitary). Serum GPL-core IgA (MAC) antibody were elevated in 8 of 9 patients. Pseudomonas aeruginosa were cultured in 5 of 33 RA with complicated sinusitis (sino-bronchial syndrome). Among 9 MAC patients, 4 received prior MAC therapy (CAM, RF, EB) were no exacerbation of pulmonary MAC (negative sputum culture and CT findings) by biologics. However, 5 patients preceding biologics without MAC therapy were exacerbated pulmonary MAC, and stopped biologics. These 5 patients were re-started biologics with continuing MAC therapy. Although RA patients was complicated with respiratory tract (airway) including pulmonary MAC, biologics can be carefully used with low immunogenicity and possible on-off setting of biologics. NTM can spread from preexisting abnormal structural lung lesions. RA patients received inadequate RA therapy (MTX or biologics) has been thought to be progressed destructive articular and lung change resulted as cylindrical bronchiectasis or NSIP/UIP like manifestations associated continuous pulmonary inflammation.

S18-4

Perioperative DMARDs therapy and surgical site infection

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Conflict of interest: None

Surgical site infection (SSI) is one of the most severe complications of orthopaedic surgeries. Previous studies have tried to elucidate whether rheumatoid arthritis (RA) patients treated with disease modifying antirheumatic drugs (DMARDs) could be high risk cases of SSI and delayed wound healing (DWH). The consensus about perioperative continuation of methotrexate (MTX) use has been already described in the guidelines set by JCR. On the other hand, several studies reached conflicting conclusions about biologic DMARDs (bDMARDs) use in this decade. Bibbo et al. reported in 2004 that the use of TNF-alpha inhibitors did not increase the risk of SSI or DWH without perioperative discontinuation (Bibbo, Foot Ankle Int, 2004). We also investigated 1036 procedures performed for RA patients in our department, and reported that the foot and ankle surgery (OR:3.16, 95%CL:1.256-7.986), and the total knee arthroplasty (OR:4.04, 95%CL:1.43-11.38) were risk factors of SSI and DWH, respectively, but not bDMARDs use with adequate discontinuation periods (Kadota, Mod Rheumatol, 2015). However, we have to note the relatively low frequency of SSI or DWH after orthopaedic surgeries for adequate statistical evaluations. Ito et al. reported the result of meta-analysis (Ito, Mod Rheumatol, 2015), and concluded that the bDMARDs might slightly increase the relative risk of SSI (RR:2.03, 95%CL:1.40-2.96). At present, surgeons are recommended to stop the use of bDMARDs during perioperative periods. The relevant period of discontinuation should be decided considering the half-life of each drugs. Along with the discontinuation of DMARDs we have to care about the risk of flare-up the disease. We have already experienced many cases of flare-up especially in etanercept cases because of its short half-life. Hereafter, small molecule drugs come to be used in more cases, then further investigations are needed for the proper management of each agent according to the invasiveness of surgical procedure.

S18-5

Viral reactivation under immunosuppressive treatment for CTD

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Conflict of interest: None

In Overarching principles on 2016 Eular Recommendation for RA treatment, “Treatment of decisions are based on disease activity and other patient factors, such as progression of structural damage, comorbidities and safety issues.” Recently new comorbidities have been appeared. Among them, Hepatitis B virus (HBV) and herpes zoster (HZ) infection is a major issue in RA patients under bDMARDs or tsDMARDs treatment. Reactivation of HBV refers to a rise in the hepatitis B viral load caused by immunosuppressive therapy including bDMARDs in a patient with HBV infection. Reactivation of HBV is classified into reactivation from the carrier state and reactivation in a patient with resolved HBV infection. Hepatitis associated with this reactivation in a patient with resolved HBV infection is called “de novo hepatitis B”. Japan College of Rheumatology has published“A proposal for management of rheumatic disease patients with hepatitis B virus infection receiving immunosuppressive therapy”. Serological examination for HBV infection is necessary before starting immunosuppressive therapy for all patients with CTD. Immunosuppressant agents known to be associated HBV reactivation include corticosteroids, immunosuppressant agents, anti-rheumatic agents with immunosuppressive activity, and biological agents such as anti-TNF-α agents. HZ induced VZV reactivation is also important complication for CTD patients under immunosuppressive treatment. It is well known that several RCTs revealed an increased rate of herpes zoster with JAK inhibitor. The incidence of HZ under JAK inhibitor treatment is high in Japanese population significantly. The Herpes zoster incident rate associated tsDMARDs treatment is suggested to increase compared with that associated with biologics.

S18-6

Infectious disease management in connective tissue disease

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Conflict of interest: None

Infectious disease management is an essential skill for rheumatologist. It is important to understand diagnosis and infection control for management of infectious diseases. Patients with connective tissue diseases have various biological changes. In addition to aging, the following biological changes are known. (1) Immune disorder due to the disease itself, (2) Immune disorder caused by therapeutic drugs such as steroids, immunosuppressive drugs, biological preparations, etc. (3) Diabetes and hypertension renal injury / failure, liver disorder / failure caused by therapeutic drugs. Patients with connective tissue diseases are immunocompromised due to these changes. We consider two axes to diagnose infection. Two axes are infected organs and causative microorganisms. Due to host factors, we are difficlut to diagnose patient infection with connective tissue diseases. Microbial burden, a major determinant of severity of the infection, is significantly increased in patients with connective tissue diseases. Owing to anti-inflammatory effects of the immunosuppressive therapy, symptoms of infections are greatly muted and presentation occult, until the infection is far advanced, with a poor prognosis. We predict infections with which immune disorder my patient have. We can divide 4 immune disorders, neutropenia, cellular immunodeficiency, humoral immunodeficiency, failure of the barrier function. Patient with connective tissue diseases can have multiple infected organ lesions. Infection control is also an essential. It is important we understand standard precaution such as hand hygiene. We also need airborne precaution for patients with pneumocystis pneumonia and disseminated herpes zoster. It is important collaboration between infectious disease specialists and rheumatologists.

S19-1

New insights into the pathogenesis of systemic lupus erythematosus : Finding novel players and therapeutic targets

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Conflict of interest: None

Genetic and epigenetic components play the critical roles on the development;of SLE. Recently we have defined functional variant in NCF1, encoding the subunit of the phagocyte NADPH oxidase (NOX2), as the putative underlying causal variant that drives a strong SLE-associated signal detected by the Immunochip in the GTF2IRD1–GTF2I region at 7q11.23 with a complex genomic structure. We show that the p.Arg90His substitution, which can cause reduced reactive oxygen species (ROS) production, predisposes to SLE in multiple populations. Our findings highlight the pathogenic role of reduced NOX2-derived ROS levels in autoimmune diseases. A hallmark of SLE is high titers of circulating autoantibodies. Recent study identified a novel $CD11c^+$ B cell subset in aged female mice that is critical for the development of autoimmunity. However, the role of $CD11c^+$ B cells in the development of lupus is still unknown. We explored the function and regulation of this novel B cell subset. The number of $CD11c^+$ B cell and titer of anti-chromatin IgG2a was significantly increased in induced SLE mice model (cGVHD). In vitro study demonstrated that $CD11c^+$ plasma cells produced large amounts of anti-chromatin IgG2a upon stimulation. In vivo depletion of $CD11c^+$ B cells significantly reduced anti-chromatin IgG and IgG2a production. Moreover, T-bet expression was remarkably increased in $CD11c^+$ B cells during cGVHD. Knockout T-bet in B cell alleviated the progression of cGVHD. Finally, the percentage of $T\text{-}bet^+CD11c^+$ B cells were significantly elevated in lupus patients, which are positively correlated with anti-chromatin levels and nephritis. Our data demonstrated that $T\text{-}bet^+CD11c^+$ B cells are critical for the anti-chromatin autoantibody production, which might be explored as a therapeutic target for rectifying the abnormally produced anti-chromatin in SLE.

S19-2

Clinical practice and management of systemic lupus erythematosus in Japan

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Conflict of interest: Yes

Systemic lupus erythematosus (SLE) is a prototype of systemic autoimmune disease. Multiple organs and tissues are affected in patients with SLE in a different way, and such heterogeneity of clinical aspect of this syndrome is making difficult to standardise the management of lupus patients in clinical practice. In fact, assessment of patients with SLE highly depends upon the experience of the treating physicians, thus being subject to large variability between centres. Amongst the lupus organ involvements, lupus nephritis (LN) is one of the most common and important manifestations, affecting the mortality and morbidity in patients with SLE. A number of immunosuppressants has been used for the treatment of systemic lupus erythematosus in daily practice, and they contribute to improve the prognosis of the affected patients. Mycophenolate mofetil (MMF) has been recommended for the initial and maintenance treatment. In order to clarify the real-world use of MMF as a treatment for LN in Japan, Japan College of Rheumatology surveyed the use of MMF in daily clinical practice. Last year, as a result, MMF was approved for treating LN in Japan. Considering the background, solid data on the efficacy and safety of MMF for the treatment of LN has not been available. Cyclophosphamide (CY) and tacrolimus (TAC) are potent immunosuppressants, frequently used for serious organ involvements in SLE patients. Apart from LN, most serious diseases in SLE, such as neuropsychiatric lupus, thrombotic microangiopathy, are treated by CY. For LN, CY was listed as the first choice for active class III/IV LN in parallel with MMF. We should consider advantages/ disadvantages for both drugs. TAC has been approved for LN in a maintenance phase of the treatment in Japan. In clinical practice, however, TAC is often considered as a potent supporter for MMF or CY in the induction phase for cases with insufficient response for MMF or CY. We should establish a strategy how to use those potent immunosuppressants to improve the outcome of lupus treatments.

S19-3

Update on the therapy of lupus nephritis

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Conflict of interest: None

Renal disease in SLE carries significant morbidity and mortality. Conventional cyclophosphamide (CYC) and azathioprine (AZA) is not ideal in terms of efficacy and toxicity. Mycophenolate mofetil (MMF) has emerged as an alternative agent for induction therapy of lupus nephritis because of its lower gonadal toxicity, although it is not superior to CYC in efficacy. In the past decade, newer immunosuppressive biological agents are being tested in lupus nephritis (LN). Tacrolimus (TAC) has been shown to be equally effective to CYC or MMF for induction therapy of LN. Low-dose combination of MMF and TAC appears to be superior to intravenous pulse CYC as induction in Chinese patients with LN. The same regimen is also effective as salvage therapy of refractory disease. A number of biological agents, including rituximab, ocrelizumab, atacicept and abatacept have been tried in LN but none of them could meet the primary efficacy end-point as compared to placebo. Therapeutic drug monitoring (TDM) may help to optimize dosing to enhance efficacy but reduce toxicity in patients with SLE receiving MMF or TAC. Novel agents are being developed and shown promise in LN. These include voclosporin and monoclonals against the type I interferons. New studies of belimumab and rituximab are being performed in patients with LN. Finally, omics-based techniques have enabled discovery of novel serum and urinary biomarkers that are being validated for diagnosis, prognostic stratification and early detection of flares in LN. As there is considerable interethnic variation in the efficacy and tolerability of various regimens, treatment of LN has to be individualized.

S19-4

Upcoming treatment of SLE

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Conflict of interest: Yes

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease with heterogeneous clinical manifestations, and pathologically characterized by activation of autoreactive T cells and overproduction of autoantibodies by B cells. The overarching principle of Treat-to-target-in SLE recommendations documents that the treatment of SLE should aim at ensuring long-term survival, preventing organ damage, and optimizing health-related quality-of-life, by controlling disease activity and minimizing comorbidities and drug toxicity. When a patient has life-threatening organ damage or high disease activity, high dose glucocorticoids, hydroxychloroquine and immunosuppressants are widely used for the treatment. As immunosuppressants, mycophenolate mofetil, cyclophosphamide, azathioprine and tacrolimus are approved in Japan. However, patients refractory to these drugs are often experienced and safer and more effective therapies are needed. Biological agents have been emerged for the treatment of SLE. Among them, belimumab reveals sustained safety and tolerability documented in a long-term extension and is globally approved in many countries. Treatment with rituximab, an anti-CD20 antibody, results in reconstitution of B cells in the periphery, which in turn leads to long-term remission SLE. Anifrolumab, an anti-IFNAR antibody demonstrated efficacy especially in patients with higher IFN gene signature and tolerability and is currently under the phase 3 trial. Orally available kinase inhibitors targeting JAK, Syk and Btk also gather their attention for the treatment of SLE. A phase 2 trial of baricitinib, a JAK1/2 inhibitor, has commenced in lupus nephritis. Despite inherent obstacles, there are infinite unmet needs for the treatment of SLE. However, we have to understand the reasons for failed many trials and have to move forward with lessons from the past.

S20-1

Medical cooperation and hand surgery for RA patients

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Conflict of interest: None

(Introduction) It has been reported that biologic agents inhibit the

progression of the joint destruction in rheumatoid arthritis (RA). For this reason, these agents have been often used for the treatment of RA recently. The purpose of this study is to evaluate the effectiveness of orthopaedic surgery in RA patients, especially RA hand surgery. (Indication of RA hand surgery) Sometimes a few of arthritis are remained under controlled RA patients. For these patients, surgical treatment is better choice than medication. Moreover, for destructive joint cases, surgical intervention is needed. Especially for RA patients, hand deformity is big problem, and appearance is very important. One finger joint swelling is very likely to cause joint deformity. Therefore surgical treatment is needed for these cases, however a few patients know about it. We, orthopaedic surgeons, have to give correct information about surgical indication for RA patients. (Medical cooperation) In these days, medical cooperation is necessary for RA treatment. Combination of medication, surgical treatment, and rehabilitation is thought to be important. Best timing of surgical intervention is needed to all of them. (Conclusion) In this era, RA hand surgery is thought to be important under tight control with medical therapy. Medical cooperation is also important for RA patients satisfaction.

S20-2

Combinations of medication and surgery. From the stand point of an internal rheumatologist

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Conflict of interest: Yes

Internal rheumatologists tend to focus on laboratory data and ignore joint destruction or tendon rupture. They should not miss the timing for joint surgery. In order to be aware of the good timing for surgery, not only pay attention to joint destruction by X ray, but also they should obtain and maintain the consultation system to the orthopaedic rheumatologists. With the advance in medication such as methotrexate or biological disease modifying anti-rheumatic drug (bDMARD), and the prevalence of the concept of treat to target (T2T), it became easier to achieve clinical remission (CR) these days. However, there still exist the patients who had joint pain, restriction of joint mobility, or with decreased quality of life even with CR by composite measures such as disease activity score 28 (DAS-28). In this meeting (JCR 2017), Nomura Y will present the effectiveness of the joint surgeries in such patients at our rheumatic center. In 2016, new recommendation of T2T was published, and the importance of surgery and physiotherapy was clearly written (Smolen JS, Bleedveld FC, Burmestar GR et al.:Treating rheumatoid arthritis to target: 2014 update of the recommendations of an international task force, Ann Rheum Dis 1:3-15, 2016). Especially, foot care and the surgery to prevent tendon rupture were recommended. I will present my patients who achieved and maintained CR, but who required a surgical intervention. Conversely, in order to get a favorable result of surgery, disease activity of RA should be controlled with an adequate medication. In conclusion, internal rheumatologists should know the orthopaedic knowledge about joint surgery not to miss the timing of operation. They should build a consultation system to orthopaedic rheumatologist. Of course they should be good at medication to control disease activity of RA.

S20-3

Indication for surgical therapy of foot in rheumatoid arthritis from the view point of physicians through efforts on multidisciplinary team approach

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Conflict of interest: None

The therapeutic goal of rheumatoid arthritis (RA) is to improve patient's QOL and prognosis. This depends on their pain control and improvement of physical function. Furthermore, it is necessary to be done safely, and achieved in consideration of social and economic aspects. Recently, the development of new therapeutic agents and advances in therapeutic methods have shown that remission by medication have been prepared, but there are a lot of other requirements including surgical therapy. Therefore, the team approach is necessary, and our hospital has been working on building team approach, as the center for rheumatic disease. The core of team approach must be collaboration between physicians and surgeons, which is the key point for success. In our hospital, outpatient unit / wards are common, and case conference are also held jointly. Physicians are required to have ability of diagnosis, medication, management of complications, early treatment of infectious diseases, but at the same time it is also necessary to evaluate the physical dysfunction. As a major factor of their decline in ADL, physical dysfunction of lower limb, gait disturbance due to pain can be considered. In our hospital, we established "Locomo Check for RA patients" responsible for surgeon, physician can easily introduce to surgeon by selecting patients who recognized dysfunction. In the "Locomo Check for RA patients", surgeon provides information for function of joints, proposals for orthosis, surgical therapy. In the case of revision joint surgery, "Total Care Team in Revision Surgery" composed of various medical staff will perform preoperative and postoperative evaluation. Local evaluation and treatment of the lower limbs are also conducted in collaboration with professional nurses of "Foot Care for RA patients", dermatologists and orthotics. I would like to discuss indication for surgical therapy of foot in RA from the view point of a physician through efforts on team approach.

S20-4

Changes of surgical indication for hip and knee in RA patients

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Conflict of interest: Yes

【Purpose】In daily practice with improved medication, we feel various changes in the joint of rheumatoid arthritis (RA). We analyzed the trend of total hip arthroplasty (THA) and total knee arthroplasty (TKA) cases in recent years, then the changes of surgical indication will be discussed.【Methods】Between 2000 and 2015, all RA surgeries were reviewed. For THA and TKA, the number of surgery, patients' background, and disease activity were analyzed. 239 joints of TKA and 81 joints of THA were further investigated for perioperative changes of C-reactive protein, white blood cell count, and changes in use of MTX and prednisolone (PSL). The main focus of radiological findings was osteophyte formation in TKA, on the other hand, acetabular Protrusion and cortical index in THA.【Results】The number of RA surgery were increased over time. The rates of the number of lower limb surgery was decreasing, on the other hand, surgery number for upper limb surgery showed continual increase. The use of biologics were maintained around 30% after 2010, but the cases with remission were increased. In TKA and THA cases, the average age at the time of surgery have been increasing. In THA cases, CRP value was decreased with time. The averaged doses of MTX were increased, and averaged doses of PSL was decreased in both groups. In radiographic analyses, most of TKA cases showed osteophyte formation. In THA cases, osteophyte formation around the acetabulum and improved cortical index were observed in recent cases. Although some cases showed rapid destruction of the joints, most of cases in both groups showed gradual changes of joint destruction more than two years before surgery.【Discussion and conclusion】The cases of RA surgery increased over time, with use of biologics about 30%. In the near future, surgical cases in remission may increase. Also, it is important to perform surgery during patient's ADL is maintained in lower limb.

S20-5

Indications for surgical intervention and patient satisfaction in rheumatoid arthritis: Current view from rheumatologist

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Conflict of interest: None

For patients with rheumatoid arthritis (RA), the current concept of "treat-to-target" is the primary treatment goal aiming to achieve clinical remission. Clinical trials have demonstrated that early treatment reduces

inflammation, resulting in limited structural damage and better long-term outcomes. However, patients who fail to respond to pharmaceutical therapies, require surgical intervention to prevent further loss of function. We have analyzed he relationship between inflammation and joint destruction in RA. We reported that positive Power Doppler signal detected by ultrasound (US) reflected active synovitis in patients undergoing arthroplasty. Furthermore, we and other groups have reported US-detected synovitis with power Doppler signal is associated with joint destruction, even in RA patients in clinical remission. Although RA is generally an inflammatory process of the synovium, structural or mechanical derangement is a frequent cause of pain or loss of joint function. Pain and joint mobility may be improved by surgical treatment. Recently, as a result of the introduction of effective new drugs, the goals of surgical intervention for patients with RA have changed. However, there is lack of definitive evidence for the surgical management in RA. The decision for orthopedic intervention should be established by an interdisciplinary team that includes rheumatologists and orthopedic surgeons, and we need further consideration to achieve higher patient satisfaction in RA.

S20-6

Achievements of rehabilitation for the higher satisfaction on orthopedic surgeries for patients with rheumatoid arthritis

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Conflict of interest: Yes

Aggressive early treatment of rheumatoid arthritis (RA) based on an early diagnosis with a concept of tight controls (treat RA to target; T2T), more specifically pharmacotherapies with methotrexate (MTX) and biologic agents enable most of patients with RA to spend unlimited daily living similar to premorbid states without disabilities. However, a certain number of patients with RA have been still suffering from disabilities caused by the onset before the era of paradigm shift on RA pharmacotherapies, the delay of confirmed diagnosis or initiation of therapy, or the difficulty on the application of MTX or biologic agents. Artificial joint replacement surgeries on weight bearing joints are frequently performed for older patients with a long RA history, in contrast, hand surgeries to improve functions and appearance are sometimes done for younger patients with a relatively short history. Rehabilitation, composing one of the four main therapies for RA, includes the instruction of activities of daily living for joint protection, the instruction of exercise therapy for the maintenance of physical functions, and psychological supports such as music therapies for mood improvement through patient education aimed for all the patients with RA including early patients. Rehabilitation is closely related to orthopedic surgeries and plays a significant role for the good performance of surgeries and the high patient satisfaction level. The better outcome from surgeries assisted with preferable occupational and physical therapy is likely to increase the motivation for surgeries in both surgeons and patients. In addition, rehabilitation can improve physical function on the disabilities remaining even after the surgeries by training and using an orthosis or a self-help device, resulting in further increased satisfaction. In the presentation of this symposium, current rehabilitation for patients with RA will be illustrated with a couple of case reports.

S21-1

Patient reported outcomes in clinical rheumatology

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Conflict of interest: None

In recent years, patient reported outcome (PRO) has been regarded as an important indicator of treatment effectiveness in general medical treatment. In rheumatoid arthritis (RA) treatment, definition of remission established by the ACR/EULAR in 2011 include a PRO such as patients global assessment (PtGA), as well as clinical findings and examination values. However, PtGA has characteristics such that correlation with other RA activity indicators is not high, changes are difficult to evaluate, "how to ask" has not been decided. Therefore, it is necessary to be verified whether it is appropriate as an epidemiological indicator of therapeutic effect. From March to August 2013, a questionnaire survey was conducted on 90 rheumatologists and 761 patients. Total of 68.8% of doctors regularly evaluate PtGA in daily practice. The answer to the question of how much consideration PtGA should be taken in therapeutic decision making was widely distributed from 10% to 90%, but the average value was 51.6 ± 18.9. Sixty percent of rheumatologists change the way how to ask PtGA according to patient characteristics such as age, disease activity, comprehension ability. The patient's PtGA showed a high correlation with Pain-VAS ($r = 0.87$, $p < 0.001$), showing a reverse correlation with age, duration of significant significance, satisfaction with medical care. People who responded that their disease duration was long (over 14 years) or who became worse than one year ago had increased PtGA over the degree of Pain-VAS. This study suggested that PtGA in RA patients may cause deviation with Pain-VAS when they have long RA history and/or major changes in symptoms. Such patient characteristics were consistent with the reasons why RA doctors changed their way of asking PtGA at daily practice. To use PtGA as an epidemiological index, it is necessary to standardize inquiries according to the purpose. However, PtGA can be a useful communication tool between RA patients and their doctors to share therapeutic goals. For that purpose, PtGA could be asked in various manners.

S21-2

Patient Global Assessment in RA practice

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Conflict of interest: None

Patient global assessment (PtGA) is one of the most used patient reported outcomes (PROs) in rheumatoid arthritis (RA) practice. Needless to say, PtGA is important in assessing disease activity and therapeutic response in daily clinical practice. Even in clinical trial, the experts from ACR, EULAR and OMERACT endorsed PtGA as "Core Set" of PROs, along with physical function and pain assessment. In addition, PtGA is commonly incorporated into many composite measures of disease activity in RA such as DAS 28, SDAI, CDAI, RAPID 3. Although PtGA is simple and widely used, there is no so-called "Gold Standard" of PtGA. Based on the difference of the wording/phrasing (state of arthritis / health condition), the time period (on the day/ 7 days / 14 days.) and evaluation method (VAS / NRS), PtGA is far from homogeneous. PtGA is used for purpose of comprehensively evaluating the disease activity of RA, but it is affected not only by short-term disease activity but also by changes in joint structure, mental stress. In addition, it is reported that even factors that are not directly related to the activity of RA (comorbidities and socioeconomic factors such as education level) can influence the PtGA. Also, discordance between PtGA and PhyGA has been reported. PtGA is very often scored higher than PhyGA. While RA treatment based on a shared decision between physicians and patients is required, the discordance of disease activity assessment between physicians and patients has potential becomes a problem. In this session, we review the importance and the problems of PtGA once again, then present our data about the factors cause fluctuation in PtGA.

S21-3

QoL assessment of rheumatoid arthritis patients

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Conflict of interest: None

There is a growing interest in patient-reported outcomes (PROs) in rheumatology, which goes with a global trend for patient-centered care. Among PROs, 3 domains, namely pain, function, and patient global assessment, are established in most of the rheumatic diseases and the sum of the 3 domains are also used as disease activity indices (RAPID3 and PAS-II). MHAQ is still used widely in Japan however it failed to reflect

the higher level of activity in the era of remission. In the NinJa 2015 database, MHAQ was 0.23 lower than HAQ-DI and patients with MHAQ score of zero became 48% whereas patients with HAQ-DI of zero were 35%. In patients with HAQ-DI of zero, 12% had difficulty in "Walk two miles or three kilometers, if you wish? "and 21% had difficulty in "Participate in recreational activities and sports as you wish? "If we use MDHAQ which consisted of 8 items of MHAQ and 2 items as above, the gap between MDHAQ and HAQ-DI decreased to 0.12 and the patients with MDHAQ of zero were 31%. MHAQ should be replaced to MDHAQ in Japan as stated in the ACR 2015 recommendation. Recently, more PROs such as psychological well-being and fatigue are highlighted in addition to pain and physical function. SF36 is used most frequently in research but most of the validated outcomes are not intended for the use in daily practice. Dr. Pincus, a developer of MHAQ, created MDHAQ and its questionnaire to solve the floor effect of MHAQ in 1999. The Japanese version is now available. Modification for each practice is also allowed. If we ask patients to answer PRO (MDHAQ questionnaire) using their waiting time, we can assess each patients' QoL beyond joint.

S21-4

Evaluation of satisfaction in patients with rheumatoid arthritis

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Conflict of interest: None

Evaluation of patient satisfaction is often used when we assess the quality of medical services. Quality is often evaluated based on 3 components: structure, process and outcome. Studies have reported that the higher the quality of structure and process is, the higher the outcome is. The ideal outcome is to improve the disease condition and maximize patient satisfaction. Satisfaction is assessed by patients themselves considering aspects such as treatment procedures and interactions with health professionals; therefore, it reflects a patient-centered perspective. Patient satisfaction increases significantly in correlation with the volume of information provided by health professionals, as well as time spent in consultation. Concern shown by doctors highly influences the evaluation of satisfaction. In the field of RA, EULAR has proposed T2T strategies with the aim of achieving the best possible outcome. T2T focuses on appropriate and most effective treatment based on the assessment of disease activity. T2T also highly recommends RA treatment based on a shared decision making with patients. The degree of patient participation in shared decision making is strongly related with patient satisfaction. Kaneko and colleagues reported that while most rheumatologists in Japan agree with T2T recommendations, their implementation still requires some improvement. Support is required for better patient understanding of RA and its treatment, and adequate participation in decision-making. Studies from other countries indicate that not only medical skills but also the health professionals' attitude is related to patient satisfaction. Satisfaction in patients with RA in Japan also showed correlation with positive interactions with opportunities for "face to face" consultation and health professionals' efforts to ensure patient understanding. Better communication improves the patients' adherence to the prescribed treatment, resulting in continuity of better treatment and better outcomes. We discuss the significance for evaluation of patient satisfaction based on previous studies.

S21-5

The Relationship Between Physical Function and Patient Reported Outcomes

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Conflict of interest: None

In DAS-28 or SDAI, evaluator's global assessment and patient's global assessment are one of the components. The main determinants for the PGA are pain, function, and number of swollen joints. Physical functions will affair clinical remission. With the advent of methotrexate and biological disease-modifying antirheumatic drugs, clinical remission has been a realistic goal in rheumatoid arthritis (RA). In 2011 ACR/EULAR Boolean-based definition of remission in RA, patient global assessment (PGA) is often the limiting factor for reaching remission. In the real world, there are not few patients with no swollen joints, nor tenderness joints, nor CRP, only PGA is high. PGA had a most strong correlation with the HAQ-DI in the components of the DAS28-CRP (r=0.395). Of the patients who were in functional remission (HAQ-DI ≤0.5), mean PGA was 0.51, of the patients whose HQA-DI >0.5; 4.2. 50.3% of the former fulfilled PGA 0 or 1, on the other hand, only 16.0% of the latter fulfilled PGA 0 or 1. By Receiver Operating Characteristic analysis of the 277 patients fulfilled swollen joint count, tenderness joint count, and CRP 1 or less, cut off value that satisfies PGA 0 or 1 was HAQ-DI=0.18. The Ishiguro group from the Ministry of Health, Labour and Welfare characterized functional impairment in surgical patients. Patients noted most remarkable ADL disabilities for the following items on the HAQ-DI: HAQ2 (shampoo hair), HAQ4 (arising), HAQ11 (tub bathing), and HAQ16 (opening and closing a wide mouth jar). As the level of disability increased, a concomitant decrease was observed in each joint's range of motion. Following ROMs of the joints which represented nearly non-existent levels of disability, are needed; wrist, flexion-extension as well as 150° pronation and supination, 130° elbow flexion, and 140° shoulder flexion. Physical function had an impact on PGA. Physical function is one of the determinants for the PGA.

S21-6

The usefulness of surgical intervention examined by patient's subjective evaluation in patients with rheumatoid arthritis

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Conflict of interest: None

【Objectives】Clinically beneficial effects of biologic disease-modifying anti-rheumatic drugs (b-DMARDs) have been reported in disease control as well as prevention of the joint destruction. Surgical procedures for joint deformities of rheumatoid arthritis (RA) have been aimed to achieve the functional remission for the joint. Patient's subjective evaluation systems are important tools not only for assessment of post-operative outcomes of the joint, but for the assessment of whole extremity or whole body. We aimed to investigate the usefulness of surgical intervention with patient's subjective evaluation systems (Disability of Arm, Shoulder, and Hand (DASH), Hand20 questionnaire (Hand20), Self-Administered Foot Evaluation Questionnaire (SAFE-Q), body image (BI) and Beck Depression Inventory-II(BDI-II)).【The usefulness of upper extremity surgeries evaluated by DASH and Hand20】158 RA patients underwent the surgical treatment on upper extremities. We examined the postoperative changes in each items of DASH and Hand20, and found the significant improvements in items about weakness in elbow group, pain in wrist group, and delicate movement and cosmetic factor in finger group.【The usefulness of foot surgeries evaluated by SAFE-Q】24 RA patients underwent surgery on the forefoot deformities. In the subscale of SAFE-Q, pain and pain-related, physical functioning and daily-living, social functioning, shoe-related and general health and well-being significantly improved at one year after the surgery.【The usefulness of surgical intervention on BI】90 RA patients underwent the surgical intervention for large and small joints of the upper and lower limbs. In patients of the large joints of the upper and lower limbs groups, the disturbed body-cathexis significantly improved. The low body-esteem significantly improved in patients of the small joints of the upper and lower limbs groups.【Discussion】Among the patients who underwent the surgery for large joints, the improvement of ADL contributed to improve the BI and depression. The

improvement of cosmetic appearance contributed to improve the BI among the patients who underwent the surgery for small joints.

Educational Lecture

EL1

Comprehensive pain care in rheumatoid arthritis

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Conflict of interest: Yes

Rheumatoid arthritis (RA) treatment has dramatically changed using by biological DMARDs and methotrexate. We are able to hold down disease activity, and it became the treatment goal to protect joint destruction. Although many patients can achieve remission, it is a fact that there remain patients who cannot. Sometimes we could not provide enough treatment because of an escape phenomenon of DMARDs, second failure of biologics, or adverse events. It is still difficult to maintain remission throughout the life. We may use glucocorticoid to achieve, at least, low disease activity. Under such an inflammatory situation, the joint destruction gradually progresses. In addition, even if we would maintain remission and protect joint destruction for several years, we could not protect degenerative osteoarthritis or spondylosis for several decades. The chief complaint of the RA patient is 'pain'. Pain limits ADL and reduce QOL. Pain care is not mere the start, but also 'a key' for treatment. We should distinguish nociceptive pain because of joint inflammation or deformity, from neuropathic pain due to the compression of nerve. It is necessary to prescribe an appropriate medicine, such as NSAIDs, acetaminophen, or pregabalin. When it is difficult to control the sharp pain at the time of the exercise using only medicines, it is required orthosis or surgery to get rid of pain due to deformity or instability of joints. The cause of the pain greatly varies according to an individual, and it is important to provide the comprehensive pain care.

EL2

Rheumatic diseases and Pregnancy

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Conflict of interest: Yes

The theory of Developmental Origins of Health and Disease (DOHaD) that is the fetal origins of adult disorders shows that the condition in the uterus is important for human beings. Active disease in patients with rheumatoid arthritis (RA) and systematic lupus erythematosus (SLE) tend to result in poor outcomes during pregnancy. Therefore, we must strive to achieve a good outcome by safely using medicine. Many RA patients in remission can stop medication after conception because RA tends to improve during pregnancy. However, SLE patients must continue medication throughout pregnancy. We must, therefore, pay attention to the teratogenicity in the 1st trimester and to fetal toxicity in the 2nd and 3rd trimesters. SLE has a tendency to cause complications during pregnancy, such as preeclampsia and intrauterine growth restriction, especially with antiphospholipid antibodies syndrome. We would like to introduce the findings of the research team for surveillance concerning the pregnancy outcome of mothers positive for anti-SS-A antibodies and antiphospholipid antibodies.

EL3

Current status of malignant disorders complicated by connective tissue disorders

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Conflict of interest: None

Patients with connective tissue disorders (CTDs), including RA and SLE, have a higher risk of malignancy. PM/DM and polymyalgia rheumatica are associated with a particularly high incidence of malignancy. Many reports have stated that the risk of malignancy in patients with SSc

is increased, although the standardized incidence ratio (SIR) for malignancy varies (0.910; 95% CI, 0.66–1.22 and 1.75; 95% CI, 1.41–2.18). Although the relationship between CTDs and malignant disorders is unclear, paraneoplastic syndrome or the mechanism of malignancy development based on fibrosis are considered. Furthermore, malignant lymphoma (ML) is common in CTD patients. Many reports have described ML in patients with RA, SLE, and Sjögren syndrome (SS). Histologically, most cases of ML in RA patients are diffuse large B-cell lymphoma. However, one complication of SS is a marginal-zone B-cell lymphoma called mucosa-associated lymphoid tissue lymphoma. We suggest that this discrepancy is caused by the onset mechanism associated with the presence of the underlying disease. Additionally, malignant disorders may be related to medications in CTD patients. In particular, methotrexate-associated lymphoproliferative disorder (MTX-LPD), which develops during treatment with MTX in RA patients, has been a recent focus of attention. Some cases of MTX-LPD spontaneously regress with only MTX withdrawal, and this rate is higher in patients with Epstein–Barr virus infection. Moreover, patients with MTX-LPD have more extranodal lesions than do patients with common lymphoma. Some reports have described a negative association between MTX and LPD onset. However, we epidemiologically proved that the mean MTX dose is a risk factor for LPD onset. Current problems include resolution of the predictive factors for spontaneous regression and decisions regarding established treatment for RA after LPD onset. In this lecture, we review past reports and discuss the association between CTDs and malignant disorders.

EL4

Diagnosis and treatment of polymyalgia rheumatica (PMR) ～All rheumatologyists must be familiar with this disease

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Conflict of interest: Yes

PMR is a systemic inflammatory disease of unknown etiology exclusively in the elderly. In 1957 Barber used the name PMR for his 12 cases for the first time. Estimated annual incidence varies from 0.01% to 0.08% in those aged 40 years and over in UK and the life-time risk of PMR in the US to be 2.4% for females and 1.7% for the males. Incidence of PMR is higher in northern Europe than in southern Europe, Africa and Asia. Ethnic predisposition and HLA-DRB1 association may suggest genetic factors are involved in the pathogenesis of PMR. The onset of clinical symptomes and signs are usually acute, which start with shoulder girdle myalgia and develop trunk myalgia with systemic symptoms such as fever within a few weeks. Laboratorical features show high serum CRP levels, elevated ESR, negative rheumatoid factor and normal myogenic enzymes such as CK in spite of severe myalgia. Giant cell arteritis (GCA) is frequently complicated with PMR and latent GCA complication detected by PET/CT should be kept in mind. Recently new classification criteria by ACR/EULAR was introduced in 2012 instead of Bird's criteria. Differential diagnosis of PMR from other diseases such as polymyositis, systemic vasculitis, drug-induced myopathies, infectious diseases and malignancies must be meticulously excluded. Glucocorticoids (GC) are definitely a mainstay of treatment for PMR. According to the 2015 recommendations for the management of PMR, GC should be started with 12.5 ~25 mg/day prednisolone equivalent and be tapered to 10 mg/day within 4 ~ 8 weeks. Dramatic response may be obtained but relapses are frequent. In addition adverse events of GC may be a significant matter. Concomitant use of methotrexate is recommended in such cases. Recently there are many reports showing efficacy of tocilizumab (TCZ) for PMR, not only for refractory cases but also for the first-line therapy. I will report a result of a prospective pilot study of TCZ mono-therapy in 13 PMR patients done in our institute. TCZ may be a promising alternative therapy for PMR patients with comorbidities.

EL5

Autoinflammatory diseases: Diagnosis and Therapy

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Conflict of interest: Yes

Autoinflammatory diseases are firstly proposed by Kastner et al. in which unprovoked, pathological activation of the innate immune system is triggered in the absence of autoantibodies or autoreactive T cells. Discovery of the causative mutations underlying several monogenic autoinflammatory diseases, those originally reported as autoinflammatory diseases, has identified key regulators of innate immune responses. The importance of autoinflammatory diseases in clinical practice is growing since some of the diseases or pathological conditions, considered as unknown etiologies, are now recognized as autoinflammatory diseases. Such diseases or pathological conditions resemble with infectious or autoimmune diseases, however, infectious pathogens or specific autoimmune reactions are not found that are characteristic in autoinflammatory diseases. Most frequent autoinflammatory disease is a familial Mediterranean fever (FMF). FMF is characterized by short, recurrent bouts of fever with systemic inflammation which last a few days. FMF is associated with a number of mutations of the *Mediterranean Fever (MEFV)* gene, which codes for a protein named pyrin. There appears to be a difference between Mediterranean/Middle Eastern populations and Japanese populations regarding genetic/phenotypic characteristic of FMF. The identification of double *MEFV* mutations in patients with FMF symtoms confirms the disease analysis, but it is not uncommon for no mutated alleles or only a single mutated allele to be detected, even in Mediterranean FMF patients. Moreover, in Japanese FMF patients, *MEFV* exon 10 mutations, most disease-related alleles and usually associated with sure disease phenotypes, even in heterozygous carriage. A high proportion of asymptomatic carriers of *MEFV* exon 2 or 3 variants is also observed. Therefore, we have been investigating the precise role of *MEFV* gene and other candidate genes associated with FMF. In this lecture, the recent advances and topics of autoinflammatory diseases will be discussed.

EL6

Animal models of rheumatic diseases

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Conflict of interest: Yes

Animal models are useful for clarifying the mechanism of rheumatic diseases. Previously, 'induced models' such as type2 collagen induced arthritis (CIA) were mainly used as animal models of rheumatoid arthritis (RA). Recently, 'spontaneous models' including genetically engineered mice have been established, such as TNF-a transgenic mouse, K/BxN mouse, and SKG mouse. These 'spontaneous models' have contributed to explore the mechanisms of disease onset of RA. Those include cytokine-dependent autonomous proliferation of synovial fibroblasts, osteoclast differentiation and bone destruction, role of auto-antibody and immune-complex, and newly identified helper CD4 T cell subsets such as regulatory T cells, Th17 cells, and follicular helper T cells. Role of innate immunity and intestinal microbiota for the regulation of helper T cell subsets are also recent research topics. On the other hand, given the fact that immune system of mouse and that of human are not identical, findings obtained from animal studies cannot always be applied to human diseases. Therefore, translational researches has been increasingly conducted, based on the findings obtained from human samples and utilizing animal models as a tool to disclose the precise mechanism of diseases. In this seminar, it will be reviewed how animal models have contributed to clarifying the pathogenesis of rheumatic diseases and how to utilize them for drug discovery.

EL7

Ideal timing of orthopaedic surgery for recent RA patients

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Conflict of interest: Yes

【Purpose】The recommendations for surgical treatment of rheumatoid arthritis (RA) were published from the Japan College of Rheumatology in, but clear recommendations regarding the timings of the surgery based on the surgical site were not available. In general, the decision of the sur-

gery for RA tends to late, which may result in further joint destruction, disturbance of activities of daily living, and the quality of life. In this session, the best timing and changes of indications of RA surgery will be discussed based on recent patients' back ground and the changes of joint destruction.【Methods】Between 2000 and 2015, all RA surgery in our hospital were carefully reviewed. For lower leg, total hip arthroplasty (THA), total knee arthroplasty (TKA), and toe surgery were analyzed. For upper limbs, surgery for shoulder, elbow, wrist, and finger joint were analyzed regarding recent trend of surgery.【Results】The number of RA surgery were increased with years. The proportion of upper limb surgery showed increase, on the other hand, surgery for lower limbs showed continual decrease. In lower limbs, THA and TKA showed continual decrease, but toe surgery showed increase with time. In upper-limb surgery, most of the patients showed low disease activity or remission. In THA and TKA, many patients showed slow progressive joint space narrowing more than two years. In toe surgery, joint preserve surgery was increased compared to artificial toe implant or resection arthroplasty. The rates of the patients who underwent RA surgery with use of biologics were 30% in recent years. This trend may continue for a while, and surgical cases with low disease activity or remission thought to be increase. Also, it is important to perform surgery during patient's ADL is maintained in lower limb.

EL8

Update of the treatment of osteoporosis

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Conflict of interest: Yes

Osteoporosis includes primary and secondary osteoporosis, and causes of secondary osteoporosis include rheumatoid arthritis and glucocorticoid, etc. In Japan, guidelines for prevention and treatment of osteoporosis were revised in 2015 and 2014 revised guidelines on the management and treatment of glucocorticoid-induced osteoporosis of the Japanese Society for Bone and Mineral Research was published in 2015. In 2016, the report of a task force of American Society for Bone and Mineral Research (ASBMR) about managing osteoporosis in patients on long-term bisphosphonate treatment was published and revised position paper of anti-resorptive agent-related osteonecrosis of the jaw was published by the Japanese Allied Committee of the jaw. In November of 2016, a progress report about goal-directed treatment of osteoporosis was published from the ASBMR-National Osteoporosis Foundation working group and once yearly intravenous zoledronic acid was newly released in Japan. The treatment objective of osteoporosis is prevention of osteoporotic fractures, and the important fractures that should be prevented include hip fractures in the older patients and vertebral fractures in the younger patients. About primary osteoporosis, the evidence of the hip fracture preventive effect is found in alendronate, risedronate, zoledronic acid, denosumab and the evidence of the vertebral fracture preventive effect is found in bisphosphonates, SERMs, eldecalcitol, teriparatides, denosumab. Also, about male osteoporosis, alendronate, risedronate, zoledronic acid, recominant teriparatide have preventive effect of vertebral fracture. In addition of these drugs, ibandronate, alfacalcidol, calcitriol have preventive effect of vertebral fracture in glucocorticoid-induced osteoporosis. It is necessary to consider the dosage forms of the drugs on the occasion of drug choice.

EL9

Precepts from reoperation of upper extremity surgery for rheumatoid arthritis

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Conflict of interest: None

In rheumatoid arthritis (RA), wrist and fingers are commonly affected, and disfunctions of wrist, shoulder and elbow joints frequently contribute the increase of HAQ score. Fifteen years of experience of biologic DMARDs still found increasing number of the surgeries for upper extremity in RA patients. Disappointingly, there is a range of frequencies in the occurrence of post-operative complications. Infection, loosening of the implant, joint contracture, adhesion around the tendon, periprosthethic fractures are representative complications which require reoperations. Residual pain after total joint arthroplasty is less common, but may require revision surgery. Specifically, intraoperative humeral shaft fracture can be occurred during the total shoulder arthroplasty due to adduction contracture of the gleno-humeral joint and osteoporosis of humerus. Careful surgical procedure is also required for total elbow arthroplasty to avoid intraoperative fracture. Attention should be paid for the rotational alignment of the prosthesis, otherwise mal-rotaion may cause polyethylene wear, resulting implant loosening or dislocation of the elbow joint. Height of implant relative to the original joint line may affect the postoperative range of motion, and may cause the dislocation or flexion contracture. After the partial or total arthrodesis of the wrist joint, reoperation may be needed for recurrence of deformity or pain due to poor fixation. Early tenolys or tendon transfer is indicated for the adhesion or tendon rupture, respectively, after the reconstruction surgery for extensor tendon rupture. After the implant arthroplasty of the fingers, the rate of breakage of silicon implant is relatively high, and dislocation of the components might be seen in unlinked finger joint implant. Surgeons should always verify whether these complications were inevitable or not, and endeavor to improve our surgical skills, and not to repeat thoughtless procedures, in order to minimize the rate of reoperation.

EL10

Recent Advances of Relapsing Polychondritis (RP) Research

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Conflict of interest: None

Relapsing polychondritis (RP) is a rare intractable inflammatory disease with unknown causes. Antitype 2 collagen antibody is suspected to associate with a possible cause of RP. Epidemiological information is insufficient, especially in Japan. Although several diagnostic criteria are known, none of them have sufficient sensitivity of RP. Guidelines for the treatment have not been established. We conducted epidemiological survey on RP in Japan and reported clinical characteristics of the patients. Our survey suggests use of immunosuppressive drugs in respiratory involvement, one of the most severe forms of RP. We conducted an international multicenter study on RP with Dr. Arnaud of France and proposed disease activity index of RP, RPDAI, as an indicator for evaluating disease activity. We are currently preparing RP severity classification (draft) by comparing the result of RPDAI with the result of our epidemiological investigation. We constructed a patient registration website in collaboration with Relapsing Polychondritis Patient Association, in 2012/2013. We have been promoting the construction of a clinical information database using this system, as a part of initiating efforts to establish treatment guidelines for RP. Although the research responsible official underwent changes, we continues to collect patient information until now. We found an increase in monocyte/myeloid cell-derived factor TREM1 as a disease activity marker of RP by comprehensive analysis using sera of patient specimen bank. Making diagnosis of RP is not necessarily easy for practical clinicians. It is an absolute necessity to establish the items suggesting the possibility of RP using clinical examinations such as blood sampling. Collectively, since patients with organ involvement are sometimes fatal, the establishment of a better diagnostic criterion and therapeutic guidelines are awaited.

EL11

Spinal lesions associated with rheumatoid arthritis: current treatment strategy and challenges ahead

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Conflict of interest: None

Spinal lesions associated with rheumatoid arthritis (RA) commonly affect the cervical spine with reported incidences ranging from 40% to

80%. The progressive destruction of the spine may cause intractable pain, a loss of natural motion, and instability of the spine. Further destruction may result in a compromise of the spinal cord and subsequent paralysis. Recent advances in medical treatment have greatly improved the care of patients with RA. Modern biologics not only suppress the progression of joint destruction, but also can reduce the occurrence of spinal lesions. Nevertheless, surgical treatment remains the treatment of choice for those presenting with advanced destruction of the spine. For the last few decades, the surgical treatment of spinal lesions in RA patients has become increasingly safer due to such factors as: 1) the wide use of computer navigation-assisted surgery, 2) advances in spinal instrumentation, and 3) an increased awareness of potential complications. Despite the marked improvement in both treatment and patient care, there remain numerous problems to be solved. One of these issues is the delay in starting appropriate treatment. Therefore, close collaboration between physicians and spinal surgeons is crucial to ensure the treatment is provided in a timely manner.

EL12

Chest CT imaging for rheumatologists

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Conflict of interest: None

In this review, I present knowledge required for interpretation of report by radiologists and pulmonologists. Then, I present CT image in two critical conditions requiring immediate therapy; one is when RA patients reveal acute diffuse pulmonary infiltrates and the other is when myositis patients developed acute/ subacute interstitial lung disease (ILD). **Fundamentals of Chest CT imaging** *CT is a sensitive tool to detect pulmonary lesions. To analyze detail characteristics of the lesions, high resolution C imaging is required. CT scan detects pulmonary structure/lesions larger than 0.5mm. * Understanding concept and anatomical structure of pulmonary lobule is essential to interpret HRCT imaging. Understanding chest CT findings is also important which include ground glass opacities (GGO), consolidation, reticular pattern, and bronchial lesions. * ILD are classified into 4 category, 1) usual interstitial pneumonia (UIP), which is characterized by honey combing lesion; 2) non-specific interstitial pneumonia (NSIP), which is indicated by GGO/consolidation without honeycombing.; 3) diffuse alveolar damage (DAD), which presents diffuse GGO/ consolidation without interlobular septa thickening and 4) organizing pneumonia. Moreover, traction-ectasia of bronchus indicates existence of fibrosis. * Interstitial pneumonia, particular UIP, developed acute exacerbation of ILD (DAD in pathologically). In RA, UIP is domiinant ILD and patients frequently developed acute exacerbation of ILD. **When RA patients developed acute diffuse pulmonary infiltrates;** Acute diffuse pulmonary infiltrates are caused by RA itself including acute exacerbation of ILD, infection such as pneumocystis pneumonia and drug-induced lung disease such as MTX-ILD. Notably, infection or drug can induce acute exacerbation of ILD. It is impossible to distinguish these 3 causes by CT imaging. **ILD in myositis patients;** Acute/subacute ILD are frequently developed in patients with anti- ARS Abs or anti-MDA5 Ab that is rapidly progressive, and resistant to usual therapy. CT in ILD with anti-ARS Abs is essentially NSIP pattern. In contrast, ILD with anti-MDA5 Ab is characterized by randomly scattered GGO/ consolidation.

EL13

Practical use of musculoskeletal ultrasound in the management of rheumatic diseases

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Conflict of interest: None

Most of the rheumatologists today already understand the usefulness of musculoskeletal ultrasound (MSUS) in patients with rheumatoid arthritis (RA) both in clinical practice and research. With MSUS, we can evaluate the presence of subclinical synovitis and subradiographic bone erosion. It is true that RA cannot be diagnosed solely with MSUS without other clinical information, but there is no doubt that the information shown by MSUS helps us to make the early diagnosis of RA, monitor disease activity and evaluate the state of clinical remission. In this lecture, I would like to discuss how to best integrate MSUS into daily clinical practice with the aim to improve the diagnostic algorithms, the daily patient care and the disease's outcome.

EL14

Infection prevention and control measures useful for orthopedists

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Conflict of interest: Yes

Recent advances in the treatment of rheumatoid arthritis (RA) including biological agents such as tumor necrosis factor inhibitors brought about significant improvement in the patients' functional prognosis and QOL. RA patients are likely to be complicated by infectious diseases because of immune dysfunctions of RA itself, comorbid conditions, adverse reactions of the therapeutic drugs. Use of corticosteroids or methotrexate, potent immunosuppressants, are known to be risk factors for infections. Moreover, biological agents are reported to increase in the risk of infections, such as pneumonia, tuberculosis, nontuberculous mycobacteriosis, and *Pneumocystis jirovecii* pneumonia, so that we need to prevent, diagnose and treat properly such respiratory complications during follow-up of RA patients especially in the cases of biological agents users. The spread of drug-resistant bacteria is a growing threat in the clinical settings. Especially, multidrug resistant (MDR) bacteria including carbapenem-resistant Enterobacteriaceae cause several difficult-to-treat healthcare associated infections. Problem is not only for the patients of medical infectious diseases, but also perioperative infections, which deteriorate the patients' prognosis. The National Action Plan on Antimicrobial Resistance was established last April in Japan, and several prevention measures are now promoting in many ways. Appropriate infection control measures to prevent transmission of MDR bacteria and judicious use of antimicrobials to suppress the selection and emergence of MDR bacteria are required. In this lecture, I'd like to talk about the management of infectious complications of RA patients, and control measures against MDR bacteria, which are useful for orthopedists.

EL15

Clinical characteristics and the management of elderly rheumatoid arthritis

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Conflict of interest: Yes

Rheumatoid arthritis (RA) is a chronic and systemic inflammatory disease characterized by erosive synovitis and subsequent joint destruction. Although the peak onset of RA is between the ages of 30 and 50 in females, the number of elderly RA patients of long disease duration has been increasing in association with growing of the aging population. Furthermore, elderly-onset RA patients are also thought to be increasing. Elderly patients usually have more complications, impaired drug metabolism, and declined immunological function, which is called immnosenescene, causing increased risk of infection and malignancy. In addition, cognitive impairment in elderly patients can cause the adherence of medication or excessive administration of disease modifying antirheumatic drugs (DMARDs). Because of the actual complications and the apprehension of possible adverse effects, especially life-threatening severe infections, in elderly patients, less aggressive therapy is likely to be selected even if the disease activity is beyond moderate. The continuation of the disease activity may result in impaired physical functions, unstable mental conditions, poor nutrition, and deterioration of social activity, leading to increased mortality. In particular, methotrexate, a standard drug in RA, is less frequently used in the elderly RA, while glucocorticoid is prescribed more commonly. Since glucocorticoid has been reported as a potent risk factor of severe infections in RA, the long-term glucocorticoid use should be avoided as possible. Treatment of elderly RA

should be determined individually based on the disease severity and the existence of renal dysfunction, lung disease and other complications, with sharing the determination with the patient, according to the Japan College of Rheumatology guideline. Patient education and collaboration among multiple specialties are essential to prevent and manage the side effects. On the other hand, decreasing the dose and the interval or withdraw of DMARDs should be considered once therapeutic goal is achieved. In this lecture, I would like to talk characteristics of elderly RA and the management in daily practice.

EL16

Recent updates on hemostasis and thrombosis: essentials for rheumatologists

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Conflict of interest: Yes

Since episodes of bleeding and thromboembolism frequently occur in patients with connective tissue diseases, it is necessary for rheumatologists to update knowledge on hemostasis and thrombosis to make appropriate diagnosis, pathologic process assessment, treatment, and prevention. Thrombocytopenia is a common laboratory abnormality in patients with connective tissue diseases, especially in those with systemic lupus erythematosus. This condition is induced by a variety of mechanisms, including immune thrombocytopenia (ITP) and amegakaryocytic thrombocytopenia, which are mediated by autoantibodies. Other mechanisms include thrombotic microangiopathy (TMA), disseminated intravascular coagulation, macrophage-activation hemophagocytic syndrome, drug-mediated and infection-related conditions. The prompt differential diagnosis of these conditions is required in clinical setting. Immunosuppressants have been used mainly for ITP inadequately responsive to corticosteroids, but many other treatment options are available, including splenectomy, hydroxylchloroquine, rituximab, and thrombopoietin receptor agonists, which have a potential to induce immune tolerance but increase a thromboembolic risk. On the other hand, classification of TMA has been updated and is now categorized into three major groups based on the pathogenic process: thrombotic thrombocytopenic purpura (TTP) due to ADAMTS 13 deficiency, and hemolytic uremic syndrome (HUS) due to infection with Shia toxin-producing *E. coli*, and atypical HUS, which is now identified as the condition induced by dysregulation of the complement pathway. Recent accumulating data show efficacy of rituximab for acquired TTP and anti-C5 antibody eculizumab for atypical HUS. Finally, introduction of a series of direct oral anticoagulants targeting prothrombin or factor Xa into clinics results in large selection of the anti-coagulation therapy, but proper use still remains undetermined.

EL17

Ophthalmic disorders associated with rheumatoid disease: useful information for rheumatologists

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Conflict of interest: None

Intraocular inflammatory diseases including uveitis and retinitis are relatively rarely encountered in daily clinical practice of ophthalmology clinics. In general, it is difficult to clarify the cause of these inflammatory disorders, unlikely inflammations that affect the ocular surface such as conjunctivitis. Corticosteroids are the mainstay for the treatment of these diseases, although systemic and local corticosteroid therapies may develop various adverse events. We ophthalmologists need cooperation from rheumatologists to manage these ocular inflammatory disorders when they are associated with rheumatoid disease. In this session, basic knowledge regarding ocular anatomy and function, various ocular disorders associated with rheumatoid disease, symptoms and signs caused by ocular inflammation, and local treatment for the eye are introduced. In addition, current topics in diagnosis and management of representative diseases such as Behcet disease, sarcoidosis, Vogt-Koyanagi Harada disease, non-infectious scleritis, and IgG4-related ophthalmic disease will be discussed.

EL18

How to look at Renal Involvement in rheumatic diseases for rheumatologists

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Conflict of interest: None

A variety of renal diseases are seen in rheumatic diseases. These are mainly classified into two groups, a complication of specific rheumatic diseases and a nephrotoxicity caused by the drugs used for the rheumatic diseases. The former include lupus nephritis, ANCA-associated glomerulonephritis, IgA vasculitis (purpura nephritis), anti-GBM disease, IgG4-related renal disease, and other infrequent complications such as scleroderma renal crisis, renal tubular acidosis (Sjogren syndrome), and also thrombotic microangiopathy for some of the rheumatic diseases. The complicated renal diseases may appear in glomeruli, tubulointerstitum and/or vascular systems and by the autoimmune, allergic or vascular mechanisms. Also, some drugs may cause nephrotoxicity; non-steroidal anti-inflammatory drugs (NSAIDs) that are most frequent nephrotoxic drugs with many presentations. It is of note that nephrotic syndrome (membranous nephropathy) are sometimes seen by some DMARDs, in particularly bucillamine. In this educational lecture, I will summarize some of the renal complications that may be important for rheumatologist while seeing the patients.

EL19

Spondyloarthritis

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Conflict of interest: Yes

Spondyloarthritis refers to a group of related diseases that have particular clinical manifestations and genetic association with HLA-B27. These shared clinical features are consisted with axial involvement, peripheral arthritis, enthesitis and dacyltis as articular findings and psoriasis, inflammatory bowel diseases and uveitis as extra-articular manifestations. Clinically, spondyloarthritis is consisted of ankylosing spondylitis, psoriatic arthritis, arthritis related to inflammatory bowel disease, reactive arthritis and a part of juvenile idiopathic arthritis. In the recent ten to fifteen years, the understanding of the pathophysiology of inflammation using MRI and ultrasonography and the basic pathogenesis facilitates the early diagnosis, the development of outcome measures and guidelines/recommendations. The advance has an effect on terminology and now some experts prefer (radiographic) axial spondyloarthritis to ankylosing spondylitis. The classification criteria developed by the Assessment of Spondyloarthritis International Society (ASAS) may be a useful tool for the research or clinical trials of early axial spondyloarthritis, however, some modification may be necessary. The introduction of biologics is also one of the major topics in this field. Interestingly, unlike rheumatoid arthritis, conventional synthetic DMARDs and biologics inhibiting IL-6 and T-cell costimulation are not effective. It has been shown that TNF inhibitors suppress the inflammation and may have a role to inhibit structural damages. Recently, interleukin-17/23 pathway has been focused as new treatment targets in axial involvement of spondyloarthritis. The understanding of spondyloarthritis is important component in the rheumatological clinical practice. In the review, the concept of spondyloarthritis and problems in the clinical practice will be discussed.

EL20

Rehabilitation of rheumatoid arthritis –to live a well-filled life–

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Conflict of interest: None

Rheumatoid arthritis (RA) was defined as a chronic and progressive disease in the past. Rehabilitation of RA was different for each stage; the stage of RA was divided into early stage, advanced stage and late stage, and rehabilitation suitable for each stage was intervened. Biological

agents and other drugs have currently been improving control of disease activity and joint damage in early RA patients. However, Joint swelling may remain and joint destruction may progress, even if drug therapy is successful. Therefore, rehabilitation of early stage should be performed concurrently with the start of drug therapy. Furthermore, progressive RA in the middle stage is required to cope with overuse syndrome due to excessive exercise and use, and therefore, joint protection law and daily management are important. It is necessary to support the measure for returning to workplace and social status, and the home care through team medical care and health /medical cooperation in the late stage. Previously, there was no evidence that leads to the effectiveness of rehabilitation interventions in RA. In the era of biological agents, it has been reported as definite evidence that significant improvements were obtained in hand function, activities of daily living and work capacity as a result of large-scale randomized controlled trial of finger movement therapy (SARAH: Lancet 385, 2015). Further evidence for the effectiveness of general rehabilitation interventions is also anticipated other than therapeutic exercise in the future.

EL21

Clinical rearch designs and data analysis

Satoshi Morita
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Conflict of interest: None

This lecture will talk about how to design clinical researches and how to analyze data from them.

EL22

From stagnation to turbulence: we should know the history of rheumatoid arthritis to understand the pathological situation of this disease

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Conflict of interest: Yes

Rheumatoid arthritis (RA) is an immune-mediated process involving the joints and is associated with marked functional disability. In recent years, disease-modifying antirheumatic drugs (DMARDs) have been used to inhibit or halt the underlying immune process and prevent long-term damage. However, the cause of RA remains poorly understood and may involve a combination of genetic, environmental and stochastic factors. Therefore, it is important to know the history of this disease. In around 1500 BC, the Ebers Papyrus already described a condition that is similar to RA. There is evidence of RA in the Egyptian mummies as found in several studies. It is known world widely that Hippocrates described arthritis in general in 400 BC. Actually, the first series of patients with RA appeared in 1800s. The term "rheumatoid arthritis" was introduced by Garrod in 1859. However, it can be argued that RA was at least uncommon before the 19th century. Therefore, at first investigators wondered about a "slow virus" infection as a cause of RA. Others thought about other microbes or lifestyle changes or consequences of the industrial revolution. Among them, lately some people hypothesized that importation of sugar from the West Indies to Europe and a resultant epidemic of periodontal disease was linked to the appearance of RA. The connection, Porphyromonas gingivalis, occuring in peridontitis, produces peptidyl arginine deiminase, which citrullinates proteins leading to inflammation and consequent RA. There is a possibility to be a link between sugar, periodontal disease, and RA. In this lecture, I aim to analyze these things with respect to the types and conclusions of the research that has been conducted.

EL23

Nursing Practices to Support Patients with Chronic Illness

Kazuko Nin
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Conflict of interest: None

What do we think of when we hear the phrase "chronic illness"? Disease that cannot be cured, restriction imposed on life, no change, uncertain future, and so on, are some of the examples. What is central to the care under chronic condition is not recovery but to live with the disease. Supporting patients so that they can cope with symptoms and live a normal life yet enduring the sufferings is the role of nursing. It is the goal of nursing to decrease the social and psychological burden caused by chronicity of the illness and to minimize difficulties in life. Here I called "Chronic illness." There are similar terms such as "Chronic disease," "Chronic conditions," and "Long term conditions.""Disease" and "illness" have similar meanings; we can use them differently. For example, there are many patients who wonder, "Why did I come to suffer from rheumatoid arthritis?" If we consider it a disease, we will explain it like: "The cause is genetic factors, smoking, stress, and so on." On the other hand, if we consider it as illness, we will focus on such issues as why the patient is questioning that, how the patient is considering his/her illness and pain, and so on. I would like to use this presentation as an opportunity to think once more about nursing done to support living with chronic illness as well as provide knowledge that I obtained at the Rheumatology Center of the Kyoto University Hospital.

EL24

JCR guideline for the methotrexate treatment of rheumatoid arthritis

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Conflict of interest: Yes

In Japan, an increased dose (>8mg weekly) of methotrexate (MTX) for the treatment of rheumatoid arthritis (RA) patients was approved in 2011. Then, Japanese rheumatologists used enough amounts of MTX even for disease-modifying anti-rheumatic drug (DMARD)-naïve patients. MTX is the anchor drug for RA, whereas some biological DMARD, which have different modes of action, can be used. More than 70% of RA patients received MTX, which is sometimes effective as a monotherapy for early RA and as a combination for patients using other conventional synthetic, targeted synthetic, and biological DMARD. The Japan College of Rheumatology published "Guideline for the MTX treatment of RA" in 2011. Recently, 2016 version was proposed because some clinical evidences in MTX treatment have appeared for 5 years. In 2016 version, some statements were changed as follows: 1) Result of CORRA study, in which a rapid dose escalation of MTX was indicated in MTX-naïve and very early RA patients, was referred, 2) risks of mycobacterium tuberculosis in patients receiving MTX was added, 3) combination treatments of MTX with iguratimod or tofacitinib, which was not approved in 2011, were included, 4) imaging data of typical cases with MTX-associated adverse reactions were shown, and 5) chapter of lymphoproliferative disorders associated with MTX was revised. Actually, the revised guideline can support clinical practice but not interfere a decision make of the experienced doctors. In the present lecture, the revised points will be discussed including the updated ACR/EULAR guidelines.

EL25

Differential diagnosis of unknown fever for rheumatologist

Hiroaki Ida
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Conflict of interest: None

Unknown fever was defined by 1) a temperature greater than 38.3°C (101°F), 2) more than 3 weeks' duration of fever, 3) failure to reach a diagnosis despite 3 days of inpatient or outpatient investigation. Autoinflammatory syndrome is a syndrome that causes systemic inflammation. Main symptom is fever, accompanied by inflammation of the site, such as joint, skin, intestine, eye, and bone. As symptom is similar to that of in-

fectious diseases and collagen diseases; however, pathogenic microorganisms cannot be identified, and autoantibodies or antigen specific T cells is also not detected. Recently, it is known that there are many patients with autoinflammatory syndrome in Japan, and has been fairly recognized to clinicians. In these reasons, autoinflammatory syndrome might be "Forth unknown fever" following to three major unknown fever (infection, malignancy, and collagen disease). We must diagnose the patient with unknown fever in order from 1) to 5) as following; 1) Infection; Representative diseases are abscess, tuberculosis, and infectious endocarditis. 2) Malignancy; malignant lymphoma, leukemia, and intravascular lymphomatosis, etc. 3) Collagen disease; systemic lupus erythematosus and angitis, etc. 4) Other disease; sarcoidosis, drug fever, Castleman's disease, and Kikuchi disease, etc. 5) Autoinflammatory disease (extensive definition); Behcet disease, adult onset Still disease, Crohn disease, and gout, etc. 6) Autoinflammatory disease (narrow definition); familial Mediterranean fever (FMF), TNF receptor-associated periodic fever (TRAPS), and cryopyrin-associated periodic syndrome (CAPS), etc. It is desirable that it is used the Japanese genetic diagnosis guidelines and flowchart ("autoinflammatory disease site" http://aid.kazusa.or.jp/2013/) as a reference. In this meeting, I focus the diagnostic points for unknown fever.

EL26

Genetic analysis of rheumatic diseases

Koichiro Ohmura
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Conflict of interest: Yes

Genetic analysis of rheumatic diseases has revolutionarily developed in this decade. Human genome sequence was revealed in 2001, and the discovery of many single nucleotide polymorphisms (SNPs) and the progress of typing technology enabled us to perform genome-wide association study (GWAS). Many susceptibility genes or loci were found to be associated with rheumatic diseases and some were within our thought, but many were unexpectedly found. So far, more than 100 susceptibility genes/loci were reported in rheumatoid arthritis (RA) and more than 60 in systemic lupus erythematosus (SLE) and around 20 in systemic sclerosis (SSc). Some of them are shared in several rheumatic diseases, and some are uniquely seen in particular rheumatic disease. For example, BLK, TNFAIP3, IRF5 in addition to HLA are shared in RA, SLE and SSc and those common genes are related to both innate and adaptive immune systems. Particular example of disease-specific genes/loci in RA is PADI4, which is related to citrullination, and CDK2 and CDK6, which are related to cell cycle, and B3GNT2, which is related to glycosylation, are interestingly unique to RA. In SLE, RAD51B, which is related to DNA repair, is specifically associated, and many of the interferon pathway genes including IFIH1, IRF5, IRF7 and IRF8 are listed as SLE susceptibility genes, which will be the characteristic of this disease. The number of SSc susceptibility genes is limited probably due to the absence of large GWAS studies, but many of the genes are shared by RA and SLE. So far, genes/loci related to fibrosis or vasculopathy, which are the characteristics of SSc, have not yet identified. Looking at these common and unique genes will tell us the pathogenesis of each disease. In this educational seminar, I will overview the recent advances of the genetic analysis and will introduce the pathogenic mechanism of each rheumatic disease from the view of susceptibility genes.

Meet The Expert

MTE1

Effect of biologics on occurrence of infectious diseases

Kazuhiro Tateda
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Conflict of interest: None

History of discovery and development of antibiotics has stated from early 20 century. So far more than 150 antibiotics, such as b-lactam, macrolide, quinolone and aminoglycoside, became available and they were broadly used not only hospitals, but also a variety of field like livestock and agriculture. On the other hand, we are facing to a serious problem. That is appearance and spreading of antibiotics resistant bacteria. Especially, several immunomodulatory compounds are well known to sensitize hosts to opportunistic pathogens, including antibiotic resistant bacteria. Recent progress in introduction of several biologics to a variety of diseases, such as rheumatism and inflammatory bowel diseases, brought significant improvement in patient's care and treatment, even cure has been achieved in some patients. But unfortunately, we are facing to another issue, which is increase of risk of infectious diseases in patients treated with biologics. Accumulating reports demonstrated vulnerability of these patients to several microbial infections. The important and representative organisms may include *Mycobacterium tuberculosis*, non-TB mycobacterium, Legionella and *Pneumocystis jirovecii*. In this talk, risk of infectious diseases in biologics' era will be reviewed. Also the mechanisms of pathogenesis of these infectious diseases will be summarized.

MTE2

Treatment of difficult SLE

Seiji Minota
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Conflict of interest: None

SLE is so heterogeneous in the expression of symptoms and organ damage that it might be viewed as a syndrome instead of a disease. Underlying pathophysiology is immune complexes formation composed of mainly nuclear antigens and the corresponding autoantibodies. Immune complexes are delivered via blood stream to virtually all organs in the body and this accounts for the heterogeneity of organ involvement. What is difficult SLE? There is no definition on it. In each organ involvement, the pathology spans from very slight to very severe, and severe involvement is always difficult for treatment. As a speaker of MTE in the JCR meeting, I select, arbitrarily, 1) lupus nephritis, 2) neuropsychiatric SLE (NPSLE), and 3) anti-phospholipid antibody syndrome (APS) as difficult SLE. 1) Kidneys are small and they weigh ~0.3 kg, albeit, they receive ~25% of cardiac output. Therefore, they receive ~50 times more blood supply per weight compared to the other organs in the body; plenty of blood. Organs receiving more blood supply are more susceptible to inflammation caused by immune complexes delivered by blood stream. To mitigate lupus nephritis, immune complexes must be reduced in amount. To do so, immunosuppressant is usually employed along with glucocorticoid as a base drug. Cyclophosphamide has been the mainstay of immunosuppressant. Mycophenolate mofetil was recently approved for the treatment of lupus nephritis in Japan, which gave us a stronger armamentarium and the method to prevent adverse effects incurred by cyclophosphamide. 2) NPSLE is very difficult in making diagnosis in the first place, because it spans real organic brain damage caused by SLE to mood change caused by drugs. Infection may be the cause of neuropsychiatric symptoms. Treatment needs help from psychiatrists. Lastly comes 3) APS, which is well-known for biological false positive in serological test for syphilis. Catastrophic APS is the severest form and often fatal.

MTE3

Diagnosis and treatment strategy in juvenile idiopathic arthritis (JIA) in the biologic era. How does it differ from rheumatoid arthritis (RA)

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Kagoshima, Japan

Conflict of interest: None

JIA is a chronic disease characterized by joint inflammation of unknown cause which occurs before 16 years of age. It affects about 1 individuals in every 10,000 Japanese children; the incident is about 1/40 of RA. Therefore, JIA is not a rare disease and adult rheumatologists may encounter a child with JIA at the first referral. The diagnosis of JIA is difficult because there are no specific laboratory tests including RF and ACPA. Inflammatory markers such as CRP sometimes remains normal range in children. In addition, some patient do not complain any symptoms, therefore, even their mothers do not realize their joint pain. Therefore, diagnosis should be made based on careful physical examination with excluding other arthritic diseases in children. On the other hand, several progressions were made in the treatment of strategy and evaluation of the disease activity. Treatment strategy has been established separately for both systemic JIA and arthritic JIA by Pediatric Rheumatology Association in USA, EU, and Japan. Biologic DMARDs (bDMARDs) were induced in JIA patients resistant to the conventional therapy including MTX. As the result, there are less children with joint destruction and more children who attained off medication remission. At present, tocilizumab, etanercept, and adalimumab is approved for use, and the clinical study for abatacept and canakinumab is now undergoing. In addition, disease remission was defined with 6 parameters, and disease activity was evaluated by Juvenile Arthritis Disease Activity Score (JDAS). These objective tools provide useful information for evaluating the efficacy of the treatment which JIA children receive. Prognosis of JIA has dramatically improved by newly developed biologic agents. Rheumatologists in the biologic era should aware that major cause of poor prognosis is not due to disease severity but due to the delay or inappropriate treatment in JIA.

MTE4

The key point of rehabilitation for Rheumatoid Arthritis

Naohisa Kikuchi
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Conflict of interest: None

Recently, treatment for Rheumatoid Arthritis has remarkably advanced. Thus the patients who has some trouble with daily life due to joint deformity and contracture seem to be decreasing. However, many patients who has associated with a Rheumatoid Arthritis for a long time and patients who needs management to joint inflammation still exist. I have worked for medical rehabilitation of rheumatoid patients with rheumatoid specialists at the university hospital. In this lecture, I focus 4 point of view, such as the guidance of a joint protection, the splinting for finger and wrist deformity, devices for ADL and housework, and the orthosis for foot and toe deformity. It's necessary to be guiding in a joint protection by the level of the joint inflammation and the loading amount by the daily movement. We use proper splints for joint protection, and we also use devices in daily living movement. We usually request occupational therapists to make splints for deformity of fingers and wrists. We mainly use the wrist supporters with soft material for wrist deformity. We sometimes use soft material or rigid orthosis for ulnar deviation. We use 3-point supporting orthosis for swan-neck and button-hole deformity. And as a handy splint, we use taping method by a self-sedentary elastic bandage. I introduce some typical devices. There are a base mounted nail clipper, a plastic bottle opener, a medicine covering opener (Kusuripon), a shaft brush used for a haircut, Reacher used for change clothes, Button-aid, Socks-aid, a thicken shaft of spoon or fork, and a tweezer type chopstick. We request prosthetists and orthotists for foot and toe deformity to make custom-making slippers, sandals and shoes. Patients can use public financial supporting by medical insurance and Support for Persons with Disability for making these orthosis. We use medial arch support and sole device for pes planovalgus. We use metatarsal pad, front foot decompression, and widen shoes for toe deformity.

MTE5

Management of patients with refractory RA

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

MTE6

Examination method and treatment of rheumatoid foot

Koichiro Yano
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Conflict of interest: None

Although the introduction of powerful antirheumatic drugs has dramatically improved the treatment of rheumatoid arthritis (RA), many patients still experience progressive joint destruction. Painful forefoot deformities are prevalent in 80-90% of patients with RA, many of whom undergo surgery to treat them. Surgeries for the rheumatoid foot, including joint-preserving surgery, have been widely performed in Japan. However, in many cases, conservative therapy might have been effective if the physicians had previously noticed the foot deformities. One of the reasons for the failure to diagnose foot deformities is that scales evaluating 28 joints to determine the disease activity, such as the DAS28, do not include the foot and ankle. As a result, the disorders of the foot and ankle have been neglected. Indeed, I experienced a case in which foot surgery was finally performed, even though the patient's DAS28 indicated the maintenance of clinical remission over a long period. On the other hand, there are some patients who experience treatment delays due to the physicians' lack of knowledge of the various treatments for the rheumatoid foot, even though the physicians are aware of the progression of the foot deformities. To reduce such unfortunate cases, this presentation includes the following topics:(1) The critical points of clinical examination of the rheumatoid foot, (2) Conservative treatment that anybody is able to perform, (3) The timing of the consultation from the internist to the orthopedic surgeon, and (4) The latest developments in foot surgery for the rheumatoid foot.

MTE7

Early diagnosis and intervention in systemic sclerosis

Masataka Kuwana
Department of Allergy and Rheumatology, Nippon Medical School

Conflict of interest: Yes

Currently, there is no practical guideline for patients with systemic sclerosis (SSc) because of paucity of treatment evidence. Due to highly variable clinical presentation among patients, it is necessary to proceed with personalized medicine based on expert opinions. To manage SSc patients in routine clinical practice, it is essential to know natural history of the disease. Since acute exacerbation is very rare during the course of SSc except renal crisis, future organ involvement and prognosis can be predictable in most cases based on detailed clinical evaluations at diagnosis. In addition, early detection and treatment is crucial for SSc patients since functional impairment is hardly reversible once normal tissue architecture has been replaced by fibrotic scarring tissue. In this regard, patients with Raynaud's phenomenon with nailfold capillary changes and/or SSc-related anti-nuclear antibodies should be regarded as pre-SSc even in the absence of apparent skin thickness. This session is aimed to understand how to predict future outcomes in SSc patients by presenting typical case scenarios.

MTE8

Therapeutic strategy for multiple joint disorders in patients with rheumatoid arthritis

Asami Abe
Department of Rheumatology, Niigata Rheumatic Center, Niigata, Japan

Conflict of interest: None

Recently, the classification criteria of rheumatoid arthritis (RA) has enabled us to diagnose RA in the early stage. The composite measures for the disease activity and newly developed medications (bDMARD, tsDMARD etc.) has now made it possible to effectively control the disease

activity. As a result, it is no longer a dream that many RA patients can now lead an ordinary life. However, there are still some patients whose joint deterioration has progressed due to a delayed diagnosis and/or an insufficient medication. Other patients in the clinical remission might develop the secondary osteoarthritic changes due to the overuse of painless joints after the acute inflammation. In addition, some patients can not be treated by strong medications because of concurrent infectious diseases and other comorbidities. Additionally, some patients may develop multiple joint disorders. Before selecting the treatment strategy for disabled patients, it is important to assess the patient's disease activity, ADL, QOL and comorbidities, and to obtain sufficient information regarding the patient's background including age, gender, family, job and interests, etc. For diseases in which a radical cure proves to be impossible, total management should thus be adopted. Systemic treatment should be administered according to basic therapy and the 4 factors of medication, rehabilitation, surgery and patient care. Ishiguro et al. recommended establishing a treatment goal by considering the patient's satisfaction using an assessment of mentality and QOL, and then evaluating the therapeutic effect from each individual patient's stand point. It is also important to allow patients to select the treatment from various therapeutic options depending on their various disease conditions and other related factors.

MTE9

Treatment for the intractable ANCA associated vasculitis

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Conflict of interest: None

Anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV) includes microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA) and eosinophilic GPA. These 3 diseases became specified as incurable diseases. Eearlier diagnosis with the ANCA detection and cyclophosphamide (CY) treatment with a combination of glucocorticoids used for the induction of AAV improved the outcome of AAV. However, some patients have not achieved remission and required repeated treatment for relapses. Recently, several biological agents have been used for the treatment of AAV. Rituximab, which is an anti-CD20 monoclonal antibody, has demonstrated efficacy in patients with GPA and MPA. Rituximab and cyclophosphamide are considered to have similar efficacy, but rituximab was found to be superior to cyclophosphamide for patients with relapsing disease. Several studies have indicated that rituximab is also effective and safe for remission maintenance of MPA and GPA. Multicenter clinical trials for AAV, using agents such as anti-complement 5-a receptor antagonist, IL-6 receptor inhibitor for MPA and for GPA and anti-IL5 for EGPA are now ongoing. In this symposium, I will talk about the management of AAV on the basis of our cases of AAV and the revised AAV guideline 2017 published by research committee of intractable vasculitis syndrome of MHLW. At the end of this meeting, participants will understand some treatment strategies for patients with AAV.

MTE10

The update for the pathophysiology and treatment of osteoarthritis of the knee

Muneaki Ishijima[1,2,3], Haruka Kaneko[1], Yasunori Okada[3], Kazuo Kaneko[1,2,3]
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Conflict of interest: Yes

The recent epidemiological studies revealed that the one fourth of the reasons for requiring special assistance or nursing care in elderlies is currently the locomotive disorders. Osteoarthritis of the knee (knee OA), as well as the osteoporotic fragility fractures and the spinal canal stenosis due to spondylosis, is the one of three major locomotive disorders those are related to the requiring special assistance or nursing care in elderlies. The knee OA is an age-related progressive joint disease, which is characterized primarily by cartilage degradation. However, the subchondral bone, meniscus, synovium and ligament, in addition to the cartilage, have been known to be also involved in the pathophysiology of knee OA. OA is an increasingly important public health concern, as the prevalence of the disease is increasing with the aging of society, and is one of the representative age-related chronic motor organ diseases responsible for the locomotive syndrome. The ideal management of knee OA is illustrated as a sequential, pyramidal approach. While it has been estimated that there are 25 million people with radiographic knee OA, it has been speculated that eight million have knee pain. Among the patients with painful knee OA, eighty-five thousand cases of total knee arthroplasty (TKA) are currently being performed each year in Japan. The concept of locomotive syndrome should therefore be promoted to allow for the earlier identification of patients with symptomatic knee OA to prevent the development of locomotive syndrome by providing adequate pain relief. Moreover, the development of pathophysiology of knee OA should be promoted to facilitate the earlier identification of asymptomatic knee OA and the development of novel treatment methods including in new drugs and interventions. In this session, based on the evidence found recently by the clinical researches, I'd like to focus broadly on from the pathophysiology to the treatment of knee OA.

MTE11

Differential Diagnosis of Rheumatoid Arthritis in Daily Practice

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Conflict of interest: None

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

MTE12

Practicing ultrasonography in the assessment of synovial inflammation

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Conflict of interest: Yes

Musculoskeletal ultrasound visualizes low-echoic synovial infiltration (i.e. synovial hypertrophy) and abnormally increased vascularization which accompanies synovial hypertrophy (i.e. synovial Doppler signal) and determines the presence/absence and the severity of synovitis, tenosynovitis, and bursitis. However, sonographic assessment has pitfalls as do other clinical investigations and needs training and experience. The accurate assessment of synovitis is possible only when clear images are acquired, and a certain degree of knowledge and understanding of joint anatomy and ultrasound physics are necessary to acquire clear images. Pitfalls exist in each process of machine/setting, image acquisition, or interpretation and may cause either false-negative/underestimation or false-positive/overestimation. In this session, these factors related to pitfalls and their representative ultrasound images will be presented and how to avoid them will be discussed.

MTE13

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

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Conflict of interest: None

Connective tissue diseases (CTD) including rheumatoid arthritis (RA) are well known as systemic autoimmune disorders, because high tiers of autoantibodies (auto Abs) are frequently observed in sera from CTD patients. Actually, lots of auto Abs, of which clinical significance is clearly identified, are examined in clinical practice. 1) Auto Abs associated with disease diagnosis Anti-CCP Abs in RA, anti-Sm and dsDNA Abs in systemic lupus erythematosus, and anti-topoisomerase I Abs in systemic sclerosis are marker Abs. These Abs are highly specific and included in the international classification criteria. 2) Auto Abs associated with specific manifestations Anti-aminoacyl tRNA synthetase (ARS) Abs including anti-Jo-1 are recognized in polymyositis/dermatomyositis. Patients with anti-ARS Abs, however, often show the similar clinical manifestations (anti-synthetase syndrome), which consist of fever, Raynaud's phenomenon, polyarthritis, and interstitial pneumonia (IP) in addition to myositis. 3) Auto Abs associated with severe clinical disorders Anti-melanoma differentiation-associated gene 5 (MDA5) Abs are closely associated with life-threatening IP especially in clinically amyopathic dermatomyositis. Also, anti-transcription intermediary factor 1-γ(TIF1-γ) are linked to the cancer-associated dermatomyositis, so clinicians should check the malignancy before an immunosuppressive treatment. 4) Auto Abs associated with disease activity Titers of anti-DNA Abs and MPO/PR3-ANCA correlate with disease activity in SLE and ANCA-associated vasculitis, respectively. Such auto Abs may be repeatedly determined during the remission induction treatment. In the present seminar, we can discuss the best way to interpret the autoantibody testing according to the International recommendations for the assessment of autoantibodies to cellular antigens referred to as anti-nuclear antibodies (*ARD,* 2014).

MTE14

Elderly rheumatic diseases

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Conflict of interest: None

With the improvement of life expectancy in the general population and advent of the super-aging society, the number of patients with elderly rheumatoid diseases is anticipated to increase. Although rheumatoid arthritis (RA) is commonly diagnosed between the ages of 30 and 50, the mean age at diagnosis has increased recently. Elderly-onset RA (EORA) is a progressive disease similar to younger-onset RA. To prevent progression to irreversible geriatric syndromes, patients with EORA may undergo intensive treatment using a treat-to-target strategy. Individuals with early EORA have higher disease activity scores, and an explosive onset of shoulder arthritis, resembling polymyalgia rheumatic (PMR) is observed in 13–23% of patients with early EORA. Differentiation between anti-CCP antibody-negative EORA with PMR-like onset and PMR can be difficult and requires careful follow-up. Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) affect elderly people with an increasing incidence in individuals aged 70-80 years. 2015 recommendations for management of PMR serves to lead clinicians to best practices in the treatment of PMR. GCA with temporal arteritis is usually classified according to the American College of Rheumatology 1990 criteria. About one-fifth of patients with GCA develop large-vessel vasculitis. Interestingly, elderly patients with large-vessel involvements have a lower frequency of cranial symptoms and temporal artery abnormality. A novel treatment is expected to bring about changes in the outcome of patients with GCA. We will discuss the diagnosis and treatment strategy of EORA, PMR, and GCA in this seminar.

MTE15

The diagnosis, treatment and clinical care of fibromyalgia patients

Yoshifuji Matsumoto
Kuwana City Medical Center

Conflict of interest: None

Fibromyalgia (FM) is a rheumatic disease to develop most commonly on middle-age women (the prevalence in Japan: about1.7%). FM patients have chronic widespread pain and stiffness of general body with a various kinds of physical, neurological and mental symptoms. Recently, brain imaging studies have been disclosed the activation of microglia cells within some specific area of brain in patients with FM, and it is thought that neuroinflammation would be the pathophysiological mechanisms of FM. Moreover, Japan College of Fibromyalgia Investigation (JCFI) and Japan Agency for Medical Research and Development (AMED) published jointly "Fibromyalgia Practice Guidelines 2017th edition" by using GRADE system. We will discuss about following clinical questions (CQs) with rheumatologists participating in this seminar, for the improvement of QOL of patients with FM. CQ-1: Which diagnostic criteria should be used? CQ-2: What is activity or severity criteria? CQ-3: Which drugs are prescribed? CQ-4: Which regimens are selected for non-drug treatment? CQ-5: How are the clinical course or prognosis (functional or vital)? CQ-6: what patients should be consulted to specialists for FM practice?

MTE16

Perioperative management for patients with rheumatoid arthritis

Isao Matsushita
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Conflict of interest: Yes

A multidisciplinary approach is required to care for patients with rheumatoid arthritis (RA) in the perioperative period. In preparation for surgery, patients must have a respiratory risk assessment performed due to the high risk of lung disease in patients with RA. Rheumatologists have to assess the perioperative patient using chest radiography, spirometry, blood gas analysis and sometimes CT scan. Renal functions often decrease in long-standing RA patients. It is necessary for assessment renal function to use GFR and/or CCr. After total hip/knee arthroplasty, the use of small molecular weight heparin or Factor Xa inhibitors is recommended to prevent thromboembolism. However, anticoagulants are contraindication when the value of CCr of patient is below 30ml/min. RA can involve the cervical spine with important implications for perioperative management, particularly positioning for anesthesia. Rheumatologists must be aware of the risk of cervical instability which may be asymptomatic. If performed, radiology imaging should include at least flexion-extension views of the cervical spine. Methotrexate is widely considered the cornerstone of RA management. Cohort studies did not demonstrate any difference in perioperative infection between those who continued or discontinued methotrexate. JCR guideline for the management of rheumatoid arthritis 2014 demonstrates that discontinuation of MTX is not necessary in the perioperative period. On the other hand, in some reports comparing patients who used traditional DMARDs versus TNF-α inhibitors, there was an increased risk of surgical site infection (SSI) with TNF-α inhibitors. JCR guideline demonstrates that biological DMARDs slightly increase the risk of SSI, and recommends the discontinuation of biological DMARDs in the perioperative period. In this opportunity, I would like to talk about the knack and pitfalls of perioperative managements for patients with RA.

MTE17

How to use Hydroxychloroquine in daily practice

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Conflict of interest: None

The effect of hydroxychloroquine (HCQ) on cutaneous lupus erythe-

matosus (CLE) was recently reported from Japan. Also, many ameliorative effects on aspects of SLE including lupus activity, recurrence rate, organ damage and survival, glucose and lipid profiles, infection, and malignancy have been reported. Although HCQ can cross the placental barrier, teratogenicity and fetal toxicity have not been reported. Maintaining HCQ administration during pregnancy is important for preventing lupus flare. HCQ reduces the risk of congenital heart block in infants born to mothers with anti-SSA antibodies. A nation-wide registry of anti-SSA antibody-associated congenital heart block has been launched to investigate the effect of HCQ. Lupus experts from around the world now recommend using HCQ for all lupus patients. In Japan, in contrast, corticosteroids are still used as first-line therapy for mild SLE. However, life-long treatment with low dose corticosteroids (PSL 5-7.5mg/d) is associated with adverse events such as atherosclerosis, infection, osteoporosis, metabolic abnormalities, and cataracts. On the other hand, lifelong HCQ use is safe provided regular ophthalmologic screening for HCQ toxicity is conducted. Starting HCQ as a steroid-sparing agent and lowering the daily dose of PSL will help extend the life expectancy of CLE and SLE patients to that of healthy individuals.

MTE18

How to assess joints

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Conflict of interest: Yes

The most important and most basic clinical assessment in rheumatology field is joint assessment. While the utility of sensitive modality like ultrasound and magnetic resonance images has been well recognized, touching patients' joints is far important in the management of rheumatoid arthritis and other rheumatic diseases to know the place of the pain and the extent of swelling and tenderness. Is it a joint pain or arthritis? Where is the origin of the pain, inside of the joint or outside? Mild swelling or Severe? Rheumatologist should find it by palpating patients joints. The aim of this lecture is to reinforce the knowledge of how to assess joints, especially 40 joints which is composed of basic 28 joints and ankles and feet, semiquantitative assessment and the method recommended by EULAR committee.

MTE19

Update on diagnosis and treatment of idiopathic inflammatory myopathy

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Conflict of interest: None

Idiopathic inflammatory myopathy (IIM) is a disease group characterized by proximal muscle weakness and myalgia due to muscle inflammation. Polymyositis/Dermatomyositis (PM/DM) is one of representative IIM and a patient is diagnosed as DM if one has typical cutaneous lesion such as Gottron's sign or papules or Heliotrope rash. Previously it has been well known that some patients only show typical skin manifestations without or mild muscle inflammation with no obvious muscle symptoms. Nowadays these patients were called as clinically amyopathic DM (CADM) as they have no muscle weakness or myalgia clinically. PM/DM often occurred with other manifestations, polyarthritis, interstitial lung disease (ILD), myocardial involvement and malignancy during their clinical course. As mentioned above, clinical manifestations of IIM are extremely diverse as well as response to treatment and prognosis of muscle disturbance itself and complicating other organ involvement. Clinicians are also required to pay careful attention to these complications especially ILD, malignancy and cardiac involvement because these are critical factor that influences the prognosis of PM/DM. Therefore, prompt correct evaluation and subsequent appropriate treatment of muscle and other symptoms are important. In this context, autoantibodies found in patients with PM/DM are useful for diagnosis, selection of treatment, evaluation of treatment and prediction of prognosis in each patient.

MTE20

Usefulness of radiographic examination for rheumatoid arthritis in clinical practice

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Conflict of interest: Yes

Rheumatoid arthritis is characterized by arthritis which causes bone destruction. Bone destruction is caused by integrated the strength and the duration of arthritis. Therefore, if a bone destruction image is confirmed from the early stage of morbidity, disease activity is high as rheumatoid arthritis and it is judged to be poor prognosis. Since the classification criteria for rheumatoid arthritis of ACR / EUL AR revised in 2010 aim at treatment intervention from the early stage, there is no X - ray finding in the item for classification. Although sensitivity is not high, X - ray examination is a very useful examination method for detecting bone destruction in routine practice. Diagnosis of rheumatoid arthritis is easy if the structural destruction of the joint is detected. Therefore, if you become familiar with X-ray interpretation, diagnostic accuracy improves. It is necessary to constantly be aware of the comparison between left and right, comparison with the presence or absence of arthritis as a scientific finding. Also, comparison over time is important. Osteoarthritic changes such as osteophyte formation and osteosclerosis are also seen as changes after drug therapy has been successful in recent years. On the other hand, in cases where drug therapy strengthening is difficult, if there is rapid destruction progress, it is necessary to perform surgical therapy at an appropriate timing. Structural destruction of bone and cartilage is directly linked to functional deterioration. Joint stability is essential for joint function. Destruction of ligament, joint capsule should be linked to joint stability. With simple x-rays, it is possible to detect by checking abnormal mobility of a joint by dynamic imaging or stress imaging. It is important to recognize not only the damage in one joint, but also the relationship with the adjacent joint, overall alignment and balance for the spine and lower limb. In this lecture, I would like to display representative and concrete radiographs in diagnosis and treatment, and aim to deepen knowledge for X - ray interpretation.

MTE21

Total joint arthroplasty for elbow and finger in RA patients

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Conflict of interest: None

The strategy for surgical reconstruction of the upper extremity disorders in RA patients has been changed with the progression of medical treatment. The number of surgery for synovectomy, subcutaneous tendon rupture and compression neuropathy have decreased, whereas those for the finger joint deformity have increased because of functional disorders and cosmetic problems. The mutilated arthritis of the elbow, which can be reconstructed by use of linked type prosthesis, has also decreased. Although the demand for surgical treatment of finger joint deformity has been increasing, the strategy for the surgery is not easy because complicated imbalance of intrinsic muscles is involved in the deformity. The surgeon should understand the mechanism of the deformity to obtain god result. In this workshop, I will present the following surgical procedure. 1) Metacarpophalangeal joint arthroplasty using silicone implant 2) Total elbow arthroplasty; standard posterior approach using linked-type prosthesis 3) Total elbow arthroplasty; three-dimensional surgical planning and triceps splitting approach using unlinked-type prosthesis (K-NOW TEA)

MTE22

Management of Liver Injuries in Patients Receiving Immunosuppressive Therapies

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Conflict of interest: Yes

Drug-induced liver injurie (DILI) may develop in patients receiving immunosuppressive therapy, whereas the therapies could not be done in patients underling liver damage. Glucocorticoids were the most frequent causative drugs for DILI; serum ALT levels increase, but may attenuate then later due to spontaneous attenuation of fatty liver. Also, methotrexate may provoke DILI frequently in a dose-related manner, but were well controlled via dose-reduction and/or folic acid supplementation. It should be noted that any drugs may cause liver damage, and the diagnosis should be done according to the criteria by JDDW2014 and histological findings on liver biopsy specimens. HBV carriers and patients with previously resolved HBV (prHBV) infection should receive immunosuppressive therapies in accordance with the guideline regarding HBV reactivation published JSH. In patients with prHBV infection, serum HBV-DNA are to be measured repeatedly depending on serum anti-HBc levels as well as duration after the initiation of therapies. Entecavir should be administrated when serum HBV-DNA levels increased to 20 IU/mL or more. Considering economic issues, the study group supported is now conducting the prospective study to apply HBs-antigen measured by a high-sensitive method instead of HBV-DNA for monitoring of HBV reactivation. Patients with HCV infection were recommended to receive DAA therapies, since liver function improves following HCV eradication. Ribavirin and/or DAASs as NS3/4A protease inhibitors, NS5A inhibitors and a nucleotide-type or non-nucleotide-type NS5B polymerase inhibitor are administrated in combination for 12 weeks depending of HCV genotypes, NS5A-RAVs, renal and cardiac diseases and underling drugs intake. Also, in 2017, novel DAAs which can eradicate HCV within 8 weeks will be approved in Japan. Such therapies, however, were not allowed for decompensated patients. Thus, we conducted the clinical study to improve liver function in such patients by B-RTO procedures.

MTE23

Iatrogenic immunodeficiency-associated lymphoproliferative disorders in patients with rheumatic diseases

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Conflict of interest: Yes

Patients with rheumatoid arthritis (RA), systemic lupus erythematosus, and Sjogren syndrome are exposed to a higher risk of lymphoproliferative disorders (LPD) including lymphoma compared to general population. For example, a meta-analysis showed standardized incidence ratio (SIR) of 2 to 3 and Japanese epidemiological studies revealed SIR of 4 to 6 in patients with RA versus general population. WHO classification of tumours of haematopoietic and lymphoid tissues (IARC Press, 2008) creates a separate section of 'other iatrogenic immunodeficiency-associated lymphoproliferative disorders' after 'post-transplant lymphoproliferative disorders'. In this section, LPDs that arise in patients treated with immunosuppressive drugs for autoimmune diseases or conditions other than in the allograft/autograft transplant setting are described. Associated factors of other iatrogenic immunodeficiency-associated LPD include age, types of rheumatic disease, disease activity, drug use, and EB virus infection. Methotrexate (MTX) and TNF inhibitors (i.e., infliximab, etanercept, and adalimumab) are on list as immunosuppressive drugs associated with LPD. Because RA has relatively high prevalence rate among collagen diseases and the treat-to-target strategy with the use of MTX and biologics has been widely accepted, there is growing concern about immunodeficiency-associated LPD, especially those developed in patients treated with MTX. Epidemiologically, disease activity serves as a confounding factor between MTX and LPD, which makes it difficult to conclude causal relationship of the two in all patients who develop LPD during treatment with MTX. Therefore, one should be very prudent to use 'MTX-associated LPD'. In this Meet the Expert session, I would like to share recent evidence about iatrogenic immunodeficiency-associated LPD and provide an opportunity to consider about clinical management of patients with this comorbidity.

MTE24

The selection and strategy of biological DMARD in patients with rheumatoid arthritis

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Conflict of interest: None

We discuss the selection and strategy of biological DMARD in patients with rheumatoid arthritis.

EULAR Session

EUS-1

Posttranslationally modified proteins – The key to auto-immunity in RA?

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Conflict of interest: None

Rheumatoid arthritis (RA) is an autoimmune disease in genetically prone individuals where multiple environmental factors can induce the inflammatory processes. Interestingly, the specific autoimmune response is directed against a number of different antigens modified by post-translational modifications (PTMs). Here, enzymatic deimination of peptide-bound arginine to citrulline by peptidylarginine deiminases (PADs) is considered to be a key mechanism. Investigations in different cohorts of RA have revealed that tobacco exposure increases the risk of anti-citrullinated protein/ peptide antibodies (ACPAs) formation, especially in carriers of the shared HLA epitope. Another PTM that has been connected to smoking is carbamylation of lysine, creating a homologous citrulline structure that is extended by a single carbon residual, also known as homocitrulline. Various carbamylations are formed by the interaction of isocyanate (HNCO). In humans, isocyanate is formed by the decomposition of urea into ammoniac and cyanate, which is transformed to isocyanate. Thus, uremia secondary to renal diseases is a pathological state that leads to the formation of isocyanate. The second key reactant for isocyanate formation is thiocyanate (SCN^-), a metabolite of cyanide that is present in cigarette smoke. Thiocyanate increases in urine, serum and saliva dependent on the amount of cigarette smoke. Moreover, passive exposure to smoke significantly increased thiocyanate levels when compared with non-exposure. Neutrophil myeloperoxidase (MPO) represents a marker of inflammation and is significantly higher in smokers than non-smokers. It uses H_2O_2 to oxidize thiocyanate to cyanate that subsequently promotes protein carbamylation at sites of inflammation. Mice immunized with carbamylated proteins (carbP) developed arthritis and a T-cell response against corresponding antigens. Additionally, antibodies against carbP but not ACPAs were detectable in mice with collagen-induced arthritis. Sera from patients with RA contain different antibody specificities recognizing either citrulline containing or homocitrulline containing antigens, and anti-carbP as well as ACPAs are detectable even before the onset of symptoms of RA. These findings suggest that in addition to citrullination, carbamylation represents another crucial process in RA pathogenesis. Accumulating evidence suggests an involvement of modified vimentin and anti-modified vimentin antibodies in the pathogenesis of RA. Vimentin is one of the most widely expressed mammalian intermediate filament proteins. The vimentin network that extends from the nucleus to the plasma membrane is believed to act as a scaffold, providing cellular mechano-structural support and thereby maintaining cell and tissue integrity. Therefore, our group hypothesized that vimentin could serve as a substrate for carbamylation from smoking ingredients and investigated the autoantibody response against different isoforms of vimentin in patients with RA. Sera from rabbits immunized with carbamylated vimentin (carbVim), in addition to carbVim also recognized human IgG-Fc showing rheumatoid factor-like reactivity. Smoke exposed mice contained detectable amounts of carbVim and developed a broad immune response against carbamylated antigens. Although the prevalence of anti-carbamylated antibodies in smokers and non-smokers was similar, the titers of carbamylated antibodies were significantly increased in sera of smoking compared with non-smoking RA. CarbVim antibodies were observed independently of ACPAs in early phases of disease and double-positive patients for anti-mutated citrullinated vimentin (MCV) and anti-carbVim antibodies showed an extended epitope recognition pattern towards MCV. Thus, carbamylation of vimentin is inducible by cigarette smoke exposure. The polyclonal immune response against modified antigens in patients with RA is not exclusively citrulline-specific and carbamylation of antigens could be involved in the pathogenesis of disease. Reference: Ospelt C, Bang H2, Feist E, Camici G, Keller S, Detert J, Krämer A, Gay S, Ghannam K, Burmester GR. Carbamylation of vimentin is inducible by smoking and represents an independent autoantigen in rheumatoid arthritis. Ann Rheum Dis. 2017 Feb 9. pii: annrheumdis-2016-210059. doi: 10.1136/annrheumdis-2016-210059.

EUS-2

Pathway identification in inflammatory arthritis

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Conflict of interest: Yes

The progress of the last decades in the identification of novel therapeutic targets has improved clinical outcomes across the spectrum of inflammatory arthritis but has equally raised expectations of further progress. These expectations have been clearly identified in the recently disclosed EULAR RheumaMap. However, in pursuit of these ambitious goals, we face several key challenges. The optimal route to drug discovery has not yet been achieved and as such there remains considerable opportunity for the rationalization of target identification and thereafter drug discovery. Moreover, we require to revise our molecular characterization of the patients – in essence we must generate orphan diseases out of common conditions to enhance the achievement of high hurdle outcomes on a more predictable basis. In this presentation, I shall consider what our new clinical objectives should be in the investigation of inflammatory arthritis and thereafter allude to recent clinical and pre-clinical datasets to examine novel approaches. These will be considered in light of the precision medicine revolution that is moving apace across several disciplines.

EUS-3

Strategies to prevent and treat early rheumatoid arthritis

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Conflict of interest: None

PREVENTION To prevent RA requires 1) knowledge of risk factors that are strong enough to predict the occurrence 2) adequate intervention modalities to prevent the occurrence of RA in those at high risk. Risk factors: Stop smoking is a very realistic public health measure, also benefitting patients at risk for RA. Specific for RA the following risk factors have been identified (so far): presence of rheumatoid factor or anti-CCP in healthy people, family history of RA, presence of shared epitope and arthralgia. Two studies have shown that in persons presenting with arthralgia, RF and/or aCCP, positive family history and presence of shared epitope around 40% develop RA in the following 4 years. There have been published two intervention studies in these populations. In the first study half of these patients received two times (0 and 6 weeks) 100 mg dexamethasone, and the other half placebo. There was no difference in the occurrence of RA between both groups (Bos 2010). In the second study treatment consisted of either Rituximab 1000 mg i.v. or placebo i.v.. In this group 40% developed RA on placebo versus 34% on Rituximab; and the Rituximab treated patients had a 5 month later onset of their RA than the placebo group (Gerlag 2016). TREATING EARLY RA: The evidence for very effective treatment of early RA is quite strong, as described in the updated EULAR recommendations on DMARD treatment of RA (Smolen 2017). As a recent example the efficacy of IL-6 blocking treatment with Tocilizumab was evaluated in the U Act Early Study (Bijlsma 2016). Over 80% of the patients with early RA treated with Tocilizumab reached sustained remission within the first 6 months. These spectacular results are most likely due to the very well developed recognition and referral system in the Netherlands for patients suspected of early RA. CONCLUSION Presently, the gain to be won by preventing RA is too limited for daily practise; however, research in this area needs to be continued. The most gain is to be obtained by early recognition and early treatment of RA, whereby responsible use of biologicals early in the disease might prove to be cost-effective in the long run.

Special Program

SP1-1

The clinical guidelines for large vessel vasculitis

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Conflict of interest: Yes

Large vessel vasculitis (LVV) consists of Takayasu arteritis (TAK) and giant cell arteritis (GCA) according to CHCC2012. Whereas TAK is reported to be much more frequently observed than GCA in Japan, GCA is more frequently observed in the western countries. However, the frequency of TAK and GCA has not been examined for long time in Japan. To reveal the real numbers of the patients with TAK and GCA in Japan, the Research Committee on Intractable Vasculitides, supported by the Ministry of Health, Labour and Welfare, is now conducting both retrospective and prospective registry studies in Japan. Glucocorticoids (GC) still remain the mainstay for LVV. These drugs suppress the clinical signs and symptoms of inflammation when administered in moderate to high doses, but a sizable number of patients with these conditions relapse upon tapering of GC dose or discontinuation. Such patients require retreatment and high cumulative doses of GC, resulting in substantial toxicity and morbidity. Thus, immunosuppressive drugs such as methotrexate, azathioprine, cyclosporine A, cyclophosphamide, mycophenolate mofetil and TNF-alpha inhibitors have been studied with an attempt to control the disease activity and lower doses of GC, especially in the patients with TAK. However, the results of the above immunosuppressive agents for the refractory patients with TAK have not been satisfactory. Recently, interleukin-6 (IL-6) has a crucial role in the pathogenesis of large vessel vasculitis (LVV) including TAK and GCA, since the expression level of IL-6 has been reported to be greatly elevated in the patients with LVV. Several recent studies have reported that IL-6 receptor (IL-6R) blockade with the IL-6R monoclonal antibody tocilizumab (TCZ) might be effective for the refractory patients with both TAK and GCA. I would like to discuss the current therapeutic strategy according to the guideline for management of large vessel vasculitis.

SP1-2

Clinical practice guidelines for the management of adults with antineutrophil cytoplasmic antibody-associated vasculitis 2017

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Conflict of interest: Yes

Objective: To standardize the management and improve clinical outcomes of the patients with AAV, we have recently published 'The clinical practice guidelines for the management of adults with antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) 2017'. Methods: The clinical committee of small- and medium-sized vasculitides of Research Committee of Intractable Vasculitis Syndrome developed 'Clinical Practice Guideline' including clinical questions (CQs) and recommendations using Grading of Recommendations Assessment, Development and Evaluation (GRADE) system as Part 1 of the book. Research Committee of Intractable Vasculitis Syndrome of the MHLW, Research Committee of Intractable Renal Disease of the MHLW, and Research Committee of Diffuse Pulmonary Disorders of the MHLW collaborated and produced 'Basic and clinical aspects of AAV' as Part 2 of the book. Results: We addressed six sub CQs of CQ1 about remission induction treatment of AAV, and developed 5 recommendations. We dealt with two sub CQs of CQ2 about plasma exchange for remission induction treatment of AAV, and developed 2 recommendations. We tackled five sub CQs of CQ3 about maintenance treatment of AAV, and developed 1 recommendation. In all CQs, certainty/quality of evidence was low or very low, and strength of recommendation was weak. Following the recommendations of each CQs, summary of evidence, discussion by the guideline development group, related other guidelines, monitoring and evaluation of treatment, possibility of future research, and list of evaluated literatures are described. In Part 2 of the book, overview, etiology, pathogenesis, diagnostic approach, diagnosis, evaluation of disease activity, differential diagnosis, RPGN clinical practice guidelines, and prognosis are described. Conclusion: Development of clinical practice guidelines for overall AAV promotes good health of Japanese public through standardization of treatment and improvement of outcomes. Enlightenment activities, monitoring, and evaluation of quality index are listed as future challenges and should be performed in a structured way.

SP1-3

New treatment strategy for antineutrophil cytoplasmic antibody-associated vasculitis with rituximab

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Conflict of interest: None

Antineutrophil cytoplasmic antibody-associated vasculitis (AAV) is a refractory and recurrent autoimmune disease. Recently, the efficacy of glucocorticoid (GC)+rituximab (RTX) was reported in randomized controlled trials abroad. According to these results, RTX is licensed for treating granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) in Japan. However, information on RTX for treating Japanese AAV patient is insufficient due to lack of clinical trials targeting Japanese patients. These facts suggest the needs of evidence for treating Japanese AAV patients, which led to this prospective cohort study conducted by the Research Committee on Intractable Vasculitides on a strategic study group, to establish evidences for treatment guidelines on intractable vasculitis. All AAV patients treated with RTX have been enrolled from each institution and will be followed-up for 2 years. Various outcomes including efficacy and safety parameters will be analyzed. Biomarkers as useful predictors will also be searched. Until December 2016, 10 GPA and 21 MPA patients were registered. Among 10 GPA patients, 5 male and 5 female were included. Five male and 16 female were included in MPA. The mean age was 67.8 years-old in GPA and 71.6 years-old in MPA. Initial RTX administration within 2 weeks of remission induction therapy was used in 4 GPA patients and 5 MPA patients. We aim to register 50 cases by December 2017, the end of registration.

SP1-4

Clinical features and treatment manner of otitis media with antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (OMAAV)

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Conflict of interest: None

Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a necrotizing vasculitis with few or no immune deposits, characterized as predominantly affecting small to medium vessels and being associated with ANCA specific for myeloperoxidase (MPO) or proteinase 3 (PR3), that consists of 3 groups: granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA). Otitis media often occurs in AAV patients. However, the diagnostic criteria for general forms of AAV from the Japanese Ministry of Health, Labour and Welfare (JMHLW) 1998 and from the European Medicines Agency (EMEA) algorithm are not available for

diagnosis in the early stage for patients with otitis media caused by AAV, who do not show any organ involvement other than the ear, ANCAs-positivity, and histological proof. Therefore, it has already been suggested that diagnostic criteria for an upper respiratory tract-limited form of AAV are necessary, because half of the patients are ANCA-negative and only one-third of them have histological vasculitis in biopsy specimens. Furthermore, clinical features of cases of intractable otitis media reported as GPA, MPA, and EGPA did not differ. Therefore, discrimination among the three subgroups of AAV is difficult and is unlikely to be applicable for intractable otitis media caused by AAV. On the basis of these reasons, we have recently proposed that such disease should be categorized as "otitis media with AAV (OMAAV)". Recently, we proposed a definition criteria for OMAAV and performed a nationwide survey in Japan, and then presented the clinical features of 235 patients1:(1) disease onset with initial signs/symptoms due to intractable otitis media with effusion or granulation, which does not respond to ordinary treatments such as antibiotics and insertion of tympanic ventilation tubes, followed by progressive hearing loss;(2) predominantly female (73%) and older (median age: 68 years);(3) predominantly MPO-ANCA-positive (60%), followed by PR3-ANCA-positive (19%) and both ANCAs-negative (16%);(4) frequently accompanied by facial palsy (36%) and hypertrophic pachymeningitis (28%);(5) often involving lung (35%) and kidney (26%) lesions; and (6) occasionally threatening patients' hearing and lives: 14 (6%) patients experienced bilateral complete deafness and 3 (1%) patients died of the disease. In this symposium, we would like to show the clinical features and treatment manner of OMAAV.

SP1-5

Vasculitis guideline from the dermatological point of view

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Conflict of interest: None

In vasculitis guideline, the Japanese Dermatological Association referred two guidelines named by "Guideline of vasculitis and vasculopathy" and "Guidelines for the management of skin ulcers associated with connective tissue disease/vasculitis". "Guideline of vasculitis and vasculopathy" belonged to ANCA-associated vasculitis, IgA vasculitis, Cryoglobulinemic vasculitis, Urticarial vasculitis, Polyarteritis nodosa, Cutaneous leukocytoclastic angiitis, Cutaneous arteritis, Lupus vasculitis, Rheumatoid vasculitis, Sarcoid vasculitis, Hepatitis C virus-associated cryoglobulinemic vasculitis, Hepatitis B virus-associated vasculitis, Drug-associated vasculitis, Cancer-associated vasculitis, and Behçet's disease. In addition, Livedoid vasculopathy and Antiphospholipid syndrome were adopted in "Guideline of vasculitis and vasculopathy". In contrast, "Guidelines for the management of skin ulcers associated with connective tissue disease/vasculitis" belonged to various vasculitides and rheumatoid arthritis. Dermatologists considered diagnostic/therapeutic approaches appropriate for each of these disorders according to the two guidelines. When these patients with vasculitis visit dermatological department, we characterize the cutaneous manifestations at initial presentation such as palpable purpura and livedo racemose. It is the role of the dermatologist to estimate the patient's general condition from skin symptoms, clarify the patient's condition through various examinations and perform treatments accordingly. It is our hope that the present guidelines are of help in clinical situations.

SP2-1

Indications, contraindications and screening tests for MTX therapy

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Conflict of interest: Yes

Methtrexate (MTX) is the anchor drug for the treatment of rheumatoid arthritis (RA) as shown in the Guidelines for the management of RA, Japan College of Rheumatology 2014. However, many patients with RA meet any of the criteria for relative contraindication of MTX, including aging, infectious diseases, hematological, hepatic, renal or respiratory disorders, even though they do not meet the criteria for contraindication such as pregnancy. Therefore, the indication of MTX and the order of its use are determined by the risk-benefit balance in each patient. It should be noted that, among serious adverse events with MTX therapy, interstitial pneumonia and lymphoproliferative disorders are more frequent in Japan than in other countries. As the screening tests for MTX treatment, chest images, interferon γ-releasing assay or Tuberculin skin test for Mycobacterial infection; HBs-Ag, HBs-Ab, HBc-Ab and HCV-Ab for hepatitis B and C infections; and blood β-D glucan test for fungal infections including Pneumocystis jiroveci are recommended, as well as complete blood count, blood chemistries, immunoglobulin tests and urinalysis. Subsequently, isoniazide, nucleoside analogues, or trimethoprim/sulfamethoxazole may be administered for some patients, if necessary.

SP2-2

Clinical use of MTX for RA based on the 2016 updated JCR guidelines

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Conflict of interest: Yes

MTX was placed in anchor drug because of the long-term effectiveness and safety at the end of 1990s. Even if the newly developed molecular-targeted drugs were introduced into the market, the positioning of MTX does not change because of the effectiveness and the reliability in usual RA care. The Japan Rheumatism Association (JCR) updated the guidelines for clinical application of MTX in the treatment of rheumatoid arthritis after an interval of 5 years, since new evidences regarding the effectiveness and safety of high-dose MTX have been accumulated The analysis of a post marketing surveillance (PMS) of MTX with higher doses in Japanese RA patients has been completed. The results of PMS showed that remission rate increased approximately 3 times by increasing MTX from 8mg to more than 10mg/week in patients with monotherapy as well as patients in combination with biologics. The C-OPERA study, a DB-RCT comparing the effect on radiographic progression between MTX and MTX+ certolizumab groups was conducted by a rapid–dose escalation protocol up to 18mg/wk of MTX. The average MTX dose during the study was 11.6mg in both groups and only about 40% of patients was taking more than 12mg/wk of MTX at the end of study. Therefore, MTX should be started at 6-8 mg/wk, with escalation of 2 mg every 4 weeks up to 10-12 mg/wk. For patients with poor prognostic factors or high disese activity, MTX could be started at 8mg/wk, with rapid dose escalation. For patients with inadequate response to appropriate dose of MTX, MTX should be considered as the anchor for combination therapy with all classes of biologics and JAK inhibtors. In this symposium, I discuss dosage and administration of MTX and how to use MTX combined with other rheumatic drugs in the updated guidelines based on new evidences accumulated during recent 5 years.

SP2-3

Management of adverse drug reactions- hematological disorder, interstitial pneumonia, infection, and liver disorder

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Conflict of interest: Yes

Methotrexate (MTX) has been widely used in clinical practice as an anchor drug for the treatment of rheumatoid arthritis (RA). Management of adverse drug reactions (ADRs) of MTX are described in Chapter 9 of the Clinical Practice Guidelines of Treatment with MTX 2016, calling attention of physicians and medical staff to its safe use. To further enhance the education of patients which is most important for early diagnosis of ADRs of MTX, the committee has revised the booklet for patients who take MTX and highly recommends to use it at every clinics and hospitals where they see patients with RA. At the beginning of the particular sections of ADRs, recommendations summarizing the main points are shown. Up-to date information of ADRs collected by pharmaceutical companies and safety results from post-marketing surveillance programs and clinical trials are abstracted. Major changes from the 2011 version are as follows. To promote a better understanding of the management of

bone marrow suppression, a case of leukovorin rescue therapy are shown in Chapter 4. Pulmonary images of interstitial pneumonia are provided to serve as a reference for physicians, and other references are cited to aid proper diagnosis. As frequently encountered and relevant opportunistic infections, pulmonary images of Pneumocystis pneumonia, pulmonary Cryptococcosis, and non-tuberculous mycobacterium are shown. Regarding liver disorders, management of carriers and patients with prior infection of hepatitis B virus (HBV) are separated. In the light of recent advances of treatment of hepatitis C virus carriers, consultation for antivirus therapy to gastroenterologists deserves considering. I would like to touch on these revision details in this symposium and make it a good opportunity to deepen our understanding of safe use of MTX.

SP2-4

Lymphoproliferative disorders in rheumatoid arthritis patients receiving methotrexate – from rheumatologists –

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Conflict of interest: Yes

In 2011, because an increased dose (>8mg weekly) of methotrexate (MTX) for the treatment of rheumatoid arthritis (RA) was approved, Japanese rheumatologists used enough dose of MTX even for early RA patients. Development of lymphoproliferative disorders (LPD) is, however, recently recognized as one of the most serious adverse reaction in RA patients receiving MTX. Clinical issues of LPD in RA patients are as follows: 1) It is sometimes difficult for rheumatologists to find an early phase of LPD because extranodular manifestations (e.g., skin, lung, and pharynx) are frequent, 2) reactivation of Epstein-Barr virus is frequently observed, so LPD may disappear in some cases immediately after the discontinuation of MTX but aggressive chemotherapy is required in other cases, 3) LPD occur more frequently in RA patients than in normal population and the previous report indicated that disease activity not but therapeutic agents is critical for LPD development, and 4) there is no recommendation of treatment strategy after clinical remission of LPD. In Japan College of Rheumatology guideline for the MTX treatment of RA (2016), MTX is contraindicated for RA patients, who were diagnosed as having LPD in 5 years. Rheumatologists should take care of manifestations associated with LPD such as fever of unknown origin, night sweat, lymph node swelling, subcutaneous tumor, chronic pharyngeal pain, hepatosplenomegaly, and an increased level of LDH. When LPD is strongly suspected, MTX should be discontinued and consultation to specialities (e.g., hematologists, dermatologists, and otolaryngologists) must be considered. If LPD is not ameliorated after 2-week discontinuation of MTX, biopsy of LPD-suspected lesion should be considered. Before MTX administration, therefore, the informed consent regarding MTX-associated LPD, should be obtained by rheumatologists. In this presentation, clinical importance of MTX-associated LPD will be discussed.

SP2-5

MTX-LPD: a hematologist's point of view

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Conflict of interest: None

Malignant lymphoma developed in RA patients during MTX therapy is called as MTX-associated lymphoproliferative disorders (MTX-LPD). It has been controversial in western countries whether MTX could amplify risk of lymphoma, because of a higher incidence of lymphoma in RA patients than general population. A case-control study revealed that higher MTX dose was associated LPD onset in RA patients of Japan. There was, however, no obvious threshold of MTX dose or duration of administration for increasing the risk. Major histologic subtype is diffuse large B cell lymphoma (DLBCL), and other subtypes such as Hodgkin lymphoma (HL, mixed cellularity subtype is common), mantle cell lymphoma (MCL), and T cell lymphoma could be seen. Forty to fifty percent of MTX-LPD cases involve extranodal sites, which should be kept in mind, for example, in a case of gastric lymphoma without superficial lymphadenopathy. The value of soluble IL-2 receptor should be evaluated with consideration of RA activity. Lymph node biopsy is necessary for a definitive diagnosis of MTX-LPD, and is performed on a lymph node larger than 1.5 cm. PET-CT or contrast-enhanced CT and bone marrow examination are used for staging. Pathological diagnosis of lymphoma subtype and clinical stage enable us to decide on treatment strategy. Importantly, at least 30% of patients with MTX-LPD showed tumor regression within 4 weeks following cessation of MTX. More patients may experience tumor regression in extended observation period. Close watching of tumor size and laboratory findings is crucial for deciding chemotherapy in any case. Chemotherapy is suitable for patients without regression and also with relapse after regression. Regimen is selected according to subtype: R-CHOP for DLBCL and ABVD for HL. Pathological diagnosis is a key for selecting specific therapy such as bendamustine for MCL and anti-CD30 monoclonal antibody for HL. I will discuss early detection, treatment policy, and prognosis as a hematologist.

SP2-6

Lymphoproliferative disorder based on Rheumatoid arthritis with treatment

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Conflict of interest: None

Lymphoproliferative disorder associated with therapy for Rheumatoid arthritis (RA-therapy LPD) such as Methotrexate (MTX)-associated LPD varies from reactive condition to malignant lymphoma that shows same pathologic characteristics as conventional malignant lymphoma (Conventional ML). WHO classification of lymphoid neoplasm 2016 revealed that Immunodeficiency-associated lymphoproliferative disorders consists of Primary immunodeficiency-associated LPD, HIV-related lymphoma, Transplantation-associated LPD and Other iatrogenic immunodeficiency-associated LPD including RA-therapy LPD. Although diffuse large B-cell lymphoma (DLBCL) is common in both conventional ML and RA-therapy ML, classical Hodgkin lymphoma (CHL) is second in RA-therapy ML, but only 5% in conventional ML. Moreover, Hodgkin-like type having CD20 (+) Hodgkin/Reed-Sternberg cells is a special type for RA-therapy ML. EBV is frequently associated with DLBCL and CHL in RA-therapy ML. Clinicopathological study of ML occurred in RA (2006, Kojima et al.) showed there were many DLBCL, but a few CHL. DLBCLs in RA-therapy ML have mono-clonality of immunoglobulin heavy chain gene even DLBCL with spontaneous regression. In this paper, pathological findings of RA-therapy LPD, as well as clinicopathological, immunohistochemical and genetic results of RA-therapy LPD in Tokai university hospital will be reported.

International Concurrent Workshop

ICW1-1

Mucosal-associated invariant t cell deficiency in systemic lupus erythematosus is related to to an intrinsic defect in the Ca2+/calcineurin/nfat1 signaling pathway

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Conflict of interest: None

Objective Mucosal-associated invariant T (MAIT) cells contribute to protection against certain microorganism infections and play an important role in mucosal immunity. However, the role of MAIT cells remains enigmatic in autoimmune diseases. Here, we examined the level and function of MAIT cells in patients with rheumatic diseases. Design and Method Patients with systemic lupus erythematosus (SLE; n = 54), rheumatoid arthritis (RA; n = 66), Behçet's disease (n = 9), ankylosing spondylitis (n = 21), and healthy controls (n = 136) were enrolled in the study. MAIT cell, cytokine and programmed death-1 (PD-1) levels were measured by flow cytometry. Results Circulating MAIT cell levels were significantly reduced in systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) patients. In particular, this MAIT cell deficiency was more prominent in CD8+ and double-negative T cell subsets, and significantly correlated with disease activity, such as SLE disease activity index (SLEDAI) and 28-joint disease activity score (DAS28). Interestingly, MAIT cell frequency was significantly correlated with natural killer T (NKT) cell frequency in SLE patients. IFN-gamma in MAIT cells was impaired in SLE patients, which was due to an intrinsic defect in the Ca2+/calcineurin/NFAT1 signaling pathway. In SLE patients, MAIT cells were poorly activated by alpha-galactosylceramide-stimulated NKT cells, thereby showing the dysfunction between MAIT cells and NKT cells. Notably, an elevated expression of PD-1 in MAIT cells and NKT cells was associated with SLE. In RA patients, MAIT cell levels were significantly higher in synovial fluid than in peripheral blood. Conclusions Our study primarily demonstrates that MAIT cells are numerically and functionally deficient in SLE. In addition, we report a novel finding that this MAIT cell deficiency is associated with NKT cell deficiency and elevated PD-1 expression. These abnormalities possibly contribute to dysregulated mucosal immunity in SLE.

ICW1-2

The $CD4^+CD52^{low}$ T Cell Contributes to the Development of Systemic Lupus Erythematosus through the CCR8/TARC Pathway

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Conflict of interest: None

Objectives: CD52 is a cell-surface glycoprotein that is widely expressed in lymphocytes, monocytes and eosinophils. $CD4^+CD52^{high}$ T cells inhibit the activation of $CD4^+CD52^{low}$ T cells through the release of cell-surface CD52. The role of the immune regulation of these cells in systemic lupus erythematosus (SLE) is unknown. Methods: We isolated the PBMCs of 64 SLE patients, 23 rheumatoid arthritis (RA) patients and 33 healthy controls (HCs). The expressions of $CD4^+CD52^{high}$ T cells and $CD4^+CD52^{low}$ T cells were analyzed by flow cytometry. We also analyzed the correlations with clinical parameters including SLEDAI, anti-ds-DNA antibodies and complement. We then analyzed circulating follicular helper like T cells (Tfh like cells) identified as $CD4^+CXCR5^{high}ICOS^{high}PD\text{-}1^{high}$. To determine the genetic characteristics of $CD4^+CD52^{low}$ and $CD4^+CD52^{high}$ T cells from SLE, we performed cDNA microarrays (SurePrint G3 Human GE 8x60K) and examined the function of the genes in *in-vitro*. Results: We found that the expression of $CD4^+CD52^{low}$ T cells in the SLE was significantly higher than HC and non-SLE. The expression of $CD4^+CD52^{low}$ T cells of the SLE were positively correlated with SLEDAI, anti-ds-DNA antibodies and IgG. The population of Tfh like cells were increased in SLE and its expression was positively correlated with $CD4^+CD52^{low}$ T cells. The microarray analysis revealed that the expression of chemokine receptor 8 (CCR8) is significantly increased in $CD4^+CD52^{low}$ T cells. In addition, in vitro experiments using CD4 T cells from patients with SLE showed that thymus and activation-regulated chemokine (TARC), known as a ligand of CCR8, induced the conversion of $CD4^+CD52^{high}$ T cells into $CD4^+CD52^{low}$ T cells. Conclusion: Collectively, our data suggest that increased $CD4^+CD52^{low}$ T cells along with increased Tfh like cells are involved in the pathogenic autoantibodies production and that TRAC may contributes to the development of SLE via an aberrant induction of $CD4^+CD52^{low}$ cells.

ICW1-3

***Peptidylarginine deiminase 4* deficiency ameliorated Imiquimod-induced lupus model mice**

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Conflict of interest: None

[Objectives] Neutrophil extracellular trap (NET) is thought to play a pivotal role in SLE pathogenesis. However, the precise roles of NETs in SLE pathogenesis remain unclear. To elucidate detailed mechanisms, imiquimod (IMQ) -induced lupus model mice were analyzed in NET-deficient situation, *Peptidylarginine deiminase 4* knock out (*Padi4* KO) mice. **[Methods]** The ear skin of B6 mice were treated topically with IMQ. IMQ was also administered in B6 *Padi4* KO mice. Splenomegaly, proteinurea, serum anti-double-stranded DNA (anti-dsDNA) antibodies, frequencies of splenic and renal immune cells, and histopathological findings of ear skin were assessed. For human experiments, B cells and Monocytes were stimulated with immune complex (IC) composed of NETs and IgG from SLE patient and evaluated their activation. **[Results]** Compared with non-treated mice, increases in proteinurea, elevation of serum anti-dsDNA antibodies, and decreased frequencies in splenic plasmacytoid dendritic cells (pDCs) were noted in IMQ-treated mice. Significant decreases in the spleen weights and proteinurea, and pDCs restoration were observed in IMQ-treated *Padi4* KO mice. Additionally, renal myeloid cell infiltrations and epidermal immune cell infiltrations were significantly decreased in IMQ-treated *Padi4* KO mice. Notably, serum anti-dsDNA antibodies were not decreased in IMQ-treated *Padi4* KO mice. Human monocyte activation and IL-6 secretion were observed when stimulated with ICs composed of NETs and IgG derived from SLE patient, not from healthy volunteer, and this activation was enhanced with IFN-α co-stimulation. B cell activation and plasma cell differentiation by NET-ICs were not observed. **[Conclusion]** Lupus-like phenotypes were ameliorated in *Padi4* KO mice. NETs contribute to SLE pathogenesis by activation of pDCs and myeloid lineage cells, especially in the focus of inflammation. Regulation of NETs or *Padi4* inhibition can be a new therapeutic target for SLE.

ICW1-4

Preliminary attempt for subgrouping of patients with systemic lupus erythematosus in our hospital

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Conflict of interest: None

[Objectives] Prediction of outcomes of systemic lupus erythematosus (SLE) patients in advance is difficult due to clinical heterogeneity of the disease. Subgrouping of SLE patients to identify patients at high risk of developing severe outcome is important to establish precision medicine

of SLE. [Methods] We reviewed the medical records of SLE patients filed between January 2004 and September 2016. Patients followed until September 2016 in our hospital were included in this analysis. We performed the principal component analysis of disease-associated lesions, such as mucocutaneous, serositis, nephritis, and neuro-psychiatric symptoms. [Results] 101 patients were enrolled. All patients fulfilled the ACR classification criteria (1997) and SLICC classification criteria (2012). 82 patients (81.2%) were female and the mean age at onset was 33±16 years. The cumulative frequency of common clinical manifestations were mucocutaneous 77.2%, serositis 26.7%, nephritis 54.5%, neuro-psychiatric 35.6% respectively. Principal component analysis revealed two distinct groups: group A "having mucocutaneous symptoms and neuro-psychiatric SLE" and group B "having lupus nephritis and serositis". When comparing these groups, frequency of performing intravenous cyclophosphamide therapy was 75.8% in group A and 70.6% in group B. Prevalence of anti-Sm antibody was higher in group A (69.7%) than in group B (35.3%) significantly (p=0.0196). [Conclusion] The present study suggested that SLE could be subclassified into 2 major groups. Larger sample size and further examination are needed in order to establish precision medicine of SLE.

ICW1-5

Functional alteration of M2 Macrophages contributes to pathogenesis of lupus nephritis

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Conflict of interest: None

Introcuction Recently, Macrophage (Mφ) polarization has gained attention in inflammatory diseases. Mφ can be classified into two functional subsets: classically activated Mφ(M1), which are characterized by cytotoxic properties; and alternatively activated Mφ(M2), which are involeved in resolution of inflammation. We have previously reported that chemical induction of heme oxygenase (HO)-1, which are predominantly expressed in M2, led to a significant reduction of proteinuria in MRL-Faslpr mice. Objectives To analyze association of Mφ polarity in lupus nephritis (LN). Methods M1Mφ and M2Mφ were generated from peripheral monocytes with M-CSF and GM-CSF, respectively. We stimulated these cells with type1 IFN, and determined expressions of CD163 (a marker of M2Mφ) and HO-1 by realtime PCR and immunohistochemistry. Immunohistochemistry was performed on renal biopsies from 20 cases with LN, using antibodies against CD68, CD163, and HO-1. Average number of M1Mφ, M2Mφ, and HO-1 positive cells per glomeruli were counted. In addition, we generated congenic mice MRL/Faslpr. C57BL/6J-Bach1-/-(a transcriptional repressor of HO-1) and analyzed difference of survival rate and proteinuria. Result In *In vitro* analysis of GM- and M-CSF induced human Mφ, M2Mφ showed higher expression CD163 and HO-1 compared to M1Mφ. HO-1 was downregulated in type1 IFN stimulated M2Mφ. Histological examination revealed that M2Mφ was predominantly present in LN glomeruli compared with M1Mφ(M2Mφ 7.95 vs M1Mφ 1.57/glomeruli). Interestingly, HO-1 positive cells were few compared to CD163 positive cells, suggesting aberrant regulation of HO-1 in M2Mφ in LN. MRL/Faslpr. C57BL/6J-Bach1-/- showed high expression of HO-1 in *in vitro* generated M2cMφ and showed improvement of proteinuria and survival rate. Conclusion Functional alteration of M2Mφ contribute to pathogenesis of LN.

ICW1-6

The clinical and laboratory analysis of macrophage activation syndrome secondary to juvenile systemic lupus erythematosus

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Conflict of interest: None

Objective: To investigate the clinical and laboratory features of macrophage activation syndrome (MAS) associated with juvenile systemic lupus erythematosus (jSLE). **Method:** The clinical and laboratory data of 14 patients with jSLE-complicated with MAS diagnosed in Saitama Children's Medical Center from November 2003 to August 2016 were retrospectively analyzed. **Results:** Twelve patients (85.7%) were female. The average age was 12.6 (7-20 age). Twelve of 14 patients developed MAS at initial manifestation of jSLE and two patients had MAS at the same time of relapsing jSLE. The average SLE disease activity index (SLEDAI) was 13. All patients had a high fever. The serum high levels of ferritin (93%), AST (100%), and LDH (85.7%) were frequently observed in jSLE patients with MAS, while the numbers of patients with coagulation disorders, lupus enteritis, pancreatitis and neuropsychiatric symptoms were 4, 2, 1 and 4, respectively. Glucocorticoids were used in all patients, among whom three received pulse methylprednisolone therapy. Two patients were treated with IVIG. Twelve patients were treated with immunosuppressants, including cyclophosphamide and mycophemolate mofetil, azathioprine, mizoribine. None patient died of MAS. **Conclusions:** In patients with jSLE, MAS was commonly seen in the incipient stage of jSLE and active disease. Fever, hyperferritinemia and liver damage are the most remarkable clinical and laboratory manifestations. In addition, we identified in jSLE patients, a cluster of MAS associated with severe complications. Early diagnosis and intensive therapy are the important parts to improve clinical outcome.

ICW2-1

Good outcome with low-dose Sulfamethoxazole (SMX)/ Trimethoprim (TMP) therapy for Pneumocystis jirovecii pneumonia (PCP) in connective tissue disease (CTD)

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Conflict of interest: None

【Objectives】For the treatment of PCP, the recommended dosage is 75 to 100 mg/kg SMX/day and 15 to 20 mg/kg TMP/day for 2-3 weeks. However, the dosages had higher rates of adverse drug reactions and required switching to an alternative therapy. On the other hand, several studies demonstrated the effectiveness of lower-dose SMX/TMP therapy (SMX 50-75 mg/kg/day and TMP 10-15 mg/kg/day) for PCP treatment. Therefore, we evaluated efficacy and safety of a lower dose SMX/TMP therapy compared with high-dose SMX/TMP therapy in CTD patients with PCP.【Methods】We retrospectively conducted consecutive CTD patients who received SMX/TMP for PCP treatment and allocated them to the low- dose (TMP≦10mg/kg/day-SMX≦50mg/kg/day) group and the high-dose (TMP>10 mg/kg/day-SMX>50 mg/kg/day) group.【Results】A total of 68 patients were included. Nineteen patients were allocated to the low-dose group and forty nine patients were allocated to the high-dose group. Clinical characteristics were the similar except for SMX/TMP dosages in both groups. Successful treatment rate of SMX/TMP therapy was 68.4% in the low-dose group and 40.8% in the high-dose group (P=0.12). On the other hand, switching to alternative therapy rate was 53.1% in the high-dose group and 26.3% in the low-dose group (P=0.12). Kaplan-Meier method revealed that continuation rate of SMX/TMP therapy in the low-dose group was significantly higher than that of the high-dose group (P=0.02). Dose increment therapy was 0% in the low-dose group and 4.1% in the high dose group (P=1.00). The overall mortality rate was 5.2% in the low-dose group and 4.1% in the high-dose group (P=1.00). No patients relapse within 6 month after the recovery of PCP.【Conclusions】Our findings indicated that low-dose SMX/TMP therapy was as effective as high-dose therapy with lower adverse drug reactions compared with high dose therapy in CTD patients with PCP.

ICW2-2

$CD11b^{+}Gr1^{dim}$Tolerogenic Dendritic Cell-Like Cells are Expanded in Interstitial Lung Disease of SKG Mice

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Conflict of interest: None

Background/Purpose: SKG mice develop interstitial lung disease (ILD) resembling rheumatoid arthritis-associated ILD (RA-ILD) in human. We identified a new cell population, $CD11b^{+}Gr1^{dim}$tolerogenic dendritic cell-like cells (tolDC-LCs), in the lung of zymosan A (ZyA)-treated SKG mice. The aim of this study is to elucidate the role of lung-infiltrating cells, especially $CD11b^{+}Gr1^{dim}$cells, in the pathogenesis of ILD of SKG mice. **Methods:** SKG mice were induced ILD by ZyA injection. The severity of ILD was evaluated by the area of diffusely affected lesion in HE stain, as follows: histological score (HS) 0: <10%, HS1: 10-29%, HS2: 30-59% and HS3: ≥60%. Lung-infiltrating cells (myeloid cells, helper T cells (Th cells) and innate lymphoid cells (ILCs)) were evaluated by flow cytometry. In vitro, lung-infiltrating cells cultured with GM-CSF (and IL-4) for 5 days and the proliferation of CSFE-labeled naïve T cells cultured with isolated $CD11b^{+}Gr1^{dim}$cells were evaluated by flow cytometry. **Results:** Histological analysis revealed that ZyA-treated mice developed various severity of ILD; HS1: 25%, HS2: 50% and HS3: 25%. Myeloid-derived suppressor cells (MDSCs), $CD11b^{+}Gr1^{dim}$cells, Th17 cells, ILC1s and ILC3s were increased in the lung of ZyA-treated mice, and the proportion of these cells varied depending on the HS. Especially, $CD11b^{+}Gr1^{dim}$cells were expanded only in the lung of HS3. About 50% of $CD11b^{+}Gr1^{dim}$cells expressed CD11c, and the cells suppressed naïve T cell proliferation in vitro. These results indicate that $CD11b^{+}Gr1^{dim}$cells are tolDC-LCs. GM-CSF (and IL-4) induced the differentiation of $CD11b^{+}Gr1^{dim}$cells from total lung cells and $CD11b^{+}Ly6C^{high}$cells (monocytic (M)-MDSCs). GM-CSF mRNA and GM-CSF-producing Th17, ILC1s and ILC3s were increased in the lung of ZyA-treated SKG mice. **Conclusion:** We found a unique cell population, $CD11b^{+}Gr1^{dim}$tolDC-LCs, in ILD of SKG mice, and the cells may be a potential target for the treatment of RA-ILD.

ICW2-3

DNA microarray analysis of labial salivary glands in patients with Sjögren's syndrome: Comparison with IgG4-related disease

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Conflict of interest: None

Objective: To examine genes expressed specifically in labial salivary glands (LSGs) of patients with Sjögren's syndrome (SS) in comparison with those of patients with IgG4-related disease (IgG4-RD) and to identify genes involved in the pathogenesis of SS. **Methods:** 1) Gene expression was analyzed by DNA microarray in LSGs of SS, IgG4-RD and healthy controls (HC). Validation of differentially expressed genes (DEGs) up-regulated in SS was performed by quantitative PCR (qPCR) using LSGs. 2) Protein production of validated genes in LSGs from SS and IgG4-RD was examined by immunofluorescence (IF) assay. 3) Functional analysis of the DEG was performed using peripheral $CD4^{+}$ T cells of SS patients. **Results:** 1) Among 1320 DEGs up-regulated in SS, CXCL9, NR4A2, CD26, SGK1, IRF4 and PDK1 were selected as candidates for validation. qPCR validated significantly higher expression of NR4A2 and CD26 in LSGs of SS than in IgG4-RD. 2) IF staining in LSGs revealed higher production of NR4A2 and CD26 in $CD4^{+}$ T cells of SS than in those of IgG4-RD and localization of NR4A2 in nuclei of IL-17-producing cells. 3) Significantly higher NR4A2 mRNA expression was observed in peripheral $CD4^{+}$ T cells of SS than HC. IL-17-producing peripheral $CD4^{+}$ T cells under Th17-polarizing conditions were significantly increased in SS than in HC. Population of these Th17 cells was significantly correlated with NR4A2 mRNA expression at baseline. Protein expression of NR4A2 was localized in nuclei of $CD4^{+}$ T cells under Th17-polarizing conditions in comparison with Th0 conditions. Nuclear NR4A2 expression in Th17-polarized $CD4^{+}$ T cells analyzed by densitometry for cellular IF was significantly increased in SS compared with HC. In addition, an inhibitor of importin-β, importazole, inhibited nuclear transport of NR4A2 and Th17 polarization along with IL-21 expression in $CD4^{+}$ T cells under Th17-polarizing conditions. **Conclusion:** NR4A2 might be a novel molecule involved in the pathogenesis of SS via Th17 differentiation.

ICW2-4

IL-2/anti-IL-2 antibody complexes adversely affect human immune cells despite the proliferation of regulatory T cells in vivo

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Conflict of interest: None

[Background] Administration of mIL-2/anti-mIL-2 Ab (JES6-1) complexes (IL-2cxCD25) induces a selective proliferation of regulatory T cells (Treg) in mice by the specific stimulus to CD25, thereby resulting in attenuation of autoimmunity in various mouse models. **[Objective]** The purpose of this study is to clarify the regulatory effect of hIL-2cxCD25 (hrIL-2/anti-hIL-2 mAb (5344) complexes) on human immune cells, providing a basis for clinical application of novel Treg therapy for autoimmune disorders. **[Method]** We first analyzed the ability of hIL-2cxCD25 to induce expansion of Treg ($CD4^{+}CD25^{+}Foxp3^{+}$ T cells). Human PBMC were cultured with hIL-2cxCD25 and anti-CD3 Ab in vitro, and assessed the cell proliferations by flow cytometry. Next, using humanized NOG mice, we investigated in vivo the effect of hIL-2cxCD25 on donor human immune cells in recipient mice. We further investigated whether the expansion of Treg could ameliorate the severity of xenogenic-GVHD in humanized NOG mice. **[Result]** In vitro, hIL-2cxCD25 did not induce Treg proliferation (Treg/$CD4^{+}$: with vs without hIL-2cxCD25; 1.7% vs 3.1%, $p = 0.01$), while they expanded much more effector T cells (Teff: $CD4^{+}CD25^{+}Foxp3^{-}$, Teff/$CD4^{+}$: 45.8% vs 28.0%, $p = 0.01$). In vivo, administering hIL-2cxCD25 caused an increase in Treg and Teff, transiently (day4: Treg, Teff/$CD4^{+}$: 23.2%, 18.7%). Contrary to expectations, the severity of x-GVHD in humanized NOG mice was significantly worse by hIL-2cxCD25 injection (prognosis: day 27.8 vs 20.8, $p = 0.013$, weight loss: $p = 0.003$). Analysis of human 16 cytokines of the NOG mice serum (multiplex ELISA arrays) revealed that hIL-2cxCD25 induced inflammatory cytokines, such as IFN-γ, TNF-α, IL-5. **[Conclusion]** The present results using humanized mice demonstrate that hIL-2cxCD25 activate human Teff as well as Treg, and cause harmful inflammation unexpectedly, suggesting the need further study and the importance of immunological studies using human cells. No conflict of interest.

ICW2-5

Increased IgG4 and decreased IgA with higher number of organ involvement is the risk factors for relapse of IgG4-related disease

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Conflict of interest: None

Objectives: IgG4-related disease (IgG4-RD) often recurs during the glucocorticoid (GC) tapering, however there is only limited information on the risk factor of relapse. The aim of this study is to clarify the characteristics of IgG4-RD which is likely to relapse by comparing clinical characteristics of patients with relapse and those without. **Methods:** Consecutive patients with IgG4-RD receiving GC therapy in our department were enrolled. We compared patient characteristics and laboratory findings at diagnosis, extracted candidate predictors by logistic regression analysis and determined most useful cut off values of the candidate predictors by receiver operating characteristic curve analysis. **Results:** Among 38 IgG4-RD patients, 9 recurred and 29 did not. There was no difference in age, sex, disease duration, doses of induction and maintenance therapy and observation periods, between the 2 groups. Patients with recurrence had significantly higher total protein (8.2 vs 7.4 g/dl, $p = 0.03$), IgG (2470 vs 1741 mg/dl, $p = 0.005$), IgG4 (919 vs 424 mg/dl, $p < 0.001$), sIL-2R (1057 vs 639 U/ml, $p = 0.008$), ESR (83.6 vs 26.2 mm/hr, $p = 0.001$), and number of organ involvements (4.7 vs 2.8, $p = 0.04$), while the level of IgA was lower (116 vs 205 mg/dl, $p = 0.03$) compared to non-recurrent group. Among them, IgG4, IgA and the number of organ involvements were the highest three pseudo R squared values ($R^2 = 0.52$, 0.46 and 0.33) in univariate logistic regression analysis. The most useful cut-off values of IgG4, IgA and number of organ involvements were 500 mg/dl (sensitivity for patients with relapse 100%, sensitivity for patients

without relapse 31%), 145 mg/dl (78.6%, 25.0%) and 4 (88.9%, 24.1%) respectively. **Conclusion:** The high level of serum IgG4, the low level of serum IgA and more than 4 organ involvements at diagnosis are the characteristics indicating futuristic relapse of IgG4-RD during treatment with GC.

ICW2-6

Anti-C1q Antibodies Contribute to the Pathogenesis of Recurrent Pregnancy Loss via Complement Activation

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Conflict of interest: None

Objectives: Complement activation is observed in recurrent pregnancy loss (RPL) as well as antiphospholipid syndrome (APS). Anti-C1q antibodies (aC1q) has been shown to associate with complement activation in APS, but the relevance of aC1q in RPL is still unclear. The aim of this study was to explore the role of aC1q in RPL. **Methods**: We conducted a retrospective cross-sectional study comprising 134 patients with RPL of unknown etiology, 27 with obstetric APS (OAPS), 14 parous connective tissue disease patients without historical obstetric complications, and 17 parous healthy controls (HC). Serum levels of aC1q were measured using a solid-phase ELISA. In murine model, BALB/c mice were mated and the presence of vaginal plug was defined as day 1 of pregnancy. Mice were intravenously injected with aC1q monoclonal antibody (JL-1), isotype control IgG2b or PBS on day 8 and 12. To block C5a receptor (C5aR), mice were intravenously pre-treated with anti-C5aR antibody 30 minutes before the injection of JL-1 on day 8. Fetal resorption ratios, weights of fetuses and placentas, serum levels of C3a and immunohistochemical staining of complement components on placenta were compared among each group at the sacrifice on day 16. **Results**: In RPL patients, aC1q was more prevalent (35% vs 12%, $p < 0.05$) and its titer was significantly higher (12 [IQR: 8-21] vs 0 [IQR: 0-4.3], $p < 0.0001$) than in HC. In mice treated with JL-1, fetal resorption ratio was higher ($p < 0.05$), both weights of fetuses and placentas lower ($p < 0.05$) and serum levels of C3a higher ($p < 0.01$) than in control mice. Furthermore, diffuse deposition of C3 on placenta was observed in JL-1 treated mice. The additional C5aR blockade cancelled these pathogenic changes. **Conclusions**: Our study indicates that aC1q contributes to the pathogenesis of RPL and that anticomplement therapy might be effective for some groups of patients with RPL for whom specific treatment remains to be established.

ICW3-1

***FCGR2B* hypermethylation after IVIG treatment and associated with intravenous immunoglobulin treatment response in Kawasaki Disease**

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Conflict of interest: None

Objective: Kawasaki disease (KD) is a systemic autoimmune like vasculitis most affects children less than 5 years old. The Fc gamma receptor (FCGR) family contains multiple activating receptors, and a single inhibitory, FCGR2B. This study was conducted to investigate the methylation status of FCGR2B in different stage of KD. **Materials and methods:** FCGR2B methylation levels were studied from 36 patients with KD and 40 age and gender matched controls by pyrosequencing. Different stage of sample from all 36 KD patients including KD1 (24 hours before IVIG), KD2 (within 3 days after IVIG), KD3 (3 weeks to 6 months after IVIG), KD4 (6 months to one year after IVIG) and KD5 (at least one year after IVIG treatment) were collected for study. **Results:** The age (1.79 ± 1.3 vs. 2.29 ± 2.66 year-old, $p=0.147$) and male gender (19/36 vs. 23/40, $p=0.412$) distribution between KD and controls showed with significant difference. ($p>0.05$) The methylation level of FCGR2B didn't showed significant difference in KD1 (before IVIG) when compared with controls ($p>0.05$). Significantly increase of methylation levels was found in KD2, KD3, KD4 and KD5 ($p<0.001$) when compared with KD1 and controls. The most high levels of FCGR2B during the followed up period was in KD3 (3 weeks to 6 months) ($p<0.001$), then subside but still significant higher level of methylation in KD5 (1 to 2 years after acute stage) when compared with KD1 and controls. ($p<0.05$) Significant lower methylation levels was found in IVIG resistance group in KD1 (20 ± 1.7 vs. 8 ± 2.8, $p=0.02$), KD2 (29 ± 2.4 vs. 13 ± 3.3, $p=0.02$), KD3 (33 ± 2.3 vs. 19 ± 3.1, $p=0.03$), but without significant difference in KD4 and KD5 ($p>0.05$). **Conclusion:** This is the first time to report the methylation of FCGR2B and showed hypermethylation after IVIG treatment even one year after disease onset. Hypomethylation of FCGR2B is associated with IVIG resistance.

ICW3-2

Semaphorin4D inhibits neutrophil activation and is involved in the pathogenesis of neutrophil-mediated autoimmune vasculitis

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Conflict of interest: None

Object Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a refractory disease, caused by inappropriate activation of neutrophils and their interactions with endothelium. The aim of this study is to investigate the role of Semaphorin4D (SEMA4D) in regulation of neutrophil activation, and its involvement in the pathogenesis of AAV. **Methods** Serum levels of SEMA4D was evaluated by enzyme-linked immunosorbent assay. Cell-surface expression of membrane SEMA4D in AAV patients was evaluated by flow cytometric analysis. To determine the direct interaction between neutrophil SEMA4D with endothelium, WT or *SEMA4D*$^{-/-}$ mice neutrophils were cultured with an endothelial cell line (MS1), and stained with SYTOX green for neutrophil extracellular traps (NETs) formation assay. The efficacy of treatment neutrophils with recombinant plexin B2, an endothelial ligand for neutrophil SEMA4D receptor, was evaluated by measuring kinetic oxidative burst. **Results** Serum levels of soluble SEMA4D were elevated in AAV patients and were correlated with disease activity scores. Cell-surface expression of SEMA4D was significantly down-regulated in neutrophils from AAV patients, a consequence of shedding of cell-surface SEMA4D. Membranous SEMA4D on neutrophils bound to plexin B2 on endothelial cells, and this interaction decreased NETs formation. Recombinant plexin B2 suppressed neutrophil Rac1 activation through SEMA4D's intracellular domain, and inhibited AAV patient–derived IgG-induced oxidative burst. **Conclusions** Neutrophil cell-surface SEMA4D receptor negatively regulates the activation of neutrophils, and the shedding of SEMA4D leads to the aberrant neutrophil activation in the pathogenesis of AAV. SEMA4D has potential as a disease activity marker and a therapeutic target for AAV.

ICW3-3

B cell phenotype and efficacy of rituximab in patients with ANCA associated vasculitis: 6-months results of FLOW study

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Conflict of interest: None

Background: B cell depletion by rituximab (RTX) is effective treatment for ANCA associated vasculitis (AAV). However, the phenotype of peripheral B cells and the selection criteria for RTX in AAV remain un-

clear. **Methods:** Phenotypic characterization of the circulating B cells was defined by 8-color flow cytometric analysis for "Human Immunology Project" termed by NIH/FOCIS in 39 AAV patients (12 GPA and 27 MPA). Based on the analysis, the patients were considered suitable to receive immunosuppressive drugs or RTX. All patients also received high dose glucocorticoids (GC). We evaluated the efficacy and safety outcomes at 6 months after treatment. Definition of clinical improvement was a reduction of 50% or more in BVAS in vital organs. **Results:** The proportion of effector or class-switched memory B cells was increased in 15 out of 39 patients (38%). Twenty-two patients were treated with GC+RTX and all achieved clinical improvement. Seventeen patients received GC and conventional immune suppressants (including 12 intravenous cyclophosphamide and 5 azathioprine), 14 patients achieved clinical improvement. There was no significant difference in the rate of improvement between the two groups. The rate of clinical improvement in patients with circulating B cell abnormality was significantly lower than in patients without B cell abnormality. Among the patients with B cell abnormality, the rate of GC reduction was significantly higher in RTX group than in conventional immune suppressants group. Six patients in RTX group and 9 patients in conventional immune suppressants group had severe infection. **Conclusion:** The presence of B cell abnormality was associated with treatment resistance. However, among patients with circulating B cell abnormality, RTX was effective and showed rapid effect of GC tapering compared to conventional immune suppressants. The results suggested that multi-color flow cytometry might be useful for the selection of RTX therapy in AAV patients.

ICW3-4

The initial symptoms of Takayasu arteritis and its relation to delayed diagnosis and prognosis

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Conflict of interest: None

Objectives: The early diagnosis of Takayasu arteritis is sometimes difficult owing to its nonspecific initial symptoms, which could be associated with poor prognosis. The aim of this study was to clarify the characteristics of initial symptoms of Takayasu arteritis, the delay in diagnosis and its relationship with prognosis. Methods: Consecutive patients with Takayasu arteritis with enough information in our hospital were enrolled. They were retrospectively analyzed for the initial symptoms, laboratory findings at diagnosis, the period from symptom onset to diagnosis, and the prognosis. Results: Sixty two patients were enrolled with 8% of male and the mean age at diagnosis of 36 years old. The mean period from the initial symptoms to diagnosis was 970 days. The initial symptoms were generalized illness (fever, fatigue, or body weight loss, etc, 31%), cranial symptoms (dizziness, syncope, headache, or visual field loss, etc, 26%), claudication of extremities (14%), arthralgia (6%), vascular diseases (myocardial or cerebral infarction, hypertension, etc, 14%), and abnormal medical examinations (heart murmur, abnormal chest X-ray, etc, 9%). No differences were found in sex and the age at diagnosis among those with different initial symptoms. The patients without generalized illness or arthralgia showed lower CRP levels (2.5 mg/dL vs 5.8 mg/dL, P = 0.021), had a tendency of requiring a longer time before diagnosis (1017 days vs 584 days, P = 0.315), and had higher rates of undergoing subsequent major surgeries or death than the patients with those symptoms. Conclusion: Lacking inflammatory symptoms including generalize illness and arthralgia in patients with Takayasu arteritis were related with delayed diagnosis and poor prognosis.

ICW3-5

Tocilizumab monotherapy increases MDC (CCL22)/TARC (CCL17) in the serum of patients with microscopic polyangiitis and polymyalgia rheumatica but not rheumatoid arthritis

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Conflict of interest: None

Objectives To elucidate the mechanism of tocilizumab (TCZ) efficacy in patients with microscopic polyangiitis (MPA), polymyalgia rheumatica (PMR) and rheumatoid arthritis (RA). **Methods** We examined multiple serum levels of cyto- and chemokines in patients with MPA, PMR and RA at 0 (baseline), 4, 24, 52, and 78 weeks after initiating TCZ monotherapy and compared those of healthy controls (HC), by microspot-based multiplex assays using electrochemiluminescence. MPA patients newly diagnosed according to the Watts' classification algorithm (n = 8), PMR patients according to the 2012 ACR/EULAR classification criteria (n = 7) and RA patients according to the 2010 RA classification criteria (n = 6), and HC (n = 8) were employed in this study. MPA, PMR and RA patients received 8 mg/kg of intravenous TCZ monthly for one year without any corticosteroids (CSs) or immunosuppressive agents. Six out of eight patients with MPA and all patients with PMR received TCZ fortnightly for the first 2 months, and then monthly for the next 10 months. All patients were followed up without any treatment from 52 weeks. **Results** The serum IL-6 level at 4 weeks increased from the baseline and decreased gradually even after cessation of TCZ from 52 weeks to 78 weeks in MPA/PMR. The serum levels of MDC (CCL22) and TRAC (CCL17) in all patients at baseline and HC were not significantly different among the groups. However, the levels of these chemokines in MPA/PMR at 52 weeks were significantly increased from the baseline, whereas RA patients did not show any change in the levels during the period. Interestingly, all patients with MPA/PMR could keep clinical remission at 78 weeks even after cessation of TCZ. On the other hand, RA patients became flare after cessation of TCZ until 78 weeks except for one patient. **Conclusions** Our data suggested that TCZ may suppress the disease activities of MPA/PMR, which is different from RA and keep clinical remission even after cessation of TCZ by increasing MDC/TARC.

ICW3-6

Elevated Serum D-dimer at Baseline Predicts Poor in-hospital Outcome in Patients with Granulomatosis with Polyangiitis Flares

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Conflict of interest: None

Introduction: Even though the prognosis of granulomatosis with polyangiitis (GPA) got improved as understanding of vasculitis got deeper, an in-hospital mortaility result of disease flares is still high. Even worse, we don't have any good disease marker that can predict the in-hospital prognosis so far. We focused on the fact that pathogenesis of AAV is relevant to endothelial dysfunction. Because D-dimer is an indicator of coagulation/fibrinolysis activity, we investigated the association between hospitalization outcomes and the level of D-dimer in patients with GPA. **Materials and Methods**: This retrospective study included 43 patients with GPA who were due to GPA flare between January 2006 and December 2015 at Severance Hospital, Seoul, Korea. We only reviewed D-dimer level which were measured within 24 hours after the patients being hospitalized. We used BVAS version 3.0 for the evaluation of disease activity of GPA. The patients were divided into two groups by a median D-dimer level: high D-dimer and low D-dimer group. And also clinical features and hospitalization outcomes between the two groups were evaluated. And also we conducted uni – and multivariate analysis in order to find out the relevent factors related to in-hospital outcome. **Results**: D-dimer level at baseline show the direct correlation with BVAS score as a conventional disease marker of vasculitis in the Pearson correlation analysis. In the Chi-square test, ICU admission and in-hospital mortality rate were significantly higher in high D-dimer group (n=21) than low D-dimer group (n=22) (66.6% vs 36.3%, p = 0.47; 38.1% vs 4.54%, p = 0.009, respectively). Also, D-dimer was a statistically significant factor related to ICU admission in the multivariate logistic regression analysis (Hazard ratio, 2.215; 95% confidence interval, 1.166-4.206; p=0.015). **Discussion**: Elevation of D-dimer measured at admission was significantly associated with poor prognosis in hospitalized patients with GPA.

ICW4-1

Stone composition and urinary stone risk in primary gout patients: A Matched Case Comparative Study

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Conflict of interest: None

Objectives: To explore the clinical value of urinary uric acid analysis by testing the common urinary stone composition, serum and urinary biochemical features in patients with primary gout. **Materials and Methods:** All the patients diagnosed as primary gout and urolithiasis in Peking University First Hospital from 2009 to 2015 were included in the study. An age and gender matched case cohort of gout without urolithiasis was selected from our gout database. Their clinical features, baseline urinary metabolic panels and stone composition were analyzed and compared between the two group of patients. **Results** 48 male gout patients with urolithiasis and 96 male age-matched gout patients without urolithiasis as control group were enrolled in the study. Most 136 (94.4%) of patients were under excretion of uric acid. Among 48 gout patients with uric acid urolithiasis, there were 30 (62.5%) patients who had pure uric acid stones, and 18 (37.5%) mixed of both uric acid and oxalic acid stones. Compared with mixed stone group, the mean age was significantly lower in uric acid stone group (45.8 vs. 60.4 years, P=0.016); and disease duration was shorter (42.1 vs. 71.1 months, P=0.005). The 24-hour urinary uric acid were significantly higher in the uric acid stone group (5205.13 vs. 2131.7 μmol/d, P=0.020). Also, the mean of both Ccr and Cua were higher (119.2 vs. 74.7 ml/min, P=0.048, 6.3 vs. 3.2 ml/min, P=0.021). **Conclusion** Urinary analysis of 24-hour uric acid and short disease duration are risk factors for pure uric acid urolithiasis in Chinese primary gout patients.

ICW4-2

Involvement of CD163-positive Macrophages in the Pathogenesis of Arthritis via Modulation of Inflammatory Cytokine Expression in the Synovium of a Murine Model

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Conflict of interest: None

[Object] CD163, a cell-surface marker of M2 macrophages, is a glycoprotein in the group B cysteine-rich scavenger receptor family that binds to and internalizes hemoglobin-haptoglobin complexes. The restrictive expression of CD163 by macrophages has been confirmed in the affected joint tissues of patients with Rheumatoid arthritis; however, the pathogenic roles of CD163-positive macrophages in inflammatory arthritis remain unclear. We investigated the roles of CD163-positive macrophages in arthritis development in mice. [Methods] A collagen antibody induced arthritis (CAIA) mouse model was established using a combination of monoclonal anti type II collagen antibodies and lipopolysaccharide (LPS) in C57BL/6 (B6)-background CD163 knockout (KO) mice. Total RNA was isolated from the ankle joints of the mice for gene expression analysis by qRT-PCR. Peritoneal macrophages derived from B6 or CD163 KO mice were stimulated with LPS, and cytokine production was evaluated by ELISA. [Results] CD163 KO mice exhibited significant exacerbation of clinical scores during arthritis compared with control B6 mice. Histomorphometric quantification of the arthritic changes in the joint tissues confirmed the clinical assessment, with significant increases in inflammatory cell infiltration and bone erosion in CD163 KO mice. CD163 KO mice demonstrated significantly elevated IL-1β, IL-6, and CXCL1 mRNA expression levels in the inflamed synovium. Exposure of CD163 deficient peritoneal macrophages to LPS resulted in enhanced production of critical arthritogenic mediators, including IL-1β and IL-6. [Conclusions] CD163 deficiency exacerbates arthritis severity via up-regulation of synovial tissue IL- 1β and IL-6. Consistent with our *in vivo* observations, LPS markedly amplified IL-1β and IL-6 production by CD163 deficient macrophages. These findings define an inhibitory role of the CD163 antigen on the cell surface of macrophages in the pathogenesis of arthritis.

ICW4-3

Radiographic changes in Thoracic spine and facet joints were already observed at the time of diagnosis in many patients with ankylosing spondylitis

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Conflict of interest: None

Objectives: We performed this study to find out how many patients with ankylosing spondylitis (AS) have radiographic changes in T spine at first visit using computed tomography. Methods:We enrolled the patients who were diagnosed as AS by modified NY criteria in Kyung Hee university hospital at Gang dong in Seoul, South Korea from Mar 2008 to Dec 2015. We performed a whole spine CT in each patient to evaluate the radiographic involvement of spine. Total 1,170 patients were enrolled and analyzed. We examined the presence of bone spurs in vertebral bodies (VB) and radiographic changes of facet joints in L and T spine and costo-vertebral joints (CVJ). Results:Of the 1,170 enrolled patients, the 920 patients (79%) were male. Mean age was 33.0 ± 10.0 years and mean disease duration was 10.5 ± 9.5 years. 34.1% of patients had at least one bone spur and 26.3% had at least one lesion in facet joints in L spine. In T spine, 47.2% of the patients had already at least one bone spur, and 28.2% had at least one lesion in facet joints. 32.8% of the patients had already at least one lesion in CVJs. Each radiographic change is associated with one another (p=0.001). These all radiographic changes were significantly more frequently observed in the patients with old age and long disease duration at the point of diagnosis (p=0.001). The lesion of CVJs and facet joints in T spine were observed more frequently in male than female significantly (respectively p=0.02, 0.00). 19.2% of the patients had radiographic changes in T spine without in L spine. Conclusions: At the point of diagnosis, many patients already had radiographic changes in T spine. We suggest that the radiographic changes of the T spine to be included in radiographic progression score system such as mSASSS. And it is possible to early detection of radiographic progression through the observation of T spine in AS.

ICW4-4

Th17 Cells in Ankylosing Spondylitis Have a Specific miRNA Signature (miR-10b-5p is Specifically Upregulated as Part of a Feedback Loop)

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Conflict of interest: None

Objective The aim of this study was to find out Th17 cell specific microRNAs and their function in ankylosing spondylitis (AS). **Methods** IL-17A-producing CD4+ T cells from AS patients and healthy controls were FACS-sorted for miR RNA sequencing and qPCR validation. Target genes of miRNA were also screened using transcriptome analysis, then confirmed by qPCR and luciferase assay. miR-10b function was determined by miR mimic expression followed by cytokine measurement, and flow cytometry. **Results** AS Th17 cells exhibited a miR signature characterized by upregulation of miR-155-5p, miR-210-3p and miR-10b. miR-10b has not been described previously in Th17 cells and was selected for further characterization. miR-10b is transiently induced in in-vitro differentiated Th17 cells. TNF –α and IL-6 enhanced miR-10b expression by CD4+T cells. Transcriptome, qPCR and luciferase assays suggest that MAP3K7 is targeted by miR-10b. Both miR-10b over-expression and MAP3K7 silencing inhibited production of IL-17A by both total CD4 and differentiating Th17 cells. **Conclusions** AS Th17 cells have a specific miR signature and upregulate miR-10b in vitro. Our data suggest that miR-10b is upregulated by pro-inflammatory cytokines and may act as a

feedback loop to suppress IL-17A by targeting MAP3K7. miR-10b is a potential therapeutic candidate to suppress pathogenic Th17 cell function in AS patients.

ICW4-5

Characteristic phenotypes of peripheral T helper cells and efficacy of biological DMARDs in patients with psoriatic arthritis

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Conflict of interest: None

Objectives: Biological DMARDs (bDMARDs) such as adalimumab (ADA), infliximab (IFX), ustekinumab (UST) and secukinumab (SEC) become available and efficacious in patients with psoriatic arthritis (PsA). However, it remains unclear how we can differentially use these bDMARDs to individual patients. We assessed peripheral immune cell phenotypes in patients with PsA treated with bDMARDs and tried to subdivide patients by the lymphocyte phenotypic difference. **Methods:** 44 patients were treated with bDMARDs. Peripheral immune cell phenotypes were assessed by 8-color flow cytometric analysis for "Human Immunology Project Consortium" termed by NIH and FOCIS in 23 patients with PsA. **Results:** The PASI score, SDAI, DAS28 (ESR) were significantly decreased from 8.8/17.7/4.38 at baseline to 3.3/8.6/2.28 at month 6. Among $CD4^+$ T cells, proportion of $CD3^+CD4^+CXCR3^-CCR6^+CD38^+HLA\text{-}R^+$ activated Th17 cells were significantly higher in patients with PsA than in healthy volunteers. In addition, 23 patients with PsA were subdivided into 4 patterns in the phenotypes of peripheral $CD4^+$T cells: $CXCR3^+CCR6^-CD38^+HLA\text{-}DR^+$ activated-Th1 cells dominant (5 cases), $CXCR3^-CCR6^+CD38^+HLA\text{-}DR^+$ activatedTh17 cells dominant (8), high activated-Th1/Th17cells (4), and low activated-Th1/Th17 cells (6). After the 6-month treatment, activated Th1 cells decreased in patients with activated Th1 cells dominancy successfully treated with UST. In addition, activated Th17 cells decreased in patients with activated Th17 dominancy successfully treated with SEC and activated Th1 and Th17 cells decreased in both activated Th1 and Th17 high successfully treated ADA. **Conclusion:** Our study showed, peripheral immune-phenotyping could be useful tool to precision medicine in PsA. Based on lymphocyte phenotype, bDMARDs can be differentially selected as followings; UST for patients with activated Th1 dominancy, SEC for patients with activated Th17 dominancy, ADA for patients with both-high and low activated Th1/Th17 cells.

ICW4-6

Cartilage-specific deletion of ULK-1 results in inhibition of autophagy, increased expression of cartilage catabolic factors and enhanced synovial inflammation

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Conflict of interest: None

Objectives: ULK1 is the most upstream autophagy inducer. Our previous study has shown that cartilage-specific ULK-1 knockout (KO) mouse subjected to osteoarthritis (OA) surgery (DMM model) exhibit accelerated OA phenotype associated with increased chondrocyte loss and cartilage destruction in vivo (Abou et al., In Preparation). However, the mechanisms associated with the accelerated OA phenotype in ULK1 KO mice are unknown. In this study, we investigated the effects of cartilage-specific ablation of ULK1 on autophagy and catabolic cascades during OA pathogenesis. We also investigated the effect of cartilage-specific ULK1 deletion on synovial inflammation and fibrosis. **Methods**: Doxycycline-induced cartilage-specific ULK-1 KO mice were generated using Cre-Lox system. 10 weeks old control and KO mice underwent DMM surgery to induce OA. Hind limbs from mice treated with either doxycycline or PBS as control were isolated, fixed and sectioned for safranin-O/Fas green staining, HE staining, trichrome staining and immunohistochemistry. **Results**: Immunohistochemical analyses indicated that ULK1 mice exhibiting accelerated OA phenotype and articular chondrocyte loss showed significant down regulation in autophagy (LC3B staining) while significantly increased expression of MMP-13 and type II collagen depletion in ULK-1 KO mice. Characterization of synovium through HE and trichrome staining revealed an increase in synovitis (inflammatory cell influx and synovial fibrosis) in ULK-1 KO mice compared to control mice. **Conclusion**: These data suggests that ULK-1 may be crucial for maintaining joint homeostasis by controlling autophagy signalling as well as the balance between catabolic and anabolic processes.

ICW5-1

Impact of the 2011 triple disaster in Fukushima, Japan, on activities of rheumatoid arthritis: a retrospective cohort study

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Conflict of interest: None

Objective As a huge disaster threatens livelihood of the residents, it inevitably affects living environments of the residents in the affected area, thus may affect activity of rheumatoid arthritis (RA). This study aims at assessing the impact of the 2011 Fukushima Disaster on RA activity at the disaster area. **Methods** Medical records of RA patients at a hospital near the Fukushima Daiichi Nuclear Power Plant were obtained. Data of internal radiation exposure levels of radioactive cesium were also collected when available. For each clinical parameters, titres of last but one visit before the disaster (Pre-pre), the last visit before the disaster (Pre), and the first visit after the disaster (Post) were obtained. Changes in values before and after the disaster were calculated as follows. ΔPre =(Pre) -(Pre-pre) ΔPost =(Post) -(Pre) Titres of Pre and Post as well ΔPre and ΔPost were compared using paired t-test. **Results** In total 58 patients (female: 81%) were included, among whom 5 (9%) resided within no-entry zone. Average age and disease duration were 63.4 years old and 15.7 years, respectively. Tender joint counts, swollen joint counts, and titre of rheumatoid factor significantly increased after the disaster. Concomitant use of methotrexate negatively correlated with the increase in RF. Evacuation status, temporal change of doctor, and disease activity before the disaster did not appear to correlate with the exacerbation. Data of internal exposure levels of radioactive cesium were available for 16 patients and only one showed detectable level, which was minimum. **Conclusions** Exacerbation of RA activity after the triple disaster was observed. As evacuation status and radiation exposure did not seem to affect the activity, other factors such as mental stress and lifestyle change might be the causes of the deterioration. As exacerbation of RA severely affect the refuge life, care for RA after a disaster needs to be taken into consideration in relief activities.

ICW5-2

The distribution of affected joints is associated with future clinical response to tumor necrosis factor inhibitors in patients with rheumatoid arthritis –Data from ANSWER cohort-

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Conflict of interest: None

Objectives: We analyzed the prognostic significance of the distribution of affected joints in patients with rheumatoid arthritis (RA) at starting tumor necrosis factor inhibitors (TNFi) to predict remission at week 24. **Methods:** The present study was conducted using data from ANSWER (Kansai consortium for well-being of patients with rheumatic diseases) cohort. RA patients treated with TNFi for more than 3 months were enrolled. Twenty-eight joints were divided into three groups (1: PIP joints, 2: MCP joints and 3: wrist and large (elbow, shoulder and knee) joints). The affected joints of each joints group were counted at baseline in each RA patient (PIPc: PIP joints count, MCPc: MCP joints count, and LJc: wrist and large joints count). Other clinical and demographic characteristics were also collected at baseline. The disease status at baseline, weeks 12 and 24 was assessed using the disease activity score (DAS 28). The primary endpoint was clinical remission (DAS28 < 2.6) at week 24. We investigated whether the distribution of affected joints at baseline was associated with the endpoint. **Results:** Data from 250 TNFi-treated RA patients were analyzed. Among them 101 patients achieved the endpoint and these patients showed shorter disease duration, younger age, higher proportion of naïve for biologic agents, lower DAS28 and higher amount of PIPc significantly than those who did not achieve the endpoint. Multivariate logistic regression analysis with the endpoint as a dependent variable disclosed that PIPc, naïve for biologic agents, and DAS28 at baseline were associated with the endpoint independently. As the cut-off point of PIPc (calculated from ROC curve) was 1, any affected PIP joint was confirmed to be associated with higher proportion of the endpoint independently by multivariate analysis. **Conclusion:** We suggested that RA patients with PIP joints involvement were more likely to achieve clinical remission responding to TNFi than those with no PIP joints involvement.

ICW5-3

A novel concept of M1 and M2 monocytes in rheumatoid arthritis; pro-inflammatory monocyte polarization imbalance, anti–citrullinated protein antibody and osteoclastogenesis

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Conflict of interest: None

Objectives: In rheumatoid arthritis (RA), bone erosions are caused mainly by osteoclasts which are derived from monocytes. Monocytes consists of different subtypes such as M1 monocytes and M2 monocytes. We attempted to investigate relationship among M1 monocytes or M2 monocytes, ability of osteoclast differentiation and clinical characteristics in RA patients. **Methods:** Peripheral blood mononuclear cells (PBMC) were isolated from RA patients and healthy donors, then we investigated the number of M1 monocytes or M2 monocytes by fluorescence-activated cell sorting. We defined M1 monocytes as CD14, CD68 and CCR2 positive cells and M2 monocytes as CD14, CX3CR1 and CD163 positive cells. We also obtained CD14 positive cells from PBMCs from RA patients and healthy donors using CD14 beads and cultured with medium containing receptor activator for nuclear factor kappa-B ligand and macrophage colony-stimulating factor to investigate osteoclast differentiation in vitro. **Results:** This study included 40 RA patients and 20 healthy donors. Twenty two patients (55%) were ACPA positive. Median M1/M2 ratio was 0.59 (0.31-1.11, IQR). There were no differences between RA patients and healthy donors. ACPA positive patients had higher M1/M2 ratio in vivo (0.87 vs. 0.41, p=0.028) and more number of osteoclasts in vitro (97 cells per well vs. 37 cells per well, p=0.003) than ACPA negative patients. Furthermore, there was positive correlation between M1/M2 ratio and the number of differentiated osteoclasts in vitro in RA patients (ρ=0.81, p<0.01). RA patients with M1/M2 ratio >1 (having relatively more M1 monocytes) had higher erythrocyte sedimentation rate and C-reactive protein than RA patients with M1/M2 ratio ≤1 had. **Conclusion:** The presence of ACPA positively correlated with the circulating osteoclast precursors in RA patients which may attributed to M1 subtypes. Our present data may explain the preferential development of bone destruction in ACPA-positive RA patients.

ICW5-4

Polymorphisms in methotrexate pharmacokinetic pathway - A pilot Study

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Conflict of interest: None

Introduction: This study investigated the impact of seven polymorphisms in genes involved in methotrexate pharmacokinetics on response, adverse effects and methotrexate polyglutamate levels in rheumatoid arthritis. Methods: This prospective study included 117 patients with rheumatoid arthritis who were treated with methotrexate for 24 weeks. Patients were then categorized for response based on the EULAR criteria at 24 weeks. Adverse effects were ascertained using a questionnaire. *Using real time Taqman discrimination assay, this study looked at SNPs* - rs1045642 (ABCB1 3435C>T), rs1128503 (ABCB1 1236C>T), rs10106 (FPGS 1994A>G), rs1544105 (FPGS G>A), rs11545078 (GGH 452C>T), rs3758149 (GGH -401C>T) and rs1051266 (RFC1 80G>A). RBC methotrexate polyglutamate$_{1\text{-}5}$ levels were determined using HPLC. Results: There was a significant association of the GGH 452C>T CC genotype (Odds Ratio 9.5, 95% CI 1.2 to 76.0) but not the other tested SNPs with response to methotrexate. On logistic regression higher DAS28 (3) at baseline and GGH 452CC genotype were significantly associated with response; the accuracy of the model was 75%. The FPGS 1994A>G GG genotype was associated with a significantly lower risk of adverse effects to methotrexate (Odds Ratio 0.3 (95% CI 0.1 to 0.6)). On logistic regression FPGS 1994GG genotype and lower BMI were significant predictors for adverse effects with an accuracy of 66%. However, there was no association of methotrexate polyglutamate levels with any of the polymorphisms. Conclusion: GGH 452C>T CC genotype was found to be associated with response to methotrexate and FPGS 1994A>G GG with lower risk of adverse effects; however, neither influenced methotrexate polyglutamate levels.

ICW5-5

Efficacy and Safety of Sarilumab as Monotherapy or in Combination Therapy in Patients With Moderate-to-Severe RA and Intolerance or Inadequate Response to Methotrexate

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Conflict of interest: Yes

Objectives: Efficacy and safety of sarilumab, a human mAb blocking the IL-6Rα, were evaluated for both monotherapy and combination therapy in patients with active, moderate-to-severe rheumatoid arthritis (RA) in 2 phase 3 clinical studies. **Methods:** MONARCH (NCT02332590) was a randomized, active-controlled, double-blind, double-dummy, 24-week superiority study comparing subcutaneous (SC) sarilumab (200 mg every 2 weeks [q2w]) and SC adalimumab (40 mg q2w) monotherapy in patients with RA in whom, per the investigator's discretion, concomitant treatment with methotrexate (MTX) was deemed inappropriate due to intolerance or inadequate response. MOBILITY (NCT01061736) was a randomized, placebo-controlled, 52-week study in which patients with RA and inadequate response to MTX received SC placebo, sarilumab 150 mg, or sarilumab 200 mg q2w plus background MTX. **Results:** Baseline demographic and disease characteristics were generally balanced between treatment groups in each study. In each study, sarilumab provided significant improvements in efficacy endpoints, including ACR20/50/70 responses, DAS28-CRP, and CDAI scores. In MONARCH, sarilumab 200 mg q2w was superior to adalimumab 40 mg q2w in the primary endpoint of mean change from baseline to week 24 in DAS28-ESR (-3.28 vs -2.20; 49% greater improvement; P<0.0001). Treatment responses observed with sarilumab as monotherapy were generally numerically similar to those observed when used in combination with background MTX. Infections, neutropenia, and injection site reactions were among the most common TEAEs in both studies. No serious infections were associated with ANC reductions <1 x 10^9 cells/L in either study. **Conclusion:** Sarilumab

significantly improved the signs and symptoms of RA and physical function when used as monotherapy vs adalimumab or in combination with background MTX vs placebo plus background MTX. The safety profile was consistent with IL-6 signaling blockade.

ICW5-6

Filgotinib, an oral JAK1 selective inhibitor, is effective in combination with methotrexate in patients with active rheumatoid arthritis: results from a Phase 2B dose ranging study

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Conflict of interest: Yes

Objective: The purpose of this 24 wk study was to evaluate efficacy and safety of different doses and regimens of filgotinib, a JAK1 selective inhibitor. Effect of MTX dose on clinical efficacy was also analysed. **Methods**: Patients with active RA on stable dose of MTX were randomized 1:1:1:1:1:1:1 in a double blinded manner to receive either placebo (PBO) or one of 3 doses of filgotinib (50mg, 100mg or 200mg) as once or twice daily regimen for 24 wks (DARWIN 1). The primary endpoint was the proportion of patients achieving ACR 20 response at wk12. MTX dose was categorized as low (≤12.5mg/wk), moderate (>12.5 to <17.5 mg/wk) or high (≥17.5mg/wk). **Results:** Of 594 treated patients, 76-86% were females with a mean age of 52-55 yrs, mean duration of RA of 7-10 yrs and DAS28 (CRP) at baseline of 6.0-6.2. Baseline characteristics were well balanced between the different treatment and MTX subgroups. At wk 12, a statistically significant higher ACR20 response versus PBO was observed with 200mg daily dose. For other key efficacy endpoints (ACR50, ACR-N, DAS28 (CRP), CDAI, SDAI) all doses showed significant differences versus PBO. Filgotinib clinical effect was observed, irrespective of MTX dose. Clinical responses were maintained or improved between wk12 and 24. Serious adverse events and treatment-emergent adverse events (TEAE) were distributed over all groups: TEAE 51% PBO and 52% filgotinib groups. No opportunistic infections or cancers occurred; one death was reported. Infections occurred in 19% PBO and 25% filgotinib groups. Increase in haemoglobin was noted in patients on filgotinib. **Conclusion:** Filgotinib in combination with MTX demonstrated consistent efficacy on signs and symptoms of active RA irrespective of MTX dose. The safety profile was overall favorable and consistent with previous studies in RA with filgotinib.

ICW6-1

Deviation of T and B cell Subset and Its Association with Single Nucleotide Polymorphisms in Antiphospholipid Syndrome

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Conflict of interest: None

Purpose: Recent genomic studies have suggested the involvement of T and B cell differentiation in antiphospholipid syndrome (APS). We thus aimed to identify the deviation of lymphocyte subset and its association with single nucleotide polymorphisms (SNPs) in APS patients. Methods: This cross-sectional study included patients with primary APS (PAPS), APS associated with systemic lupus erythematosus (SLE/APS) and healthy controls. T cells were divided into 12 subsets with 10 cell surface markers, while B cells into 6 subsets with 6 markers. A total of 28 SNPs related to autoimmune or thrombotic diseases were analyzed by TaqMan genotyping assay. Results: Eighteen PAPS, 8 SLE/APS patients and 8 healthy controls were included in this study. Th2 cells were increased in PAPS ($p = 0.011$) and SLE/APS ($p = 0.009$) patients compared to healthy controls. Resting regulatory T cells were decreased in PAPS patients compared to healthy controls ($p = 0.043$). Pre- and post-switched memory B cells were simultaneously decreased in PAPS patients compared to healthy controls ($p = 0.030$ and $p = 0.032$, respectively). Anticardiolipin antibodies were associated with the increase of Th2 cells ($p = 0.021$), while phosphatidylserine-dependent antiprothrombin antibodies with the decrease of pre- and post-switched memory B cells ($p = 0.049$ and $p = 0.027$, respectively). Toll-like receptor 7 gene polymorphism (rs3853839) was associated with the decrease of post-switched memory B cells observed in PAPS patients ($p = 0.038$). Conclusion: In APS patients, Th2 cells were increased while resting regulatory T cells, pre- and post-switched memory B cells were decreased. Furthermore, association between Toll-like receptor 7 and a decrease of memory B cells was found in APS patients. The deviation in lymphocyte subsets in APS patients could be, in part, immunogenetically regulated, presumably contributing to the development of this syndrome.

ICW6-2

Peripheral immunophenotyping identifies three subgroups based on T cell heterogeneity in patients with Systemic lupus erythematosus (SLE)

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Conflict of interest: Yes

[Objectives] Although many treatment modalities are effective in animal models, the targeted therapies show limited efficacy in humans due to molecular heterogeneity of SLE. To elucidate the diversity of SLE, we stratified SLE patients based on immunophenotyping in peripheral blood. **[Methods]** Peripheral blood mononuclear cells were obtained from 143 SLE patients and 26 healthy individuals. Circulating B, T and dendritic cells were defined based on flow cytometric analysis for human immune system termed "the Human Immunology Project". Based on these results, the immunophenotype was visualized by principal component analysis and SLE patients classified into subgroups by cluster analysis. **[Results]** The proportions of Treg and Tfh cells, but not Th1 and Th17 cells, were higher in SLE than the control. The proportions of central memory B cells and effector B cells were higher in SLE. The largest difference relative to the control was observed in the proportion of plasmablasts, which was higher in SLE and correlated with BILAG index. Principal component analysis indicated that the immunophenotype of SLE patients was consistent with T and B cell axes. More importantly, Th17 and Treg cells were statistically close, and showed positive correlation. Furthermore, the same pattern was also noted between Tfh and plasmablasts. Cluster analysis stratified SLE patients into three subgroups (with high proportions of plasmablasts in all groups): patients who did not show the characteristic features (T cell-independent group), patients with high percentage of Tfh cells (Tfh-dominant group), and patients with high proportion of memory Treg (Treg-dominant group). The percentage of patients who showed treatment resistance was highest among the Tfh-dominant group. **[Conclusions]** Our study indicates that SLE patients can be divided into three subgroups based on T cell heterogeneity. Accumulation of further evidence will help elucidate the pathogenesis of SLE and development of new therapies.

ICW6-3

Adverse events after surgery in pediatric patients with SLE: a nationwide study

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Conflict of interest: None

Objectives: Little was know about the outcomes after surgery in pediatric patients with systemic lupus erythematosus (SLE). Our purpose is to investigate the postoperative adverse events among surgical pediatric patients with preoperative SLE in a nationwide population-based study. **Methods:** We used Taiwan's National Health Insurance Research Database to identify pediatric inpatients with SLE and 258294 controls receiving major surgery. Sociodemographic characteristics, preoperative comorbidities, postoperative 30-day in-hospital major complications and mortality were analysed among surgical patients with and without SLE. **Results:** Pediatric patients with SLE had a higher prevalence of preoperative coexisting medical conditions and postoperative major complications. The OR of 30-day postoperative mortality for surgical patients with SLE was 8.55 (95% CI 2.65-27.6) after adjustment. Among pediatric patients, SLE was associated with postoperative pneumonia (OR 8.79, 95% CI 5.54-13.9), acute renal failure (OR 30.6, 95% CI 14.8-63.2), admission to intensive care unit (OR 2.16, 95% CI 1.55-3.00), prolonged length of stay (OR 2.45, 95% CI 1.78-3.38) and increased medical expenditure (OR 2.64, 95% CI 1.92-3.63). **Conclusions:** Among pediatric population, SLE significantly increased the risks of surgical complications and mortality after major surgery. Our findings demonstrated the need for integrated care and revised protocols for perioperative management to improve outcomes for pediatric patients with SLE.

ICW6-4

Cell type-specific RNA-seq of peripheral blood mononuclear cells (PBMCs) revealed mitochondria contribution in B cells to systemic lupus erythematosus

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Conflict of interest: Yes

【Objectives】SLE is a systemic autoimmune disease. Although the roles of auto-reactive B cells and regulatory T cells in its pathogenesis have already been suggested, the precise etiology remains unknown. We explore the etiology of SLE using RNA-seq.【Methods】We picked up 50 SLE patients and 30 healthy controls (HCs). Recruited patients have history of renal disorder and take not more than 10 mg/day of PSL. Each immune cell subset in PBMCs was identified by multicolor flow cytometry and followed by RNA-seq. Pipeline was alignment to the genome with STAR, and binning of sequencing reads to genes with HTseq-count. Differentially expressed genes (DEGs) were identified by edgeR.【Results】Interferon (IFN) signature upregulation was detected in all subsets from SLE patients. The number of DEGs varied between subsets and showed remarkable increase in memory B cell subset compared to naïve B cell subset. Pathway analysis revealed mitochondria-related genes were highly included in the memory B cell DEGs. Raw read counts comparison revealed higher expression of mitochondrial respiratory chain complex genes in SLE memory B cell subsets. Weighted gene co-expression network analysis in memory B cell subsets identified mitochondria-related modules showing specific correlation with disease activity. Random Forest, one of machine learning, confirmed the importance of these modules and IFN signature as variants in distinction between SLE and HC. Transmission electron microscopy and confocal microscopy showed elevated mitochondrial mass and mitochondrial membrane potential in memory B cell subset in SLE.【Conclusions】Many SLE GWAS-identified SNPs have associated with genes related to mitochondria. Our analysis suggests the importance of mitochondria function in memory B cell for SLE pathogenesis. This result may shed new light on SLE pathogenesis. In addition, we try to analyze the SNPs which have cell specific eQTL effect by combining our NGS data and GWAS data.

ICW6-5

Association of clinical characteristics with histological parameters in patients with active lupus nephritis

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Conflict of interest: None

【Objective】To elucidate the association of clinical characteristics with histological parameters in patients with lupus nephritis (LN).【Methods】The patients with biopsy-proven active LN were enrolled. The clinical parameters for LN (serum complement levels (C3), urinalysis findings, and serum creatinine (s-Cr) levels) were compared with the histological parameters (active lesions, chronic lesions, and interstitial lesions).【Results】Among 138 enrolled patients, 25 patients were classified as class III, 98 as class IV, and 15 as class V. Serum C3 levels (mg/dl) and urine granular cast were associated with highly active lesions with significance (C3: endocapillary proliferation (EnP), p=0.0006; karyorrhexis (Kr), p=0.003; necrosis (Ne), p=0.007; extracapillary proliferation (ExP), p=0.005, cellular cast: EnP, p=0.002; Kr, p=0.02; Ne, p=0.01; ExP, p=0.01). 24-h urine protein (UP, g/day) and s-Cr (mg/dl) were associated with some chronic lesions and interstitial lesions (UP: arterial sclerosis (As), p=0.04. s-Cr: glomerular sclerosis, p=0.007; interstitial cell infiltration, p<0.0001; interstitial fibrosis, p<0.0001; As, p=0.01).【Conclusions】Serum C3 levels and urinary cast may be useful to predict active lesions while UP and s-Cr may be useful to predict chronic or interstitial lesions.

ICW6-6

Involvement of peripheral subsets of CD8 T cells in systemic lupus erythematosus

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Conflict of interest: Yes

Objectives We conducted standard immunophenotyping with peripheral blood (PB) from systemic lupus erythematosus (SLE) patients and focused on CD8 T cell subsets to elucidate the association with clinical phenotype and serological markers. **Methods** PB was obtained from inactive SLE patients and healthy subjects as controls and also from active SLE before and 3 months after treatment. CD8 T cell subsets were measured by flow cytometry. **Results** Thirty-four active SLE patients and 38 inactive patients and 22 healthy controls were enrolled. Mean SLE disease activity index (SLEDAI) was 14.2 and 1.8 in active and inactive patients, respectively. Among CD8 T cell subsets, the proportion of HLA-DR+ cells was higher in SLE and positively correlated with SLEDAI, and was also higher in patients with nephritis than patients without it. The proportion of naïve CD8 T cells negatively correlated with serum complement levels and positively correlated with C1q immune complex levels. The proportion of central memory CD8 T cells negatively correlated with SLEDAI and was lower in patients with nephritis. The proportion of effector memory CD8 T cells (Tem) was lower in SLE and negatively correlated with the titer of anti-dsDNA antibody. Sixteen active patients were treated with prednisolone (PSL) 50mg (mean) with concomitant immunosuppressant; eight were treated with cyclophosphamide (CY). The proportions of HLA-DR+ cells and Tem significantly increased, and that of naïve CD8 T cells decreased at 3 months. The proportion of Tem increased and negatively correlated with SLEDAI only with those who were treated with cyclophosphamide. **Conclusion** Pathological state of SLE positively correlated with naïve CD8 T cells and negatively correlated with Tem and both subsets were affected by treatment with PSL and immunosuppressant particularly CY. These results indicate that CD8 T cells are involved in pathophysiology and could poten-

tially become a biomarker or a treatment target in SLE patients.

ICW7-1

Detecting uric acid crystals deposition by ultrasound and dual-energy CT in different joints of lower extremity

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Conflict of interest: None

Objectives. The aim of our study was to compare the performance between the ultrasonography (US) and dual energy computed tomography (DECT) in different joint regions of lower extremity which are mostly involved in clinically diagnosed gouty patients. Second, to correlate the imaging findings with results from synovial fluid aspiration whenever possible. **Methods.** We prospectively recruited 60 patients who presented with a clinical suspicion of acute or chronic gout in joints of lower extremity. DECT scans and US examination of the knees, ankles and feet were performed. In addition, joint fluid aspiration was performed in an acute inflammatory joint if possible. **Results.** We consecutively recruited 60 patients (58 male and 2 female) with an average age of 45.2±12.1 years. The median gout duration was 114 months. Among 60 gout patients, 28 (46.7%) had been previously diagnosed with gout because of podagra (n=20) or tophi formation (n=8); and 32 (53.3%) patients was newly diagnosed with gout according to the 1977 criteria. The overall accuracy of ultrasound 81.7%(49/60) was significantly higher than that of DECT 56.7%(34/60) in patient level (P<0.001). Positive percentage in DECT images for urate crystal deposits were 48.3%, 45.9%, and 43.3% in MTP1, knee and ankle region seperately. Positive percentage in US images for DQS was 33.3%, 48.3%, and 41.7% in MTP1 region, knee region and ankle region seperately; while the positive percentage in US for tophi was 33.3%, 33.3%, and 21.7% in MTP1 region, knee region and ankle region seperately. In 29 joints the synovial fluid aspiration was positive for MSU. US and CT findings correlated in MTP1 and knee joints (κ=0.50 and 0.41, *P*<0.001). The agreement of ultrasound and SFA was very good for positive crystal deposition (κ=0.87, P=0.001), while the agreement of DECT and SFA was just fair (κ=0.28, P=0.02). **Conclusion.** US was superior to DECT for the detection of crystal deposition in gouty arthritis in a clinical setting.

ICW7-2

3-bromopyruvate ameliorate autoimmune arthritis by modulating Th17/Treg cell differentiation and suppressing dendritic cell activation

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Conflict of interest: None

Objective: Recent studies have shown that cellular metabolism plays an important role in regulating immune cell function. In the process of cell differentiation, both interleukin-17-producing helper T (Th17) cells and dendritic cells (DCs) show increase of glycolytic activity by upregulating glycolytic enzymes, such as hexokinase-2 (HK2). Blocking glycolysis by 2-deoxyglucose has recently been demonstrated to inhibits Th17 cell differentiation while promotes regulatory T (Treg) cell generation. In addition, inhibition of glycolysis by 2-deoxyglucose has been reported to suppress activation of DCs. The aim of this study is to verify the effect of **3-bromopyruvate (BrPA)**, a specific inhibitor of HK2, on the differentiation and function of immune cells and on experimental arthritis in SKG mice. **Methods:** Zymosan A (ZyA) injection induced arthritis in SKG mice. BrPA (5mg/kg) was administered subcutaneously once daily. CD4+ T cells were cultured with anti-CD3/anti-CD28, anti-IFN-γ, anti-IL-4, IL-6, TGF-β, IL-2, with and without BrPA for 5 days. Bone marrow (BM) cells were cultured with GM-CSF and IL-4 (for 3 days), and with LPS (for 1 day) with and without BrPA. Synovium from rheumatoid arthritis (RA) patients was stained by anti-HK2 antibody. **Results:** We demonstrated that BrPA significantly decreased the arthritis scores and the histological scores in SKG mice, with a significant increase in Treg cells, decrease in Th17 cells, and decrease in CD40+CD86+CD11b+CD11c+(activated) DCs in the spleen. In vitro, BrPA facilitated Treg cell differentiation, while it inhibited Th17 cell development. In addition, BrPA reduced activated DCs and inhibited the production of TNF-α, IL-6. Immunohistochemistry revealed that HK2-expressing lymphocytes were increased in RA synovium. **Conclusions:** BrPA ameliorate autoimmune arthritis in SKG mice by facilitating the differentiation of Treg cells and by inhibiting the development of Th17 cells and activation of DCs.

ICW7-3

Adipokines as Link Between Arthritis and Metabolism

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Conflict of interest: None

Objectives In the context of arthritis, immunmodulatory properties of adipokines such as adiponectin, leptin and visfatin were already described by our and other groups. The role of adipokines in obesity and hyperinsulinemia is also well known. Due to the common comorbidity of osteoarthritis (OA) with obesity and hyperinsulinemia, the DMM (destabilization of the medial meniscus) mouse model was used and combined with high-fat diet (HFD) and normal diet (ND) for evaluation of systemic vs. local adipokine effects. **Methods** Mice were fed with HFD (mainly saturated fatty acids) to induce obesity and hyperinsulinemia or ND followed by surgical OA induction through DMM. Serum levels of leptin, adiponectin, visfatin and IL-6 in mice were measured by ELISA at different time points. Arthritis scores of joints were evaluated by histological staining (H/E, safranin O, pappenheim and Masson-Goldner's trichrome). To determine the adipokine expression in joints and selected organs, imunohistochemistry for adiponectin, leptin and visfatin as well as a macrophage marker was performed. **Results** IL-6 was not increased in all studied sera excluding acute inflammation or infections due to surgery. Histological scoring of the joints showed OA induction in treated mice vs. controls which was stronger in HFD fed animals compared to ND. HFD significantly increased leptin (e.g. ND 18.4; HFD 85.9ng/ml at day 28) but not adiponectin or visfatin when compared to ND. DMM decreased leptin levels at all time points (in 3 out of 6 groups significantly) independent of the diet. Interestingly, serum adiponectin levels were increased by DMM eight weeks after surgery. **Conclusions** OA development was more severe in animals fed with HFD. DMM decreased leptin levels especially in the context of HFD, which could not be observed for visfatin. Adiponectin was increased during OA but only in the later stages of OA development. Therefore, systemic levels of selective adipokines are altered by HFD and/or OA induction.

ICW7-4

Patterns of ^{18}F-FDG Uptake in spondyloarthritis

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Conflict of interest: None

Objective: To characterize the metabolic changes on PET/CT using ^{18}F-FDG in spondyloarthritis (SpA). **Methods:** Thirty-nine PET/CT in 34 patients diagnosed with SpA were reviewed. Diagnosis of SpA was made according to the ASAS criteria. The metabolic changes found on FDG-PET/CT were evaluated. Twenty healthy controls (HC) were also included to determine if false positive findings were observed. **Results:** PET/CT detected foci of increased FDG uptake in 77% of cases in at least one of the following 5 regions in patients with SpA: lumbar spinous process, sacroiliac, sterno-clavicular, peripheral and costotransverse joints. The most frequent abnormal FDG uptake was observed in lumbar interspinous process, in 51% of cases. FDG uptake was noted at the level of the costotransverse joints in 28%, in sterno-clavicular joints in 18%, in pe-

ripheral joints 15%, and in sacroiliac joints in 10% of cases. Fifty-nine percent of patients presented sacroiliitis on computed tomography. In HC, FDG uptake was observed in one case only at the costotransverse joint. Combining information provided separately by the PET and the CT parts of the PET/CT, 95% of cases were abnormal and suggestive for SpA. **Conclusion:** These preliminary data suggest a potentially promising role for FDG-PET/CT imaging in SpA patients.

ICW7-5

Hypothyroid and Hyperthyroid status was strongly associated with musculoskeletal ultrasonographic abnormalities with arthralgia

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Conflict of interest: None

Objective: The purpose of the study was to determine whether musculoskeletal ultrasonographic (MSUS) abnormalities were observed according to the state of thyroid disease. **Methods:** Patients with thyroid disease were categorized as euthyroid, hypothyroid, or hyperthyroid status according to their disease activity and evaluated the association with MSUS abnormalities. In addition, the association of the presence of thyroid autoantibodies with MSUS abnormalities was also studied. In MSUS, an experienced rheumatologist examined the presence of synovial fluid, synovial hypertrophy, and grade of power doppler in the knee joint. **Results:** A total of 109 patients participated in the study. MSUS abnormalities were statistically significantly higher in hyperthyroid or hypothyroid status than in euthyroid status (p<0.001). However, there was no statistically significant difference between hypothyroid status and hyperthyroid status. The presence of MSUS abnormalities with abnormal thyroid function was corrected according to the presence of radiological Knee osteoarthritis. Both hypothyroid and hyperthyroid status was still associated with MSUS abnormalities regardless of knee osteoarthritis. Visual analogue scale for knee pain was higher in patients with MSUS abnormalities (p<0.001). But, there was no statistically difference of MGUS abnormalities with presence of thyroid autoantibodies. **Conclusion:** Both hypothyroid and hyperthyroid status was significantly associated with MSUS abnormalities with knee arthralgia. MSUS is a useful tool to detect clinically early joint abnormalities. We suggest that patients with diagnosed thyroid dysfunction and who remain uncontrolled, should assess the MSUS examination in patients with arthralgia. Moreover a thyroid function test for unexplained arthritis maybe warranted. **Keywords:** Musculoskeletal, ultrasonography, thyroid dysfunction, arthralgia.

ICW7-6

Angiotensin II exacerbates bone destruction in human TNF-transgenic arthritis mice

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Conflict of interest: Yes

[Objectives] Recent studies have revealed that angiotensin II (Ang II) affects skeletal system as well as vascular system. However, the role of Ang II in inflammatory bone destruction is not yet clear. The purpose of this study was to determine whether Ang II exacerbates TNF-induced bone destruction and systemic bone loss in a murine arthritis model. [Methods] To investigate in vivo effect of Ang II, Ang II was infused by osmotic pumps from 12 to 16 weeks of age in wild-type and human TNF-transgenic (hTNF-tg) mice. The swelling of the paws was graded as arthritis score once per week. The bone properties of talus, lumbar vertebra and tibia were analyzed by micro-computed tomography. To evaluate the effect of Ang II in osteoclastogenesis in vitro, we conducted primary bone marrow-derived macrophages (BMMs) culture and co-culture with primary osteoblasts. In the BMMs culture, cells were treated with Ang II and RANKL. In the co-culture, cells were treated with Ang II, prostaglandin E2 and vitamin D. [Results] Arthritis scores in hTNF-tg mice were not altered by the Ang II infusion. Interestingly, erosive bone destruction on the talus was significantly more severe in Ang II-infused hTNF-tg mice compared to vehicle-infused hTNF-tg mice. Trabecular bone volume of lumbar vertebra and proximal tibia was lower in the Ang II infusion group than that in the vehicle group. In the BMMs culture, the number of osteoclasts was not affected by Ang II stimulation, whereas osteoclasts was increased by Ang II treatment in the co-culture with osteoblasts, suggesting the stromal cells-dependent osteoclastogenic mechanisms. [Conclusion] Ang II infusion exacerbated bone destruction and systemic bone loss of hTNF-tg mice. These findings suggest Ang II attributes to the bone destructive mechanisms by increasing osteoclastogenesis in arthritis. Ang II could be a therapeutic target to ameliorate the inflammatory bone destruction in patients with rheumatoid arthritis.

ICW8-1

Immunological phenotyping of obese patients with rheumatoid arthritis

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Conflict of interest: None

Objectives: Obesity is one of the risks of worse clinical outcomes and poor response to TNF-inhibitor in patients with rheumatoid arthritis (RA). The immunological characteristics of obese patinets with RA have not been clarified in detail. This study aimed to elucidate the immunological phenotypes of obese patients with RA. Methods: The frequencies of $CD4^+$ T cell, B cell and monocyte subsets were analyzed in RA (n=81) and healthy donors (n=99) by flow cytometry, and were compared between three groups (body mass index (BMI) <20, 20<BMI<25, BMI>25). Serum cytokines were measured using multiplex ELISA. Gene expression was analyzed by quantitative PCR. Clinical information was extracted from medical records. Results: The frequencies of Th17 ($CD4^+CD45RA$-$CXCR5$-$CXCR3$-$CCR6^+$) cells and plasmablasts (PB) were significantly increased in BMI>25 RA patients. A significant correlation was demonstrated between BMI and Th17 cells in RA patients. No significant difference of immune cell subset frequencies between the three BMI groups was observed in the healthy donors. Serum interleukin (IL)-1b and IL-21 showed a significant positive correlation with BMI in RA patients. In contrast, serum interferon-gamma inversely correlated with BMI in RA patients. Gene expression in Th17 cells from obese patients with RA showed the characteristics of pathogenic Th17 cells. Conclusions: Obesity was closely associated with chronic systemic inflammation. Immunological phenotyping unveiled the quantitative and qualitative changes in Th17 cells in the obese RA patients. These results shed light on the immunological mechanisms underlying worse clinical outcomes and poor TNF-inhibitor response in the obese patients with RA.

ICW8-2

Comparison of drug tolerability and discontinuation reasons between 7 biologics in patients with rheumatoid arthritis -Data from Kansai consortium for well-being of rheumatic disease patients (ANSWER cohort)-

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Conflict of interest: Yes

[Object] More than 3 years have passed since 7 biologics became available in Japan, although lacking reliable evidence which directly compared the differences of tolerability and discontinuation reasons between the agents. [Methods] A total of 1,037 biologics treatment courses from 2009 to 2016 (female 81.8%, baseline age 59.6 y, RF positivity 81.5%, DAS28-CRP 3.6, CDAI 16.8, Bio naïve 57.1% and switched 42.9%, MTX 5.9 mg/week (68.6%), PSL 2.5 mg/day (43.5%), ABT 21.3%, TCZ 20.7%, GLM 16.9%, ETN 13.6%, ADA 11.1%, IFX 8.5%, CZP 7.9%) were included in this multi-center, retrospective study. Confounding factors which significantly affected biologics retention rates were analyzed using a Cox proportional hazards model and log-rank test. [Results] The major causes of 7 biologics treatment discontinuation were drug inefficacy (47.8%), adverse events except infusion reaction and infection (12.4%), remission (8.4%), and infection (7.6%). The discontinuation reasons and ratio in each drug were as follows. Drug inefficacy (ABT 17.4%, TCZ 18.6%, ETN 24.5%, IFX 24.9%, ADA 25.0%, GLM 29.4%, and CZP 30.5%), remission (IFX 14.2%, ADA 10.8%, GLM 3.7%, CZP 3.7%, ABT 3.4%, ETN 1.8%, and TCZ 1.6%), and infection (ABT 5.1%, ETN 5.0%, TCZ 4.4%, IFX 3.8%, CZP 3.7%, ADA 2.7%, and GLM 2.7%), respectively. Confounding factors which significantly affected biologics retention rates were sex ($P<0.01$), ACPA titer ($P<0.05$), RF titer ($P<0.01$), switched biologics number ($P<0.001$), MTX dose ($P<0.001$), and PSL dose ($P<0.001$) at baseline. Raw retention rates at 24 months were as follows. ABT 61.1%, TCZ 60.2%, ETN 57.1%, GLM 49.2%, ADA 46.6%, IFX 45.3%, and CZP 41.2%. Retention rates adjusted by above confounding factors at 24 months were as follows. TCZ 62.5%, ABT 57.4%, ETN 51.3%, CZP 45.2%, ADA 44.3%, GLM 43.9%, and IFX 40.6%. [Conclusion] TCZ and ABT showed better retention rates at 24 months compared with other biologics in both raw model and adjusted model by potent confounders.

ICW8-3

Population-specific interactive effects of HLA-DRB1 alleles on susceptibility to rheumatoid arthritis

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Conflict of interest: None

Background: HLA-DRB1, the strongest susceptibility gene to rheumatoid arthritis (RA), showed allelic interactive effects on susceptibility to RA with anti-citrullinated peptide antibody (ACPA) in Europeans. However, difference in allelic distribution among populations would lead to different HLA-DRB1 interactive effects. Objective: to evaluate HLA-DRB1 interactive effects on RA susceptibility in Japanese Methods: A total of 4,871 ACPA (+) cases and 16,065 controls were analyzeds. Both allelic non-additive effects and interactive effects of allelic combinations were analyzed in logistic model. The significant levels were set by Bonferroni's correction. Results: We got evidence of non-additive effects as a whole data set ($p=6.0\times10^{-7}$) and for HLA-DRB1*04:05, the most common susceptibility allele in Japanese, and *08:03 ($p=4.5\times10^{-8}$ and 5.0×10^{-4}, respectively). None of the HLA alleles with interactive effects in European population did not show significant results. The combination of DRB1*04:05 and *08:03 showed the most significant interactive effect ($p=5.5\times10^{-6}$). Conclusions: HLA-DRB1*04:05 and *08:03 showed non-additive effects and an interactive effect on RA susceptibility in Japanese. The allelic non-additive effects might vary among populations depending on allelic distribution.

ICW8-4

Transcriptome profiling of immune cell subsets in rheumatoid arthritis

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Conflict of interest: Yes

Objective: Rheumatoid arthritis (RA) is a systemic inflammatory disease. Although many immune cell subsets are estimated to be involved in its pathogenesis, it is not clear how they are working together. We aimed to elucidate the transcriptome profiles and interactions of immune cell subsets in RA patients. **Method:** We performed RNA sequencing of 16 peripheral blood cell subsets from 31 RA patients and 20 healthy controls. We analyzed the transcriptome with WGCNA (weighted gene co-expression network analysis) software and divided it into 10 to 20 gene sets, in which genes are regulated in a coordinated fashion, in each cell subset. Gene sets were then annotated to known genetic pathways with Ingenuity Pathway Analysis (IPA) software. Genotyping was also performed with SNP microarray. **Result:** Transcriptome analysis revealed upregulation of inflammatory pathways including interferon pathway, IL-6 pathway and JAK-STAT pathway in cell subsets of RA patients compared to healthy controls. Among RA patients, T cell receptor signaling pathway, B cell receptor signaling pathway and monocyte extravasation signaling pathway were working together and upregulated in some of the patients, and oxidative phosphorylation pathways in the immune cell subsets were downregulated in some. Further, interferon pathways were markedly upregulated in the small part of the patients. The combination of these pathways classified RA patients into some groups. The association study of these pathways and genetic polymorphisms revealed that some of the risk SNPs of RA or the other autoimmune diseases were associated with aberrant pathways like interferon pathway and oxidative phosphorylation pathway. **Conclusion:** Detailed transcriptome profiles revealed the inflammatory status in RA patients and classified RA patients based on the expression levels of pathways such as oxidative phosphorylation pathway. Genetic polymorphisms might be associated with aberrant transcriptome profiles of RA patients.

ICW8-5

18F-Fluorodeoxyglucose Positron Emission Computer Tomography and Ultrasonography for Assessing Remission in Patients with Rheumatoid Arthritis

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Conflict of interest: None

Objective: To evaluate the role of ^{18}FFluorodeoxyglucose Positron Emission Computer Tomography (^{18}F-FDG PET/CT) in assessing remission in Rheumatoid arthritis (RA). Methods: A crosssectional study was performed on 63 RA patients. A total of 1764 joints was assessed. Clinical assessment (DAS-28), ^{18}FFDG PET/CT and US were performed the same day. Patients were classified in 3 groups according to their disease status: 22 (35%) were in remission (DAS-28 < 2.6), 31 (49%) had a low or moderate disease activity (2.6 < DAS-28 ≤ 5.1) and 10 (16%) had a severe disease activity (DAS 28 > 5.1). PET/CT was analyzed first visually, then semiquantitatively by determining the Standardized Uptake Value (SUV) of the positive joints. Synovitis were considered as positive in US according to OMERACT criteria. Logistic regression analysis was applied to discriminate between severe and non-severe patients and between subjects with and without remission. Results:Of the 1724 articulations, 373 (21.2%) were tender, 242 (13.7%) were swollen, 361 (20.5%) were PET/CT positive and 152 (8.6%) were US positive. Discrimination between severe and non-severe patients was significant for PET/CT (AUC=0.77, P=0.0046) and for US (AUC=0.84, P=0.0030). Cut-off levels were 8 positive joints for PET-CT, 17.8 for the cumulative SUV and 3 positive for US. By contrast, patients in remission could not be discerned from others: AUC ranging from 0.51 to 0.60 (P > 0.05). Among the 22

RA patients in clinical remission, only 6 (27%) did not show any PET/CT positive joint and 5 (23%) had no positive joint by US. Moreover, in the remission group, 4 (18%) patients had more than 8 PET/CT positive joints and 4 (18%) more than 3 US positive joints. US and PET/CT were positive in different joints, predominantly in small joints of the hands for PET/CT. Conclusion: Both ^{18}F-FDG PET/CT and US identify subgroups of patients with highly positive imaging findings and low clinical activity.

ICW8-6

Evaluating Transfer of Certolizumab Pegol and Polyethylene Glycol into Breastmilk: Results from a Prospective, Postmarketing, Multicenter Pharmacokinetic Study

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Conflict of interest: Yes

Objective To evaluate certolizumab pegol (CZP) concentrations in breastmilk of women with chronic inflammatory diseases and to estimate Average Daily Infant Dose (ADID) of maternal CZP (the daily amount potentially ingested by infants). **Methods** CRADLE (NCT02154425) was a safety and pharmacokinetic study of lactating mothers (≥6 weeks postpartum) receiving commercial CZP for an approved indication. Decision to treat with CZP and to breastfeed was independent of study participation. At steady-state (≥3 CZP doses), breastmilk samples were collected at Days 0, 2, 4, 6, 8, 10, 12, 14 (±28) across 1 dosing period (14 days [200mg Q2W; 28 days [400mg Q4W]). Optimal methods were developed for CZP and polyethylene glycol (PEG) determination in breastmilk: CZP method utilized a mesoscale discovery platform (LLOQ=0.032µg/mL), PEG method nuclear magnetic resonance (LLOQ=0.5µg/mL). **Results** 18 CZP-treated mothers were screened, 17 entered the sampling period; 16 on 200mg Q2W; 1 on 400mg Q4W (7 RA; 5 SpA; 5 CD). 77/137 samples (56%) had no measurable CZP in breastmilk. For 4/17 mothers, samples were below LLOQ. 13/17 mothers had levels at ≥1 time point (<2xLLOQ: 52/137 samples; <3xLLOQ: 8/137 samples; highest concentration: 0.076µg/mL). Estimated ADID ranged from 0–0.0104mg/kg/day; median relative infant dose (RID): 0.125%. No PEG was detected. Infants of CZP-exposed mothers had a safety profile of events occurring in unexposed same-age infants. **Conclusion** Using the highly sensitive assay, CZP was undetectable in 56% of milk samples. Detectable CZP concentrations were <1% of expected plasma concentration of a therapeutic dose, indicating no to minimal transfer of CZP from plasma to breastmilk. RID was <0.5% of maternal dose. No transfer of PEG to breastmilk was observed. CZP absorption by infants via breast milk is unlikely due to its Fc-free molecular structure and the low bioavailability of biologics after oral administration. CZP should be used as per current label.

ICW9-1

Activation of Alternative Complement Pathway Due to Depletion of Factor H in Primary Antiphospholipid Syndrome

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Conflict of interest: None

Object: Although complement activation was proposed as one of the major thrombophilic mechanisms in antiphospholipid syndrome (APS), the origin of complement activation in APS has remained unclear. The serum levels of immune complexes (IC), a major trigger of classical pathway, were reported to be low in APS patients. We focused on complement regulatory factors (CRF), which suppressed the excessive activation of complement mainly in alternative pathway, and evaluated two major CRF, membrane cofactor protein (MCP) and factor H (FH), in APS patients. **Methods**: This study involved a cohort of patients with connective tissue diseases (CTD) who visited the Hokkaido University Hospital rheumatology clinic during 2000 and 2013. The excessive activations of alternative complement pathway were qualitatively detected using solid-phase enzyme-linked immunosorbent assays (ELISA) (Wieslab Complement system Screen, Euro Diagnostic). Serum MCP levels (MCP ELISA kit, Cloud-Clone) and FH levels (factor H human ELISA kit, Human Innovative Research) were also tested by ELISA. Autoantibodies against FH were determined by western-blotting. **Results**: Twenty-six patients with primary APS (PAPS) and 56 patients with non-systemic lupus erythematosus CTD (control) were analyzed. Serum complement levels of PAPS were lower than those of control (C3: 85.9±35.6 vs 109.4±42.8 mg/dL, $p < 0.01$). In the PAPS patients, excessive complement activations were observed in 4/26 for the alternative pathway. The serum MCP levels were within normal range in both PAPS and control. On the contrary, serum FH levels were significantly depleted in PAPS compared with control (median 180.1 vs 368.5 µg/mL, $p < 0.0001$), and serum FH levels were positively correlated with serum C3 levels ($p = 0.015$, $R^2 = 0.502$). Autoantibodies against FH were not detected in any of the PAPS patients. **Conclusions**: Activation of alternative complement pathway was found in some of the APS patients mainly due to depletion of FH.

ICW9-2

Long-Term Prognosis of Patients with Systemic Lupus Erythematosus-Associated Pulmonary Arterial Hypertension: CSTAR-PAH Cohort Study

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Conflict of interest: None

Objective: Systemic lupus erythematosus (SLE)-associated pulmonary arterial hypertension (PAH) is common in Asian countries, and the

clinical outcome of patients with SLE-associated PAH is dramatically impaired. This study aimed to identify the long-term clinical outcomes and prognostic factors of patients with SLE-associated PAH confirmed by right heart catheterization (RHC). **Methods**: A multicenter cohort of SLE-associated PAH was established. Baseline and follow-up records were collected. The primary endpoint was death from any cause. The secondary experimental end point was treatment goal achievement (TGA), defined as an integrated outcome. **Results**: Among the 310 patients enrolled from 14 PAH centers, 282 patients with confirmed mortality statuses were included in the survival analysis, and 263 patients with complete follow-up data were included in the TGA study. The median follow-up was 24.0 months. The 1-, 3- and 5-year survival rates were 92.1%, 84.8% and 72.9%, respectively. The 1-, 3- and 5-year TGA rates were 31.5%, 53.6% and 62.7%, respectively. Serositis (HR = 1.94, 95% CI: 1.26 to 3.00, $P = 0.003$), 6MWD > 380 m (HR = 1.95, 95% CI: 1.14 to 3.31, $P = 0.014$) and CI ≥ 2.5 L/min×m^2 (HR = 1.92, 95% CI: 1.16 to 3.19, $P = 0.012$) were identified as independent prognostic factors of TGA. TGA within 5 years was identified as a factor associated with survival in patients with SLE-associated PAH. **Conclusions**: Our study proved that TGA was associated with the long-term survival, which supports and provides evidence to the treat-to-target strategy in SLE-associated PAH. Early diagnosis, intervention and heart function preservation are priorities for better long-term outcomes. PAH patients with high SLE activity may benefit dramatically from immunosuppressive therapy.

ICW9-3

Expression of Interferon-Inducible Mx1 Protein in Renal Tissues in Patients with Lupus Nephritis

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Conflict of interest: None

Objectives: Severe glomerular/renal tubular injury leads to a poor prognosis in lupus nephritis (LN). Analysis of overexpressed molecules in peripheral blood from SLE patients using microarray or real-time qPCR and evaluation of histopathological biomarkers for LN would provide new insights in understanding the pathophysiology of LN. The aim of this study was to investigate the overexpressed molecules in the peripheral blood of SLE patients and in the renal tissues in LN, and to evaluate the relationship between those molecules and clinical features. **Methods:** Peripheral T cells from SLE patients and healthy controls (n=14 each group) were subjected to global gene expression analysis using exon array. Thirty-four SLE patients and 22 healthy individuals were analyzed for mRNA levels of Mx1 and RGS1 in T cells using real-time qPCR. Mx1 protein concentrations in PBMCs from SLE patients and healthy controls (n=16 each group) were measured using ELISA. Mx1 expression in renal biopsy specimens from 18 patients with LN, 18 with IgA nephropathy and 10 with ANCA-associated vasculitis were evaluated using immunohistochemistry. **Results:** Exon array revealed high expression of Mx1 and RGS1, IFN-inducible genes, in lupus peripheral T cells. Mx1 and RGS1 mRNA levels in peripheral T cells regardless of disease activity, and Mx1 protein concentrations in lysates of PBMCs were significantly higher in SLE patients compared with healthy controls. Mx1-positive area in renal tissues was significantly dominant in both glomeruli and renal tubules of LN compared with other renal diseases. Renal Mx1 protein levels were lower in LN after longer than 2 weeks' immunosuppressive treatment, compared with those from patients received biopsy before treatment. **Conclusion:** Mx1 expression levels were significantly higher in lupus peripheral blood as well as in kidneys from patients with LN, suggesting Mx1 as a marker/a novel treatment target in SLE, especially those complicated with LN.

ICW9-4

The efficacy and safety of anti-CD20 antibody rituximab for refractory patients with Systemic Lupus Erythematosus

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Conflict of interest: None

Objectives; B cells play a crucial role in pathogenesis of Systemic Lupus Erythematosus (SLE). We examined the efficacy of B cell depletion therapy rituximab for refractory patients with SLE. **Methods;** 63 eligible study subjects since 2002 until 2015 were men and women, who met the American College of Rheumatology criteria in 1987 or SLICC2012 for the classification of SLE. The protocols were approved by the Institutional Review Board of our university. Treatment protocol: 2 or 4 weekly doses of 500 mg/body, 2 biweekly doses of 1000mg/body or 4 weekly doses of 1000mg/body. **Results;** Baseline characteristics; gender M:F=6:57, age 33.9 years, disease duration 87.2 months, organ failure NPSLE:35, lupus nephritis:46, treated with IVCY 34/63. The 60/63 patients were trailable at 1 year. Primary endpoint; disease activity scores were significantly improved (SLEDAI 17.3→3.4, BAILAG 17.8→3.5; LOCF). The achievement ratio of major clinical response (MCR) defined as no BILAG A and/or B score was 60.0%. Secondary endpoint; dose of corticosteroid was decreased from 43.2 to 8.4 mg/day. Nephritis score originally designed (total 10 points; protein 3, occult blood 3, cast 4) was decreased (3 (before)→2.3 (1month)→0.8 (1year)). A total of 49 adverse drug reactions (ADRs) with suspected relationship to rituximab within 1 year were observed (grade 3; infection of urinary tract 3, fungus 1, bacterial pneumonia 1, bedsore 1, gastrointestine 4, skin 3 and bone 2, in addition, neutropenia 1, cardiac infarction 1, grade4; cerebral infarction 2). The 34/50 patients were trailable at 5 years. Primary failure: 3 (8%), secondary failure (flare): 12 (35.3%, duration: 24.3 months), MCR: 17 (50.0%), corticosteroid discontinued: 5 among 34 patients. **Conclusion;** Rituximab showed short- and long-term efficacy and tolerability in refractory patients with SLE, although some of patients had a relapse. Rituximab could be considered as a therapeutic strategy for refractory patients with SLE.

ICW9-5

Association between anti-SS-A and anti-SS-B antibodies and the clinical and histological features of lupus nephritis

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Conflict of interest: None

【Objective】Anti-SS-A and anti-SS-B antibodies are frequently positive in patients with systemic lupus erythematosus (SLE). The aim of this study was to clarify the associations of anti-SS-A and anti-SS-B antibodies with the clinical and histological features of lupus nephritis.【Methods】Consecutive lupus nephritis patients who underwent renal biopsy at our hospital since 2001 were enrolled. The patients were divided according to the presence or absence of anti-SS-A and anti-SS-B antibodies, and their associations of the clinical features and renal biopsy histological findings were examined.【Results】Forty-five patients were enrolled. Thirty-eight (84%) were female, and the mean age at SLE onset was 40.2 years. Anti-dsDNA antibody was positive in all cases, anti-Sm antibody in 24 cases (53%), anti-SS-A antibody in 31 cases (69%), and anti-SS-B antibody in 9 cases (20%). No difference was found in sex, age at SLE onset, the rates of anti-dsDNA and anti-Sm antibody positivity between the anti-SS-A/SS-B positive group and anti-SSA/SSB negative group. The period from the SLE onset to the lupus nephritis onset was significantly shorter in the anti-SS-A/SS-B positive group than the anti-SSA/SSB negative group (SS-A 4.0 years vs. 9.0 years, p = 0.0046. SS-B 0.4 years vs. 6.8 years, p = 0.0074). The anti-SS-A/SS-B positive group had significantly lower rate of renal tubular atrophy and interstitial fibrosis findings than in the anti-SSA/SSB negative group (renal tubular atrophy SS-A 8.0% vs. 16.4%, p = 0.042. SS-B 3.3% vs. 12.8%, p = 0.048. Stromal fibrosis SS-A 7.6% vs. 16.4%, p = 0.031. SS-B 2.1% vs. 12.8%, p = 0.016). Chronicity Index was significantly lower (SS-A 2.37 vs. 4.14, p = 0.0024. SS-B 1.17 vs. 3.33, p = 0.0082).【Conclusions】Anti-SS-A and anti-SS-B antibodies positive SLE patients should be followed carefully for early onset of lupus nephritis.

ICW10-1

The role of intensive immunosuppressive therapy in the management of SLE-associated PAH: a real-world review

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Conflict of interest: None

Objective: Immune and inflammatory mechanisms play significant roles in the genesis and progression of pulmonary arterial hypertension (PAH), especially in patients with systemic lupus erythematosus (SLE). This study aimed to investigate the clinical outcomes of intensive immunosuppressive therapy with or without PAH specific therapy in patients with SLE-associated PAH. **Methods:** This single-center cohort study enrolled 126 consecutive patients with SLE-associated PAH confirmed by right heart catheterization (RHC) between May 2006 and December 2015. Baseline demographics, clinical features, laboratory results, hemodynamic assessments and management were analyzed. Kaplan-Meier curves and Cox proportional hazards regression analysis were used to evaluate the role of intensive immunosuppressive therapy. **Results:** All patients received intensive immunosuppressive therapy including combination of high-dose glucocorticosteroids and cyclophosphamide or mycophenolate. 82 patients received PAH specific therapy at baseline. Survival analysis indicated that responders had better survival than nonresponders in both with and without PAH specific therapy group. Patients with shorter SLE disease duration (p=0.009) and better baseline pulmonary hemodynamics (mPAP, PVR and Cardiac index, p<0.001) were more likely to benefit from immunosuppressive therapy. **Conclusion:** Intensive immunosuppressive therapy markedly improved the long-term outcome of patients with SLE-associated PAH, especially in the early stage of PAH.

ICW10-2

Whose ITP heralds SLE? To distinguish ITP patients with high probability of SLE development by means of decision-tree model: A nationwide cohort study

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Conflict of interest: None

Objectives: Immune thrombocytopenic purpura (ITP) is an autoimmune-associated thrombocytopenia which is occasionally the initial presentation of systemic lupus erythematosus (SLE), and thus regular following up has been suggested. Whereas long-term surveillance on all ITP patients would be time and cost-consuming, and thus to distinguish those with high probability of development of SLE among ITP patients should be more practical. **Methods**: We enrolled ITP patients without previous SLE diagnosis from the National Health Insurance research database between 1997 and 2012 and identified those certificated with catastrophic illness of SLE during follow up, by which the diagnosis was reconfirmed by another rheumatologists. We also analyzed the symptoms and comorbidities as well as the dose of average oral steroid to derive the decision trees, which classified the ITP patients with different probability of development of SLE. **Results**: A total of 10,265 ITP patients were enrolled, among whom 80 patients developed SLE while following-up. The whole ITP patients were allocated to training group (7,186 patients including 57 with SLE) and testing group (3,079 patients including 23 with SLE); the former was used for derivation of the decision-tree based model and the latter for validation of the previously mentioned model, and provided high sensitivity (78.2%), specificity (99.2%) and negative prediction value (99.8%). To reduce the complexity, we also proposed another models with different complexity parameters. **Conclusions**: We derived classification decision tree exempt from the necessity of laboratory data and suitable for various clinical scenarios of ITP patients, among whom those with high probability of development of SLE would be identified.

ICW10-3

Endoplasmic reticulum stress contributes to aberrant regulatory T cell differentiation in patients with systemic lupus erythematosus

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Conflict of interest: None

Defects of regulatory T cell (Tregs) mainly contribute to loss of tolerance to self-antigen which is significantly implicated in the pathogenesis of systemic lupus erythematosus (SLE). We investigated proportion of Tregs in the peripheral blood mononuclear cells (PBMCs) of patients with SLE and differentiation difference of induced Tregs in vitro under the presence or absence of endoplasmic reticulum (ER) stress, which is one of the causal factors triggering lupus flares, compared with that of healthy controls (HCs). We isolated the PBMCs of 16 SLE patients and 11 HCs. The percentage of $CD4^+CD25^+FoxP3^+$ Tregs was analyzed using flow cytometry. The PBMCs were incubated with anti-CD3/CD28 beads, supplemented with transforming growth factor-β and interleukin-2 to induce differentiation of Tregs, with or without tunicamycin for 36 hours. The percentage of Tregs in the PBMCs of SLE patients was lower than that in the HCs (1.8 ± 0.9 versus 2.6 ± 0.7%, p=0.02). The induced differentiation of Tregs increased in both groups, and the increased proportion was greater in the SLE group (600 ± 351 versus 252 ± 95%, p=0.01). Incubation with tunicamycin in the Treg differentiation process also increased the proportion of Tregs in both groups (385 ± 259 versus 166 ± 105%, p=0.006), and the increased proportion was higher in the SLE group. In addition, the percentage of induced differentiated Tregs with or without tunicamycin in SLE group was positively correlated with SLE disease activity index (SLEDAI) (r=0.555, p=0.026 and r=0.546, p=0.029). The baseline percentage of Tregs was lower in SLE patients than in HCs. However, when Treg differentiation was induced, the differentiation of Tregs was more pronounced in the SLE group. This exaggerated differentiation may reflect the paradoxical response to the diminished suppressive capacity of Tregs in SLE patients.

ICW10-4

Prophylaxis of recurrent arterial thrombosis in patients with antiphospholipid syndrome

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Conflict of interest: None

[Objectives] Antiphospholipid syndrome (APS), one of the most common acquired thrombophilia, is characterized by the presence of arterial or venous thrombosis. However, the optimal treatment for prevention of recurrent arterial thrombosis in patients with APS is unclear. The objective of this study is to evaluate the efficacy of several prophylactic treatments for recurrent arterial thrombosis in patients with APS. [Methods] This study involved a cohort of 206 patients with APS who visited Hokkaido University Hospital rheumatology clinic between April 1990 and March 2016. Patients who were followed-up for less than 2 years and

those without arterial thrombosis were excluded. A total of 90 APS patients (female 73, age 43 years (9-79)) were analysed in this study. We retrospectively assessed the efficacy of warfarin monotherapy (wf, n=13), antiplatelet monotherapy (AP, n=41), combination therapy of warfarin and antiplatelet agent (wf+AP, n=21), and dual antiplatelet therapy (DAPT, n=15) in the secondary prevention of arterial thrombosis in patients with APS. [Results] The median follow-up period was 12 years (2-27). Thrombotic events recurred in 40 (44.4%), patients (wf, AP, wf+AP, DAPT: 11, 18, 8, 3). A total of 14 (15.6%) patients died, (wf, AP, wf+AP, DAPT: 1, 5, 4, 4), and 9 (10.0%) patients had serious bleeding events, (wf, AP, wf+AP, DAPT: 0, 5, 2, 2),. In Kaplan-Meier analysis, 10-years recurrence-free survival rate was 62%, and the treatment with warfarin monotherapy was less effective than other treatment options (Log-rank p=0.001). There were no statistically significant differences in bleeding events and mortality among the groups. [Conclusion] Antiplatelet agents, as the key drugs for the prevention of recurrent arterial thrombosis, may be necessary in patients with APS.

ICW10-5

Possible correlation between coagulation factor XIII and disease activity in systemic lupus erythematosus

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Conflict of interest: None

Objectives: Coagulation factor XIII (FXIII) is important for clot stability and acts in the subsequent wound healing. In addition to these traditional key roles, novel extracellular and intracellular functions of FXIII have been identified. Subunit A of FXIII (FXIII-A) is expressed by regulatory macrophages and cellular FXIII-A has been associated with phagocytosis and migration of macrophages. In systemic lupus erythematosus (SLE), growing evidence suggests that polarization of regulatory macrophages correlates with disease activity. Together with these insights, it is implicated that FXIII may potentially be related to disease activity in patients with SLE. Therefore, we investigated whether FXIII was associated with disease activity indices and biomarkers in SLE to evaluate the clinical significance of FXIII in SLE. **Methods:** This study involved 50 consecutive patients with SLE enrolled in a longitudinal study at University of Los Angeles, California. Blood samples were collected from these patients and serological examination was performed by standard methods. Plasma FXIII activity (FXIIIa) was measured by an ELISA kit of TECHNOCHROM FXIII (Technoclone, Austria). On the day of plasma sampling, the disease activity was assessed by the SLE Disease Activity Index (SLEDAI) and the physician's global assessment (PGA). Data were analyzed with SPSS software, version 13.0 (SPSS, Chicago, IL). **Results:** Plasma level of FXIIIa had a strong correlation with SLEDAI (r=-0.38, p=0.007), PGA (r=-0.311, p=0.028), serum C3 (r=0.44, p=0.002) and double stranded DNA antibody (r=-0.361, p=0.014). In patients with high plasma FXIIIa (>143%), SLEDAI was significantly lower (2.17±3.7 vs. 4.1±3.2, p=0.009). **Conclusions:** FXIIIa is correlated with several disease activity indices and biomarkers in SLE. Further studies are needed to determine the role of FXIII in the pathogenesis of SLE and as potential disease activity indicators.

ICW10-6

Long-term Prognosis and Predicting factors of Chinese Patients with Systemic Lupus Erythematosus: a Multi-center Cohort Study from CSTAR registry

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Conflict of interest: Yes

Objective To study the long-term outcomes, both mortality and damage, and related prognostic factors of patients with Systemic Lupus Erythematosus (SLE) in the CSTAR (Chinese SLE Treatment and Research group) registry cohort. **Methods** The patients were enrolled from April 2009 to February 2010. They were followed up at clinic and were telephone interviewed at the endpoint. We collected demographic data, clinical manifestations, activity (SLEDAI-2K), damage scores (SLLIC/Damage Index), and medications. Data were censored at the last clinic visit or telephone interview. Survival rates were studied by Kaplan-Meier method, and COX proportional hazard model was adopted to perform the analysis of predicting factors for mortality. **Results** A total of 2104 patients were recruited at baseline, and 1494 patients were successfully followed up. The cumulative 1, 3 and 5 year survival rates from diagnosis were 99.0%, 98.1% and 97.1%. 78 patients died during follow-up, and the main death causes were infection (34.6%), active disease (26.9%), cardiovascular and cerebrovascular events (6.41%) and malignancy (5.13%). At entry, 247 patients presented with irreversible organ damage and it increased to 398 patients at the endpoint. The major accumulated organ damages were renal (25.9%), musculoskeletal (20.2%), neuropsychiatric (12.4%), and pulmonary (10.8%) damage. Cox regression showed that male, late onset age (≥50y), onset to diagnosis time ≥ 1 year, previous organ damage, renal involvement, pulmonary arterial hypertension, neuropsychiatric involvement, serositis and the number of involved organ systems ≥3 predict for higher mortality. **Conclusion** Long-term survival rates have improved for Chinese SLE patients. Early diagnosis, preventing from the emerging systemic organ involvements and organ damage could be the treating target for the management of SLE patients in China.

ICW11-1

Clinical and Swallowing ability outcomes of dermatomyositis and polymyositis patients with dysphagia

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Conflict of interest: None

[objectives] To assess clinical and swallowing ability outcomes of myositis patients with dysphagia. [methods] We retrospectively conducted 220 consecutive myositis patients and assessed 22 myositis patients with dysphagia. We defined myositis with dysphagia if patients fulfilled having dysphagia symptoms and required dysphagia diet (the moderate dysphagia) or required tubefeeding or intravenous hyperalimentation (the severe dysphagia). [Results] For myositis patients with dysphagia, seventeen patients had DM and five patients had PM. Ten patients developed malignancy and that was higher prevalence of malignancy than for myositis without dysphagia (P<0.001). Ten patients developed the moderate dysphagia and twelve patients developed the severe dysphagia. All patients did swallowing rehabilitation and ten patients underwent balloon dilation. After treatment, seventeen patients (77.3%) with dysphagia demonstrated improved swallowing ability, leading to a return to normal oral feeding. However, two patients still experienced mild dysphagia intermittently and three patients showed no improvement in their swallowing ability, requiring tubefeeding or intravenous hyperalimentation. Eight patients developed aspiration pneumonia and one patient underwent cricopharyngeal myotomy because of recurrent aspiration pneumonia. Nine patients died from aspiration pneumonia (N=1), sepsis (N=1), and malignancy (N=7). Overall survival rate of myositis with dysphagia was significantly lower than for myositis without dysphagia (P<0.001). Two patients with malignancy developed dysphagia recurrence in association with malignancy relapse. [Conclusion] Most of the myositis patients with dysphagia improved their swallowing ability. But, mortality rate of myositis patients with dysphagia was significantly higher than myositis without dysphagia.

ICW11-2

RasGRP4 induces proliferation of fibroblast-like synoviocytes via Ras- MAPK pathway

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Conflict of interest: None

[Background] Ras activation, as well as MAP kinase (MAPK) phosphorylation, is known in the synovial tissues from patients with rheumatoid arthritis (RA). RasGRP4 is a guanine nucleotide exchange factor for small GTPase Ras expressed preferentially in the mast cells, monocytes and neutrophils. We previously identified ectopic expression of RasGRP4 in fibroblast-like synoviocytes (FLS) of a subset of RA patients, inducing proliferation of FLS. Farnesyltransferase inhibitors (FTIs), prevent farnesylation of Ras, are known to prevent human tumor cell proliferation and attenuate collagen-induced arthritis in animal model, but the effect of FTIs on proliferation of FLS from RA patients is still unknown. [Objective] To clarify the molecular mechanisms involved in the induction of FLS proliferation by RasGRP4 and to evaluate the effect of FTI on the proliferation of FLS. [Methods] FLS or HEK293 cells were transfected with expression vector that encodes hRasGRP4. Phosphorylation of Raf, MEK, Erk, JNK and p38MAPK was evaluated in transfected cells using Western blotting. FLS were treated with tipifarnib, one of FTIs, and cell proliferation was evaluated using BrdU Assay. Phosphorylation of Erk was also evaluated using Western blotting. [Results] In HEK293 cells forced to express RasGRP4, Raf-MEK-Erk pathway, as well as p38MAPK, was readily phosphorylated at their steady state. FLS decreased RasGRP4 expression during multiple passages. RasGRP4 transfection into such cells recovered MAPK phosphorylations, especially of Erk and p38 MAPK. FLS treated with tipifarnib down-regulated their proliferation and phosphorylation of Erk. [Conclusion] RasGRP4 expression in FLS from RA patients contributes to the activation of Erk and p38MAPK signaling pathway. Inhibition of Ras translocation using FTI was suggested as a novel treatment strategy to prevent FLS proliferation in RA.

ICW11-3

MiR-204-3p inhibits the production of TLR4-related cytokines in familial Mediterranean fever by targeting the PIK3 signaling pathway

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Conflict of interest: None

Objective: The aim of this study was to identify a serum miRNAs profile and potential biomarkers in FMF and clarify their gene targets for understanding the pathogenesis of autoinflammatory diseases. **Methods:** We performed miRNA microarray in the serum from FMF in attack and in remission. We subsequently examined the expression of candidate miRNAs in macrophages derived from THP-1 cells stimulated with toll-like receptor (TLR) ligands. Macrophages derived from THP-1 cells transfected with pre-miRNA and anti-miRNA were stimulated with TLR ligands for 24 hours. We collected the supernatants for the quantification of inflammatory cytokine production. To identify the target genes, we overexpressed its miRNA and performed Agilent expression microarray. Transfection with reporter construct and pre-miRNA and anti-miRNA was performed to confirm suppression of target mRNA. **Results:** We found that miR-204-3p was greatly decreased in the serum from FMF patients in attack. In vitro study, the expression of miR-204-3p was suppressed by LPS stimulation in macrophages derived from THP-1 cells. Inhibition of miR-204-3p significantly induced the production of TLR4-related cytokines whereas overexpression of miR-204-3p inhibited their production. Bioinformatic analysis showed that miR-204-3p is predicted to target genes implicated in TLR pathway through regulation of PIK3 signaling. Reporter assay revealed that miR-204-3p directly suppressed the luciferase activity of 3'UTR of PIK3CG reporter construct. **Conclusion:** These data suggest that serum miR-204-3p has a potential as a useful biomarker among patients with FMF and that miR-204-3p plays a critical role as a suppressor to regulate the production of TLR4-related cytokines by targeting PIK3 signaling pathway.

ICW11-4

Clinical Significance of plasma Presepsin levels in Patients with Connective Tissue Diseases

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Conflict of interest: None

【Objectives】Presepsin (PSEP: soluble CD14 subtype) has been established as a biomarker of sepsis. However, the clinical significance of its plasma levels in patients with connective tissue diseases (CTD) has remained unclear. The aim of this study is to clarify a profile of plasma PSEP levels and explore their clinical significance in patients with CTD. 【Methods】One hundred and two CTD patients with a fever greater than 37.5 degrees Celsius were enrolled in this retrospective study from August 2012 to September 2015. Plasma PSEP levels were measured by chemiluminescent enzyme immunoassay (CLEIA). Plasma PSEP levels in febrile CTD patients were compared between infection and non-infection groups. 【Results】In this study, 32 patients (31%) with systemic lupus erythematosus (SLE) and 70 patients (69%) with non-SLE CTD were analyzed. Plasma PSEP levels in SLE group were significantly higher compared with those in non-SLE group (median〔IQR〕SLE: 540pg/ml〔325.8-1725〕vs non-SLE: 295.5pg/ml〔166.3-567〕, p=0.0015). The rates of proven infection in SLE and non-SLE CTD were 41% and 47%, respectively. Among non-SLE patients, plasma PSEP levels in infection group were significantly higher than those in non-infection group (Infection: 436pg/ml〔251-975〕vs non-infection: 202pg/ml〔147.5-308〕, p=0.015). Inversely, among SLE patients, there was no significant difference of plasma PSEP levels between infection and non-infection group. In SLE patients without infection, plasma PSEP levels correlated with SLEDAI-2K (r=0.484, p=0.036). 【Conclusions】Elevated plasma PSEP levels were correlated with infection in non-SLE CTD patients, but not in SLE. On the other hand, in SLE patients, plasma PSEP levels may associate with disease activity, presumably reflecting the monocyte activation.

ICW11-5

The progression in abnormalities detected by nailfold videocapillaroscopy (NVC) in patients with systemic sclerosis (SSc)

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Conflict of interest: None

[Objectives] In SSc, capillary abnormalities cause tissue hypoxia and fibrosis. However, the precise mechanism and association between the progression of nailfold capillary abnormalities and organ involvement are still unknown. To elucidate these relationships, we evaluated nailfold capillary abnormalities in patients with SSc. [Methods] 62 patients diagnosed as SSc were enrolled. We assessed quantitative capillary changes using NVC at the point of 52 weeks and compared with the baseline data. In each case, organ involvements and progression of skin sclerosis were examined based on the severity score of Ministry of Health labor and welfare Japan and Rodnan skin score. [Results] At baseline, A score (Enlarged capillary, Giant capillary, Hemorrhage) which represent initial changes showed correlation to skin score and skin ulcer, and B score (Loss of capillary, Disorganization of the vascular array, Capillary ramification) which represent advanced changes showed a significant correlation not only to skin ulcer, but also to the severity of pulmonary hypertension and gastrointestinal involvement. In patients with NVC abnormalities at the baseline, the progressive skin sclerosis was seen at 52 weeks in contrast to patients without NVC abnormalities. Overall, 41.9% of the cases (26/62) showed progression of either A score or B score during this study. Particularly, anti Scl-70 antibody positive patients showed more rapid progression of capillary changes. Even with the use of immunosuppressants and vasodilators, the effect of suppressing the progression of NVC was not seen. [Conclusion] The progression of the nailfold capillary abnormalities reflected progression of organ involvement and skin sclerosis in patients with SSc. In general, it is known that the presence of anti Scl-70 antibody increases the risk for diffuse skin involvement. From our study, the consistent results were observed in terms of the microvascular abnormalities.

ICW11-6

The Predictive Risk Factors for Complication of Infection during the Treatment for Polymyositis and Dermatomyositis

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Conflict of interest: None

Background/Purpose: Interstitial lung disease (ILD) is one of the predominant causes of death in polymyositis/dermatomyositis (PM/DM). We have already reported that infection is one of the main causes of death in early phase and identified high initial dose of prednisolone (PSL) as an independent factor for infection. Here we investigated the association of treatment and infection with PM/DM-ILD. **Methods:** We retrospectively analyzed clinical baseline, initial therapeutic regimens, total amounts of PSL, clinical outcomes, and episode of infection of PM/DM-ILD who had received initial treatment at six hospitals associated with Yokohama City University from 2003 to 2016. **Results:** One hundred sixteen (PM 22, DM 51, and clinically amyopathic DM 43) patients were included. The mean age was 56 ± 15 years and 83 were female. As initial therapies, oral PSL, methylprednisolone (mPSL) pulse, intravenous cyclophosphamide (IVCY), and oral calcineurin inhibitor therapies were performed in 113 (97%), 80 (69%), 48 (41%) and 80 (69%), respectively. The cumulative dose of oral PSL at 2 and 6 month were 2,066 ± 733 mg, and 4,385 ± 1,488 mg, respectively. Forty-one patients had a infection at 51 ± 38 days from initiation of immunosuppressants and 10 died of infections. Old age, low $PaCO_2$ and albumin, high LDH and KL-6, high score of ILD, high initial dose of PSL, mPSL pulse, IVCY, calcineurin inhibitor and combination therapy were extracted as risk factors for infection by univariate analyses. A multivariate logistic regression analyses revealed that combination therapy (p = 0.012, OR 2.83), old age (p = 0.024, OR 2.12), high initial dose of PSL (p = 0.024, OR 2.69), low albumin (p = 0.031, OR 3.56), and low $PaCO_2$(p = 0.038, OR 2.67) were independent risk factors for infection. **Conclusion:** Although intensive therapies are required for PM/DM-ILD, appropriate monitoring, prophylaxis are important, especially in older patients with malnutrition or decreased respiratory function.

ICW12-1

Correlation factors of early adverse events by high dose glucocorticoid treatment

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Conflict of interest: None

[Objectives] Glucocorticoids (GC) are often used as a first-line therapy for various rheumatic diseases. However, they often induce various adverse events (AEs). Our study intended to find correlating factors of the AEs, such as opportunistic infection, diabetes mellitus (DiM), dyslipidemia (DL), insomnia and hypertension (HTN), induced by high dose GC treatment. [Methods] This single-center retrospective study included 110 patients (pts) with SLE (n=41), PM/DM (n=32), ANCA-associated vasculitis (n=18) and other rheumatic diseases (n=19). They were admitted to our department from Apr. 2012 to Mar. 2016 and administered high-dose PSL (around 1mg/kg/day) as the first-line treatment. The medical records were reviewed for 2 months to depict the onsets of those AEs including HTN, DiM, DL, insomnia, and positive cytomegalovirus antigenemia (CMV-Ag). Candidate predicting factors of each AEs include laboratory data and complications such as HTN, DiM, and DL. Multivariate analysis was performed by Logistic regression analysis. [Results] Among all the pts, HTN, DiM, DL, insomnia and CMV-Ag, all of which were limited to newly induced events by PSL, were found in 10%, 15%, 44%, 52%, and 38%, respectively. There were no significant differences among disease types. Logistic regression analysis revealed that high Cre levels were independently positive risk factors of DiM onset (p = 0.0192, OR = 5.484). In addition, we found high value of AST and HTN under treatment was associated with CMV-Ag positive (p = 0.0118, OR = 6.346 and p = 0.0346, OR = 4.467, respectively). We could not detect any correlating factors with DL, HTN or insomnia. [Conclusion] DL and insomnia induced by high dose GC can occur in about a half pts without any expected risk factors. On the other hand, DiM and CMV-Ag may be expected before high-dose PSL treatment.

ICW12-2

The risk of preterm delivery in women with antithyroid antibodies: an association with non-specific rheumatism

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Conflict of interest: None

[Objective] Autoimmune thyroid disease (AITD) is an organ-specific disorder known to be associated with preterm delivery (PD), but a causal relationship remains unproven. Besides, the patients may develop rheumatism. We focused on women with thyroid peroxidase antibodies (TPOAb) or thyroglobulin antibodies (TgAb), and aimed to determine the risk factors for PD. **[Methods]** The retrospective study analyzed women with singleton pregnancies who gave birth from January 2012 to July 2013 in a single center. We included patients having positive TPOAb or TgAb prenatally. Patients positive for thyrotropin-binding inhibitory immunoglobulins, anticardiolipin antibodies, lupus anticoagulant, antinuclear antibodies or rheumatoid factor, or those with a definite rheumatic disease other than AITD were excluded. Their hospital records as well as obstetric outcomes were reviewed, and compared with those of 30 randomly selected control women. **[Results]** This study included 47 patients. The rate of PD was higher than the control (23.4% versus 3.3%; p=0.023), mainly owing to preterm premature rupture of membranes. A prior history of miscarriage was associated with PD (p=0.017). The titers of TPOAb and TgAb, subclinical hypothyroidism, or group B streptococcal colonization did not significantly alter the risk of PD in the patient group. Rheumatic symptoms occurred in 18 patients (38.3%), including

sicca symptoms (29.8%), rash (14.9%), arthritis (10.6%), oral ulcers (6.4%), etc. The presence of these symptoms increased the risk of PD (relative risk, 16.1; p<0.001). It was independently associated with PD in multiple logistic regression analysis after adjusting for age and the history of miscarriage (p=0.007). By contrast, the rates of PD did not differ significantly between the patients without rheumatism and the control women. **[Conclusion]** Our data suggested that TPOAb and TgAb may not directly cause PD. The associated non-specific rheumatism seemed to play a pivotal role.

ICW12-3

Epistatic Interaction of Endoplasmic Reticulum AminoPeptidase1 (ERAP1) and HLA-B51 in Iranian Patients with Behçet's Disease

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Conflict of interest: None

Objectives: Behçet's Disease (BD) is a rare multi-organ vasculitis disorder, which is characterized by mucocutaneous and ophthalmological manifestations. Among many endogenous and exogenous factors, human leukocyte antigene-B51 (HLA-B51) molecule is the most significant intrinsic factor. According to the mentioned claims, we investigated polymorphisms of the *endoplasmic reticulum aminoendopeptidase1* (*ERAP1)*, one of the critical proteins in peptide presentation processes. We also analyzed its association with *HLA-B51* and its association with clinical manifestations of BD patients. **Methods:** In the present study, 299 patients were selected according to international criteria for BD (ICBD). Control group consisted of 302 of healthy individuals who were age, sex and ethnicity matched. SNPs genotyping were performed on 13 selected SNPs using MGB-TaqMan allelic discrimination method. **Results:** There were no significant association between the genotypes, alleles and disease susceptibility. In *HLA-B51* positive patients, TT genotype of rs30187 was significantly associated with disease susceptibility. Ophthalmological and Pulmonary manifestations are correlated with rs30187. Pseudofolliculitis is associated with rs10050860 and rs17482078. Epididymitis is the manifestation correlated with rs10050860 rs17482078. Arthritis was more prevalent among patients is associated with rs27434 and Neuro-Behçet's Disease (NBD) is associated with rs17482078. **Conclusions:** This study has confirmed that there are genetic associations between *ERAP1* and clinical manifestations of BD in Iranian population and further analysis showed that *ERAP1* might take part in disease susceptibility through an interaction with the HLA-B51 protein.

ICW12-4

The CD64 Expression on Monocytes Correlates with the Disease Activity of Adult-onset Still's Disease

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Conflict of interest: None

Objectives: Adult-onset Still's disease (AOSD) is a systemic inflammatory disease with unknown etiology accompanied by the activation of monocyte lineage cells. CD64, an Fc gamma receptor for IgG, is constitutively expressed on monocyte and upregulated upon activation. The aim of this study is to investigate whether or not monocyte CD64 (mCD64) expression correlates with the disease activity of AOSD. **Methods:** Eleven patients who fulfilled Yamaguchi criteria for a classification of AOSD enrolled in this study. We quantitatively measured the mCD64 expression levels by flow cytometry before and after treatment, and statistically analyzed their changes. Besides, we analyzed the correlation between mCD64 expression levels and serum levels of ferritin, one of well-known biomarkers for AOSD, in each individual patient. **Results:** Six were freshly diagnosed patients with AOSD and the rest were recurrent cases of the disease. The means (±SD) of mCD64 expression levels were 78,010 (±33,092) and 13,910 (±3,931) molecules/cell before and after treatment, respectively (P<0.01, Wilcoxon signed-rank test). The mCD64 expression levels were significantly decreased after treatment. In individual analysis, mCD64 expression levels positively correlated with serum levels of ferritin in 8 patients (P<0.05, Spearman's rank correlation coefficient). However, the rest showed no significant correlation and were treated with tocilizumab (TCZ). In these patients, prompt decreases of serum ferritin level were observed regardless of symptomatic improvements. **Conclusion:** The mCD64 expression may correlate with the disease activity of ASOD including the patients treated with TCZ, although a larger scale study is needed to confirm the results.

ICW12-5

High Output Flow Cytometry Array Protein Expression Profiling Facilitates Discriminant Phenotyping of Behcet's and Sarcoidosis Patient-derived Peripheral Whole Blood Cells

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Conflict of interest: None

Objectives: To develop, test and apply a multidimensional flow cytometry-based protein expression analysis approach allowing classification and grouping of states of health and disease in human autoimmune disorders. **Methods:** We utilized, developed and applied a data analysis strategy taking into account all mathematically possible combinations of protein markers in a given flow cytometry panel for the analysis of selected mined flow cytometry data generated using peripheral blood samples derived from human healthy, sarcoidosis or Behcet's patients. Original FACS data files were mined from Dryad Digital Repository http://dx.doi.org/10.5061/dryad.v6ste with reference to http://dx.doi.org/10.1371/journal.pcbi.1003215, gated utilizing FlowJo software according to population partitioning in bivariate plots. Combinatory mathematics was used to generate a matrix quantifying the representation of all possible cell populations using a given set of staining antibodies (markers) within the respective starting population. The resulting data sets were visualized in a heat map approach using R to classify patient samples according to states of health and disease. **Results:** Our approach clustered healthy vs diseased subjects with minimal error using only 4 common markers (CD3, CD8, CD197 and CD45), and allowed differential clustering of sarcoid and Behcet's patients. **Conclusions:** Multi-dimensional analysis of flow cytometry data allows meaningful large-scale screening of biologically relevant markers at the protein level enabling classification and characterization of states of health and autoimmune disease. The approach is unbiased as all mathematically possible marker combinations enter analysis, thus enabling the discovery of cell populations with relevance as potential biomarkers or biological research targets.

ICW12-6

DNA Methylation-dependent regulation of Cathepsin E gene expression by the transcription factor Kaiso in MRL/lpr mice

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Conflict of interest: None

Objectives: To identify new candidate genes regulated by DNA methylation and involved in the pathogenesis of systemic lupus erythematosus (SLE), we integrated genome-wide DNA methylation analysis

and mRNA expression profiling in CD4+ splenic T cells derived from MRL/lpr lupus-prone mice (MRL) and C57BL6/J mice (B6) as a control. **Methods**: Chromatin immunoprecipitation (ChIP)-PCR were used to investigate the binding of transcription factors to the motif. Mouse T cell line (EL-4) was treated with DNA methyltransferase inhibitor, 5-Azacytidine (5-azaC) or histone deacetylase (HDAC) inhibitor, Trichostatin A (TSA) *in vitro* study. Quantification of mRNA expression was confirmed by TaqMan Quantitative PCR (qPCR). **Results**: The mRNA expression level of Cathepsin E (Ctse) was up-regulated in MRL T cells and 583 bp region in 1st intron was hypomethylated. Bisulfite sequencing further identified that CGCG motif in this region was hypomethylated in MRL. Kaiso is known to the transcripition factor which specifically recognize methylated DNA motif (mCGmCG) by C2H2 zinc-finger domains, recruit the SMART/NCoR HDAC3 complex and cause the gene repression. We hypothesized that Kaiso is a candidate transcription factor to repress expression of *Ctse.* ChIP-PCR confirmed that the binding of Kaiso and HDAC3 to mCGmCG motif was decreased in MRL compared to B6. In addition, EL4 cells treated with 5-azaC or TSA showed the suppression of Kaiso or HDAC3 binding to the motif and the overexpression of *Ctse* demonstrated by qPCR. **Conclusion**: In lupus CD4+ T cells, hypomethylation of a Kaiso-binding site in the *Ctse* intron prevents the biding of Kaiso-HDAC3 complex, which may link to the increased histone acetylation and mRNA expression of *Ctse* gene.

ICW13-1

Tankyrase regulates bone mass and osteoclastogenesis

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Conflict of interest: Yes

[Objectives] Tankyrase is a poly (ADP-ribose) polymerase that degrades target proteins. An adaptor protein SH3BP2 has recently been reported as one of the target proteins. We have previously shown that SH-3BP2 gain-of-function mutation enhances osteoclastogenesis. Though the interaction between tankyrase and SH3BP2 is clarified, it is not fully elucidated whether tankyrase attributes to osteoclastogenesis. In this study, we investigated the role of tankyrase in bone metabolism. [Methods] Bone marrow-derived macrophages (BMMs) from wild-type (WT) mice were treated with RANKL in the presence of tankyrase inhibitors (IWR1 or G007-LK). Osteoclastogenesis was evaluated by TRAP staining and resorption assay. Protein expression of NFATc1, Syk, and SH3BP2 were examined by western blotting. To determine in vivo effect, G007-LK was administered orally to WT mice for 4 weeks, and then bone properties were analyzed by micro-CT. [Results] Tankyrase inhibitors enhanced RANKL-induced osteoclast formation and function in WT BMMs culture. Tankyrase inhibitors significantly increased SH3BP2 protein and augmented nuclear localization of NFATc1 and phosphorylation of Syk in response to RANKL. SH3BP2-deficient BMMs were also tested, and then we found that SH3BP2 deficiency completely diminished the effect of tankyrase inhibitors. Though tankyrase inihibitors are known to suppress Wnt pathway, Wnt-specific inhibitor (ICG-001) did not promote osteoclastogenesis, suggesting that tankyrase inhibitors promote osteoclastogenesis independently of Wnt pathway. Finally, administration of G007-LK to the WT mice induced trabecular bone loss in tibias and vertebras. [Conclusion] These findings suggest that tankyrase inhibition enhances osteoclastogenesis via increased SH3BP2 expression independently of Wnt pathway. This study further supports the idea that activating tankyrase activity would be a novel therapeutic option of bone destructive diseases including osteoporosis and rheumatoid arthritis.

ICW13-2

Serum sclerostin levels were related to bone mineral density and structural geometry in patients with autoimmune diseases taking prednisolone and bisphosphonate

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Conflict of interest: None

[Objectives] Sclerostin is secreted mainly by osteocytes and inhibits bone formation. This study examined whether the serum sclerostin level can serve as a marker of osteoporosis in patients with autoimmune diseases treated with prednisolone (PSL) and bisphosphonates (BP). [Methods] The study enrolled 117 patients with autoimmune diseases taking BP and PSL. Their mean age was 54.6±14.1 years, 89% were female, and the mean daily PSL dose was 10.0±3.8 mg. The mean duration of BP use was 5.0±2.7 years. The underlying diseases were systemic lupus erythematosus (65 cases), rheumatoid arthritis (16 cases), and other autoimmune diseases (36 cases). The serum sclerostin level was measured using an enzyme immunoassay. Spearman's rank correlation coefficient and stepwise multiple regression analysis were used for the analyses. [Results] The mean serum sclerostin level was 0.70±0.38 ng/mL. The serum sclerostin level was positively correlated with age, body weight and the Z-score and negatively correlated with the estimated glomerular filtration rate and daily PSL dose. The hip structural analysis (HSA) score was also correlated with the serum sclerostin levels. Partial correlation coefficients controlled by age revealed that the serum sclerostin level was positively correlated with the T- and Z-scores of the left femoral neck (r=0.769, p=0.043 and r=0.758, p=0.048) and HSA section modulus (r=0.867, p=0.011 at the intertrochanteric region and r=0.802, p=0.030 at the femoral shaft), but was not correlated with bone metabolic markers. Stepwise multiple regression analysis indicated that the Z-score of the femoral neck was the factor most significantly related to the serum sclerostin level (β=0.675, p=0.046). [Conclusion] The serum sclerostin level was associated with the bone mineral density and structural geometry independently of age. The serum sclerostin level might serve as a marker of bone strength in patients with autoimmune diseases taking PSL and BP.

ICW13-4

Zinc Finger Protein 440 is Highly Expressed in Human Knee and Facet Osteoarthritis Cartilage and Regulates the Expression of Inflammatory, Cartilage Catablolic and Cell Death Markers Through the Positive Feedback Loop to Sustain NF-kB Signaling Pathway

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Conflict of interest: None

Objectives: We previously showed that zinc finger protein 440 (ZNF440) is the common target of both microRNA-181a-5p and microRNA-4454 which are significantly highly expressed in facet joint osteoarthritis (OA) cartilage and markedly correlated with disease severity of facet joint OA. We aimed to investigate the role of ZNF440 in the pathophysiology of cartilage degeneration in human facet and knee joints. **Methods:** Expression of *ZNF440* in osteoarthritic and normal cartilage obtained from human knee and facet joints were determined by immunohistochemistry/qPCR. Human chondrocytes isolated from knee/facet OA cartilage were cultured and transfected with ZNF440 siRNA or control siRNA with/without interleukin (IL)-1β, or miR-181a-5p and miR-4454 mimic to see the effect of ZNF440 on the activities of inflammatory/catabolic/cell death markers and NF-kB signaling pathway using qPCR/Western blotting. **Results:** We observed a markedly increase in the expression of *ZNF440* both in knee and facet joint OA cartilage compared to normal cartilage. Treatment with ZNF440 siRNA significantly sup-

pressed the expression of inflammatory*(IL6*/*MCP1)*/catabolic (*MMP13)*/cell death (*PARP p85*) markers in human knee and facet chondrocytes treated with IL-1β. Induction of NF-kB signaling using IL-1β treatment elevated miR-181a-5p/miR-4454 expression, which mediated a feedback loop to sustain NF-kB signaling through *ZNF440* expression. OA chondrocytes co-transfected with miR-181a-5p or miR-4454 mimic and ZNF440 siRNA regulated phosphorylation of Ser536 NF-kB-p65 and reduction of IkB expression compared to control. **Conclusions:** We have uniquely identified that the expression of *ZNF440* is markedly increased in the human knee/facet cartilage and regulates the expression inflammatory/catabolic/cell death markers through the feedback loop to sustain NF-kB signaling. These results indicate ZNF440 may be a potential target for stopping/delaying cartilage degeneration during knee and facet joint OA in human.

ICW13-5

Identification of Metabolite Profiles Linked to Gender and Obesity in Plasma of Patients with Knee Osteoarthritis

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Conflict of interest: None

Objective: Identify plasma phosphatidylcholine (PC) and lysophosphatidylcholine (lysoPC) profiles from patients with osteoarthritis (OA) compared to normal volunteers. **Methods:** PC and lysoPC concentrations were measured in plasma from OA patients or normal adult volunteers. Cohorts were segregated by obesity (BMI ≥ 30) and gender, and restricted to age ≥ 50. Analysis was performed with Metaboanalyst v3.0. PCs and lysoPCs in normal vs OA plasma were compared by Student's t- test and variable importance in projection (VIP) scores were determined by PLS-DA analysis. For each subgroup, a list of metabolites with significantly different concentrations ($p<0.05$) between groups and VIP scores ≥ 1 was generated. Metabolites common to multiple lists were identified and entered in multiple logistic regression models for predicting OA. Potential biomarkers were those with odds ratios significantly different from 1. **Results:** Plasma from 262 individuals (114 normal, 148 OA) was analyzed. Subgroups included 62 non-obese men (32 normal, 30 OA); 62 obese men (20 normal, 42 OA); 62 non-obese women (33 normal, 29 OA); and 76 obese women (29 normal, 47 OA). Non-obese men and women had no PCs or lysoPCs in common as predictors of OA; a single metabolite was common between obese men and women. Six metabolites were common predictors between obese and non-obese men, while none were common between obese and non-obese women. Four metabolites were identified as common predictors of OA across males and females (regardless of obesity). Logistic regression identified three of these (PCae 38:0, lysoPCa C16:0 and PCae C38:2) as potential biomarkers for OA, with model area under ROC of 0.75 (CI:0.674-0.814) and odds ratios of 0.27, 2.69 and 0.09, respectively (all $p \leq 0.001$). **Conclusions:** Gender and obesity are sources of variation with respect to metabolite biomarkers for knee OA. Selected metabolites show promise as plasma biomarkers for knee OA irrespective of gender and obesity.

ICW13-6

Identification of a longitudinally regulated metabolite signature uncovers a novel mechanism regulating high-fat diet induced acceleration of osteoarthritis in mice

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Conflict of interest: None

Objectives: To determine the effect of diet on longitudinal changes in metabolomics and their contributions to the pathogenesis of OA. **Methods:** 9wk old C57BL6 mice were fed high fat diet (HFD) or lean diet (LD) for 18 wks followed by a normal chow diet. Mice were evaluated longitudinally up to 12 months of age. Body composition and metabolic indices, including BMI, fasting blood glucose level, body weight, adipokine and metabolite levels were measured. Knee joints were harvested and analyzed by histopathology (OARSI scoring) for OA pathogenesis. Mice were also subjected to surgically-induced OA at the end of diet and knee joints were similarly analyzed. Primary human chondrocytes were treated with leptin, autotaxin (ATX inhibitor and expression of MMP13 were determined. **Results:** HFD-fed mice had significant increases in physical parameters as compared to LD-fed mice. Knee joints of HFD-fed mice had more severe spontaneous and surgically-induced OA compared to LD-fed mice. In addition to longitudinal increases in plasma leptin, metabolomic analysis of plasma from mice on differential diet regimes showed that select lysophosphatidyl choline (lysoPC) and phosphatidylcholine analogues increased longitudinally in the HFD-fed mice compared to LD-fed mice. Consistently, knee joints from HFD-fed mice also had increased expression of leptin and treatment of human chondrocytes with leptin increased the release of lysoPCs, expression of MMP13 and ATX. Treatment of human chondrocytes with ATX inhibitor ± leptin showed decreased expression of MMP13. **Conclusion:** HFD induces and maintains selective metabolic changes and increases OA progression in both OA models. Presently we are examining sPLA2 as an upstream target of leptin contributing to changes in the LysoPC/ATX/LPA axis in chondrocytes. Future studies will define the role of this leptin-modulated axis on OA pathogenesis.

ICW14-1

Reciprocal protein stabilization of ABL and TAZ regulates osteoblastogenesis and embryonic bone development through transcription factor RUNX2

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Conflict of interest: None

Objectives: Cellular identity in metazoan organisms is frequently established through lineage-specifying transcription factors, which control their own expression through transcriptional positive feedback while antagonizing developmental networks of competing lineages. Here, we show a distinct positive feedback model that arises from the reciprocal protein stabilization required for osteoblastogenesis and embryonic skeletal formation. **Methods:** We examined the calvarium and limb bones from newborn pups by micro-CT and histomorphometric analysis. To investigate the molecular mechanism, we isolated and cultured murine calvarial osteoblasts from *Sh3bp2*$^{-/-}$, *Smurf1*$^{-/-}$, *Abl*$^{fl/fl}$, *Abl*$^{-/-}$ and TAZ-deficient mice for *in vitro* study. Co-IP, ChIP, pulse chase, luciferase assay, BrdU assay, ubiquitin assay, cell growth assay and differentiation assay were performed in this study. **Results:** We found a unique positive feedback loop between the tyrosine kinase ABL and the transcriptional co-activator TAZ. During osteoblastogenesis, ABL and TAZ reciprocally stabilized each other at the protein level through the exclusion of their respective E3-ubiquitin ligases, SMURF1 and β-TrCP. Stabilized and active ABL potentiated the assembly and activation of the RUNX2-TAZ master transcription factor complex that is required for osteoblastogenesis and embryonic bone formation while antagonizing PPARγ-mediated adipogenesis. ABL also enhanced TAZ nuclear localization and the formation of the TAZ-TEAD complex that is required for osteoblast expansion. Lastly, we have provided genetic data showing that the regulation of the ABL-TAZ amplification loop lies downstream of the adaptor protein 3BP2, which is mutated in the craniofacial dysmorphia syndrome cherubism. **Conclusion:** A unique interplay between ABL and TAZ, which promotes the osteoblast maturation program, highlights a link between tissue-specific activation of these proteins in osteoblasts and a potential therapeutic strategy for osteoporosis.

ICW14-2

Th22 cells induce osteoclast differentiation through production of IL-22

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Conflict of interest: None

Background: Although elevated levels of IL-22 in the synovial fluids of rheumatoid arthritis (RA) patients were reported, its pathological roles remain unclear. Recently, IL-22–producing Th22 cells have been identified. We reported previously that Th22 cells highly accumulated into synovial tissues in patients with RA. In this study, we focused on the effect of Th22 cells on osteoclastogenesis in the pathogenesis of RA. **Methods:** Human monocytes were cultured with IL-22, IL-17 or IFN-γ in the presence of macrophage colony stimulating factor (M-CSF) and receptor activator of nuclear factor kappa-B ligand (RANKL) for 12 days. Th1 cells, Th17 cells and Th22 cells were sorted from peripheral blood, and co-cultured with monocytes in the presence of M-CSF and RANKL. **Results:** Addition of IL-22 to the in vitro culture of monocytes with M-CSF and RANKL markedly increased numbers of tartrate-resistant acid phosphatase (TRAP)-positive osteoclasts formation. The addition of IFN-γ to the culture significantly decreased TRAP-positive osteoclasts number, whereas IL-17 had marginal effects. The g[YT1] ene expression of NFATc1 and cathepsin K was significantly increased by addition with IL-22 in a dose dependent manner. Co-culture of Th22 cells with monocytes in the presence of M-CSF and RANKL induced TRAP-positive osteoclasts formation more efficiently than that of either Th1 cells or Th17 cells. **Conclusion:** Th22 cells, which co-express chemokine receptors CCR4, CCR6 and CCR10, therefore, possess strong potency of tissue migration and accumulate into inflamed synovial tissues where the ligands such as CCL20 are highly expressed. The results indicated that Th22 cells have the capacity to promote osteoclast differentiation through production of IL-22. Thus, Th22 cells may play a pivotal role in the pathogenesis of RA by bone resorption in RA synovitis.

ICW14-3

PLEKHM1-DEF8-RAB7 complex regulates lysosome positioning and bone homeostasis

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Conflict of interest: None

(Objectives) As bone loss caused by osteoclasts (OCs) results in a serious problem in rheumatoid arthritis (RA) patients, the control of OC function is an essential strategy for the treatment of RA. Here, we focused on a lysosome adaptor protein, PLEKHM1, whose mutation causes osteopetrosis in humans and incisor-absent rats, due to diminished lysosome trafficking and ruffled border (RB) formation in OCs. (Methods) To elucidate the mechanism (s) by which PLK1 regulates lysosomal secretion in OCs, we generated germline and Cathepsin K (CTSK)-Cre conditional PLK1 deficient C57BL/6J mice. We analyzed the bone structure by micro CT of femurs and vertebrae (in vivo) and these OC function by cultured bone marrow macrophages with RANKL and M-CSF from wild type and knockout mice (in vitro). (Results) All mice grew normally. Both germline and CTSK-cre conditional PLK1 deficient mice increased bone volume as compared to their controls. In vitro, OC formation, actin-ring formation, and microtubule organization were normal in PLK1 null OCs. However, the resorptive capacity of PLK1 null OCs was markedly reduced. Specifically, a series of morphological, functional, and live cell imaging studies revealed that loss of PLK1 abrogates the peripheral distribution of lysosomes and bone resorption in OCs Using immunoprecipitation and mass spectrometry we identified several novel PLK1 interacting proteins in OCs, including DEF8, FAM98A, and NDEL1. Further, we determined DEF8 binding to the C-terminal part of PLK1 and promoting PLK1's interaction with RAB7, a lysosome-associated small GTPase. FAM98A and NDEL1 with PLK1 connects lysosomes to microtubules. Moreover, suppression of these genes in OCs by shRNAs dramatically inhibited lysosome secretion and bone resorption similar to PLK1 null OCs. (Conclusion) Thus, PLHKEM1, DEF8, FAM98A, and NDEL1 comprise a molecular complex that regulates lysosome positioning and secretion through RAB7.

ICW14-4

Identification of microRNA-181a-5p and microRNA-4454 as mediators of facet cartilage degeneration through the activation of zinc finger protein 440 mediated NF-kB signaling pathway and potential circulating biomarkers for detecting the severity of facet j

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Conflict of interest: None

Objectives: To investigate the role of microRNAs (miRNAs) in the pathophysiology of facet joint osteoarthritis (FJOA) and the potential as biomarkers for detecting FJOA severity in blood. **Methods:** Based on MRI and histopathology, a large and unique patient cohort (n=203) ([Control group]: normal-mild FJ cartilage degeneration and [FJOA group]: moderate-severe FJ cartilage degeneration) was established. Using this cohort, 2,100 miRNAs were screened using miRNAarray/qPCR to identify differentially regulated miRNAs in cartilage and investigated their correlation with FJOA disease severity based on MRI grading. Human FJOA chondrocytes were cultured and transfected with miRNA mimics/inhibitors to determine the effect *in vitro*. Signaling pathways modulated by miRNAs were also identified using mirDIP/pathDIP. Further, miR-181a-5p mimic was injected into FJs of rats to see the effect *in vivo*. Finally, the expression of two miRNAs were tested in human plasma. **Results:** Out of 2,100 miRNAs tested, we identified 2 miRNAs (miR-181a-5p/miR-4454) whose expressions markedly increased in FJOA cartilage with exhibiting significant correlation with clinical FJOA severity based on MRI. *In-vitro* study, miR-181a-5p and miR-4454 were involved in promoting inflammatory/catabolic/cell death activity in FJ chondrocytes. We further identified that in FJ cartilage both miR-181a-5p and miR-4454 signal by ZNF440 via modulation of the NFκB pathway. By injecting miR-181a-5p mimic in rat FJs, we clearly observed a FJOA phenotype in FJ cartilage associated with enhanced catabolic activity and chondrocyte apoptosis *in vivo*. Finally, circulating forms of both miRNAs in human plasma are detectable and elevated with increased degree of FJOA disease severity. **Conclusions:** Using clinical, *in vitro* functional and *in vivo* studies, we for the first time have identified miR-181a-5p and miR-4454 as mediators of FJ cartilage degeneration and potential biomarkers to detect and determine the stage of FJOA disease.

ICW14-5

Microdamage accumulation is the most dominant factor influencing bisphosphonate related atypical femoral fractures; from bone histomorphometric findings of iliac bone and cortex of fracture site

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Conflict of interest: None

To explore the mechanism of bisphosphonate (BP)-related atypical femoral fractures (AFFs) by evaluating the degree of microcracks and osteocyte necrosis in the cortex of the fracture sites and bone metabolism in iliac bone with bone histomorphometric analysis, 11 AFFs patients who fulfilled with ASBMR clinical features were registered. All cases were female, and age was 77 ± 9 years old on average. Primary diseases were osteoporosis in 9, rheumatoid arthritis in 1, PMR in 1. Average duration of BPs was 6.4 ±3.5 years. At the surgery, the specimens were collected from the fracture sites and ilium. Microcracks were detected in the fracture site of each specimen. The average crack density (Cr.Dn) was 1.11±1.1/mm^2, and the average crack surface density (Cr.S.Dn) was 110.8±100/mm^2. Both Cr.Dn and Cr.S.Dn were remarkably higher than reference data; Cr.Dn was 0.21 (/mm^2) and Cr.S.Dn was 19.5 (μm/mm^2) based on the previous report (Norman TL, et al. Bone 1997;20:375-9). Empty lacuna density was higher than osteocyte density in 6 of 11 cases (56%), suggesting the decrease in osteocytic function. Iliac bone findings showed that both bone formation and bone resorption parameter were decreased in 2 of 9 cases (22%), suggesting severely suppressed bone turnover was not essential factor of the incidence of AFFs. In conclusion, microdamage accumulation was the most dominant factor influencing BP-related AFFs.

ICW14-6

Influence of Previous Knee Symptom History in Knee Osteoarthritis on Present and Future Knee Symptoms – Data from the Osteoarthritis Initiative

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Conflict of interest: None

The duration of previous osteoarthritis-related knee pain, aching, or stiffness is generally not considered in current and future therapeutic strategies. Therefore, we investigated the relationship between the duration of previous knee symptom history and current and future knee symptomology in a subsample of the Osteoarthritis Initiative. We investigated 1765 individuals (56% females, BMI 28.6kg/m2, 59.3 years) for their previous knee symptom history and included a total of 2548 knees. Measures of pain, stiffness, disability (WOMAC scores), pain intensity, and quality of life (KOOS score) were recorded at baseline and at every consecutive annual follow-up screening visit for a period of 9 years. No significant differences at baseline were observed between categories of previous knee symptom duration (<1year, 2-5years, >5 years) in respect to measures of pain, stiffness, disability and quality of life. After the 2-year follow-up visit, a significant worsening in knee symptomology was detected in those with >5 years and 2-5 years when compared to those with <1year. This effect was consistent throughout the next 9 years of follow up. However, a longitudinal trend was observed towards lesser worsening in those with <1year as compared to greater worsening or same worse symptom state in those with 2-5years or >5 years. Radiographic grading in a subsample of 961 knees revealed no significant differences between the investigated categories at baseline and at every consecutive visit. The results of our analyses reveal that the duration of previously-experienced symptoms in knee osteoarthritis do influence present and future symptomology. Individuals with <1 year of symptom history have less pain, better function and increased quality of life compared to those with >1 years of symptoms. Symptom history did not influence longitudinal radiographic structural change during the investigated 9-years period.

ICW15-1

Efficient regeneration of cartilaginous tissue after application of IL-6R-stimulated mesenchymal stem cells with a novel delivering scaffold for the treatment of RA

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Conflict of interest: None

Objectives. Mesenchymal stem cells (MSCs) differentiate into many types of cells, including chondrocytes. MSC are considered as an ideal tool for joint repair of rheumatoid arthritis (RA). Although local delivery of MSCs is prerequisite to aim tissue repair, the methodology of local delivery remain unclear. Aim in this study is to establish how to implant poly-lactic-co-glycolic acid (PLGA) nano-fiber with MSC into joint tissues in a novel method to regenerate cartilaginous tissues efficiently. **Methods.** Human bone marrow-derived MSCs treated with or without IL-6R were implanted into bilateral knees from antigen-induced arthritis (AIA) rats after seeded on PLGA. After 8 weeks, effects of the implant on cartilaginous regeneration/repair were assessed by X-ray and mCT image, HE and Safranin O staining, or immunohistochemistry to detect human chondrocytes. **Results.** X-ray or mCT images revealed that joint image of knees from AIA rats implanted with (MSCs+IL-6R)+PLGA, but not PLGA alone or MSCs+PLGA, were comparable with those of wild-type (WT) rats. HE or safranin O staining revealed that knee's joints from AIA rats implanted with (MSCs+IL-6R)+PLGA, but not PLGA alone or MSCs+PLGA, showed similar positive image to those of WT ones. Human aggrecan was detected in knee's cartilaginous tissues from AIA rats implanted with (MSCs+IL-6R)+PLGA, but not PLGA only or MSCs+PLGA. **Conclusion.** After co-implantation of (MSCs+IL-6R)+PLGA into AIA rat's joint space, MSCs efficiently differentiate into chondrocytes, and reside within damaged cartilaginous tissues. The chondrocytes produce cartilage matrix, leading to efficient repair and regeneration of cartilaginous tissue. These results suggest a potential clinical application of MSC-based treatment by utilizing PLGA for cartilage regeneration in patients with RA.

ICW15-2

Epidemiology of Rheumatoid Arthritis and Association with Coronary Artery Disease in the Korean Population: A Nationwide Study

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Conflict of interest: None

Objectives: Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease and is known to be associated with coronary artery diseases (CAD). However, previous studies of the association between RA and CAD were reported mainly in non-Asian groups, although some Asians appear to have a higher independent risk for cardiovascular diseases. Thus, we aimed to examine the prevalence of RA and the relationship between RA and CAD in South Korea. **Methods:** Data were collected from the 2008–2012 Korea National Health and Nutrition Examination Surveys. A total of 25,828 eligible participants were included. The current diagnostic status of RA and CAD determined by a physician was based on self-reports. CAD included myocardial infarction and angina pectoris. Because there were significant differences in the baseline characteristics between the patients with RA and those without RA, we used propensity score-matching to adjust for such differences. We calculated the odds ratios (ORs) and 95% confidence intervals (95% CI) for the odds of the participants with RA on CAD development. **Results:** The prevalence of RA in Korea from 2008 to 2012 was 1.9%. After propensity score-matching, the multivariable logistic regression model showed that the OR of the patients with RA on CAD was 2.67 (95% CI 1.60–4.45, p <0.001) compared to the patients without RA. **Conclusion:** The prevalence of RA in South Korea was similar to the worldwide data, and the presence of RA increased the risks of CAD.

ICW15-3

Autophagy Promotes Citrullination of Vimentin in Synovial Fibroblasts

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Conflict of interest: None

Background: Citrullinated vimentin (cVIM) is a major antigen of rheumatoid arthritis (RA) targeted by anti-citrullinated protein antibodies. Autophagy is a self-cannibalism system which regulates not only metabolism but also various cellular functions. Since autophagy is involved in major histocompatibility complex class II antigen presentation and has peptidylarginine deiminase activity, we hypothesized that activation of autophagy causes citrullination of vimentin in synovial fibroblasts (SF), one of the effector cells in RA. **Objective:** To clarify the relationship between autophagy and citrullination of vimentin. **Methods**: cVIM was generated by incubating recombinant human VIM with rabbit muscle peptidylarginine deiminase. Among 6 sera from RA patients one serum with the highest anti-cVIM was identified. SF from three RA patients and three osteoarthritis patients were treated with a proteasome inhibitor MG132 to activate autophagy. Intracellular cVIM was quantified by western blotting using anti-VIM, anti-citrulline and anti-beta-actin antibodies as well as anti-cVIM positive serum. **Results**: MG132 activated autophagy in SF with both dose-(1 nM to 10 microM) and time-(3, 6, 12, 24, 48 h) dependent manner, evaluated by conversion of LC3-I to LC3-II. Anti-VIM antibody, anti-citrulline antibody, and anti-cVIM positive serum all detected 54 kDa protein in SF lysates, indicating the presence of cVIM in SF. The amount of cVIM in SF, evaluated by the ration between 54 kDa citrulline and beta-actin, was increased dose-dependently following the treatment with MG132 ($p = 0.03$ at 10 microM, 24 h). **Conclusions**: Our study indicates that autophagy may promote citrullination of vimentin in SF, presumably contributing the initiation of autoimmunity in RA.

ICW15-4

IL-17 inhibits the migration and invasion of rheumatoid fibroblast-like synoviocytes through activation of autophagy via PI3K/AKT/mTOR signaling pathway

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Conflict of interest: Yes

Objectives: Interleukin-17A (IL-17A) plays a critical role in the pathogenesis of rheumatoid arthritis (RA). Autophagy is required to ensure cellular homeostasis. Here, we hypothesized that IL-17A might have an impact on autophagic flux and that modulation of autophagy might be involved in migration and proliferation of synovial fibroblasts in the patients with RA under inflammatory condition. **Methods:** Synovial tissue was obtained from the patients with RA or osteoarthritis (OA). FLS was cultured with IL-17A, autophagy inducer or inhibitor. The expression of marker proteins for autophagic flux and PI3K/AKT/mTOR signaling pathway were analyzed by western blot. A migration scratch assay was used to assess FLS migration in response to stimulation with IL-17A. Inflammatory cytokine release was measured by enzyme-linked immunosorbent assay. **Results**: The expression of autophagy markers (LC3B, Beclin1, Atg5 and p62) was time- and dose-dependently increased in the synovium of the patients with RA than in that of the patients with OA. Autophagy was also enhanced in RA-FLS compared with OA-FLS. IL-17A upregulated the expression of LC3B, Atg5, Beclin1 and Lysosomal-associated membrane protein 1 (LAMP1) in RA-FLS. IL-17A-induced accumulation of p62 was prominent in RA-FLS. Inflammatory cytokine and expansion of FLS stimulated by IL-17A was suppressed by the inhibition of autophagy. IL-17A increased expression of phosphorylation-Akt and decreased mTOR signaling pathway. **Conclusion**: Our findings demonstrated that IL-17A could induce activate autophagy, induce inflammatory response, and eventually lead to proliferation of synoviocytes. This results also provide additional evidence for a significant role of autophagy in the pathogenesis of RA.

ICW15-5

Prevalence and Associated Factors for Non-adherence in Patients with Rheumatoid Arthritis

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Conflict of interest: None

Objective: To estimate the prevalence of nonadherence to anti-rheumatoid arthritis (RA) treatment and to identify the associated factors for non-adherence in RA patients. *Method:* Among 3,555 patients in KORONA cohort, which is a nationwide multicenter observational RA cohort, 3,523 patients who completed the questionnaire about adherence to anti-RA treatment were analyzed. Patients were divided into 2 groups; 1) adherent group as patients who had skipped their medication ≤5 days within the past 2 months, 2) nonadherent group as patients who had skipped ≥6 days. Baseline characteristics and cause of nonadherence were compared, and then multivariable regression analyses were performed to identify the associated factors for nonadherence. *Result:* The 339 patients (9.6%) were included in nonadherent group. Nonadherent patients were younger (50.9 ± 12.6 vs. 54.6 ± 11.7 years, $p<0.01$) and had experienced more adverse events (AEs, 44.2% vs. 33.3%, $p<0.01$). In multiple selection questionnaire which asked the reason of nonadherence, more patients in adherent group reported that “they forgot to take medicine”(78.7% in adherent group vs. 45.8% in nonadherent group), while more patients in nonadherent group responded that “they had a discomfort with medicine”(4.5% vs. 13.1%) or “they did not have RA symptom without medication”(5.3% vs. 24.7%). After adjusting for variables, several factors such as younger age (OR 1.02, $p<0.01$) and higher income (OR 1.70, $p<0.01$) increased the risk of nonadherence, while factors representing severe disease including higher functional disability (OR 0.68, $p<0.01$) and glucocorticoid use (OR 0.73, $p=0.02$) were associated with decreased risk of nonadherence. *Conclusion:* The 10% of patients were nonadherent to medication in RA patients. The common causes in nonadherent patients were experience of AEs and absence of RA symptom. Thus, individualized approach according to the cause of nonadherence is needed to improve the adherence.

ICW15-6

A longitudinal study of the effects of disease activity on renal function in patients with RA utilizing linear mixed effect models - ANSWER cohort study -

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Conflict of interest: None

Objective: While patients with RA have more chronic kidney diseases comparing to general population, no studies have investigated tight disease control resulted in improvement or alleviation of renal impairment because the sampling intervals in the most previous cohorts were too wide (e.g. once a year) to exclude the confounding effects of medications which may cause renal damages. Therefore, the objective of this multi-center cohort study is to identify the effects of disease activity on renal function. **Methods:** RA patients with a sampling interval of less than 150 days were enrolled. An estimated glomerular filtration rate (eGFR) was calculated using an equation officially approved by the Japanese Society of Nephrology and used as an outcome variable. Linear mixed effect models were used to evaluate the renal trajectories of patients. Time from baseline (months), disease activity, and their interaction were included as fixed effects while participant identification number and time from baseline were included as random factors. Age, sex, disease duration, RF, ACPA, and medications that were known as a cause of renal damage, such as tacrolimus, iguratimod, NSAIDs, tofacitinib, were included as covariates. **Results:** A total of 25661 samples (mean sampling interval: 2.0 months) from 2104 patients was included. Patients with lower DAS28-CRP had worse renal function at baseline, but a significantly better longitudinal trajectory on eGFR (0.0079 ml/min/1.73m^2 per month, $P = 0.025$). Although all RA patients had naturally progressive renal impairment as they got older, patients who achieved remission or low disease activity had slower renal impairment rate of -0.068 ml/min/1.73m^2 per month compared to patients with moderate or high disease activity (-0.084 ml/min/1.73m^2 per month; $P = 0.037$) These results were also similar using SDAI or CDAI. **Conclusion:** Lower disease activity results in slower renal impairment. The T2T strategy also improves renal outcome.

ICW16-1

Analysis of non-responders to TNF inhibitor: a retrospective cohort study of rheumatoid arthritis patients

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Conflict of interest: None

Objectives Biological disease-modifying anti-rheumatic drugs (bDMARDs) are highly effective treatment for rheumatoid arthritis (RA), among which TNF inhibitors are the most commonly used. However, a small proportion of patients show worsened disease activity after initiation of bDMARDs. This study aims at identifying factors that affect refractory status to TNF inhibitors. **Method** Clinical data was obtained from RA patients who were treated with TNF inhibitors (infliximab, etanercept, adalimumab, golimumab, and certolizumab) for the first time during the period of August 2009-March 2016. Patients who fell into either of the following conditions were defined as non-responders. 1. Treatment with the TNF inhibitor was stopped within 6 months due to a lack of response; or 2. The DAS28-CRP at 6 month increased by >0.6 from that at week 0. Those who quit the treatment within 6months from other reasons were excluded. **Results** In total 774 patients were included. Median age, median disease duration, and mean DAS28-CRP at week 0 were 62 years old, 24 months, and 4.73, respectively. Patients treated with etanercept showed older age, longer disease duration, and lower dose of methotrexate than those with other drugs. At 6 month, DAS28-CRP improved by 2.55 on average, but 54 (6.9%) were identified as non-responders. There was no significant difference in the proportion of non-response between the years of the treatment. Age, disease duration, methotrexate dose at week 0 were not associated with non-response, and prednisolone usage (OR 2.0, 95% CI 1.1-3.7) and high DAS28-CRP (>4.1) at week 0 (OR 2.2, 95% CI 1.1-4.8) were identified as risk factors. **Discussion** Although transient treatment with low dose corticosteroid is reported to be beneficial to prevent bone destruction, this study suggests that corticosteroid usage requires careful consideration to avoid poor outcome of TNF inhibitor in RA patients.

ICW16-2

Association Between Methotrexate Use and Effects of Treatment with a Second Biologic Agent in Rheumatoid Arthritis

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Conflict of interest: None

[Object] In general, the concomitant use of methotrexate (MTX) and biologic disease-modifying antirheumatic drugs (bDMARDS) plays an important role in treating bio-naïve patients with rheumatoid arthritis (RA); however, whether concomitant use of MTX is associated with the effects of second bDMARDS treatment in RA patients for whom first bDMARDS treatment has failed remains unclear. [Methods] We used demographic and clinical data obtained from the Tsurumai Biologics Communication Registry, which comprises the Nagoya University and 20 affiliated hospitals in Japan. Patients aged 20–80 years who fulfilled the ACR 1987 revised or the 2010 ACR/EULAR classification criteria for RA were selected, and only those switching to second bDMARDS treatment were included. Linear multiple regression analysis was used to assess the association between MTX use and effects of second bDMARDS treatment, as defined by DAS28-ESR improvement at week 24. Unstandardized coefficients were calculated. Adjustment variables included sex, age, DAS28 at pre-treatment with second bDMARDS, tumor necrosis factor inhibitor (TNFi) or non-TNFi in RA treatments with first and second bDMARDS, MTX use with first bDMARDS, and glucocorticoid use with second bDMARDS. [Results] Some baseline characteristics differed between patients with MTX use and non-use; however, they were adjusted using linear multiple regression analysis. The unstandardized coefficient of interest was 0.67 ($P < 0.05$), suggesting that DAS28 improvement in second bDMARDS treatment with MTX is superior to that without MTX. Other variables affecting the treatment effects were sex and TNFi or non-TNFi with second bDMARDS, which are well-known influential factors for biologic therapy. [Conclusion] This study demonstrated that the concomitant use of MTX was independently associated with increased effects of second bDMARDS treatment.

ICW16-3

Dose Reduction of Sarilumab in EXTEND: A Long-term Open-label Extension Study in Patients With RA

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Conflict of interest: Yes

Objectives: Sarilumab is a human mAb blocking the IL-6Rα. In the MOBILITY (NCT01061736) and TARGET (NCT01709578) studies, subcutaneous sarilumab (150 or 200 mg q2w) demonstrated efficacy in adults with RA. Infections, neutropenia, injection site reactions, and increased transaminases were among the most common TEAEs. EXTEND (NCT01146652) is an open-label, follow-up study evaluating long-term safety and efficacy of sarilumab added to csDMARDs. This analysis examined the effect of dose reduction of sarilumab 200 mg q2w to 150 mg q2w in EXTEND primarily for protocol-specified laboratory abnormalities. **Methods:** Patients entering EXTEND initially received sarilumab 150 mg weekly. After dose selection for phase 3 studies, patients were switched to or initiated on sarilumab 200 mg q2w. Per protocol, investigators could reduce the dose to 150 mg q2w for ANC ≥0.5-1.0 Giga/L, platelet count ≥50-100 Giga/L, or ALT ≥3-5 × ULN, or at investigator's discretion. Efficacy was analyzed before and 24 weeks after dose reduction for MOBILITY (n=173) and TARGET (n=60) patients. **Results:** As of January 2016 (N=1864), dose reduction occurred in 17.2% of patients (n=321), most commonly for decreased ANC (10.7%; n=199) and increased ALT (4.1%; n=76). The most common non-laboratory reason for

dose reduction was infection (0.4%; n=8). At the time of analysis, 76.9% of patients (n=247) whose dose was reduced were continuing treatment, with a median treatment duration of 2.3 years after dose reduction. Improvements in ANC and ALT were observed over the 6 months after dose reduction. Efficacy was maintained 24 weeks after dose reduction in EXTEND as assessed by ACR20 response rates and HAQ-DI scores. **Conclusion:** In patients whose sarilumab dose was reduced from 200 mg q2w to 150 mg q2w, there was an improvement in laboratory abnormalities and continuation of treatment for the majority of patients. Efficacy was maintained after dose reduction.

ICW16-5

High disease activity and inflammation were related with cognitive impairment in patients with rheumatoid arthritis and collagen induced arthritis mice

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Conflict of interest: None

Objective: To determine risk factors of cognitive impairment (CI) in RA patients and to evaluate association between CI and disease activity and inflammation. Methods: A 497 RA patients' demographic and laboratory data were assessed from 3 universities. The disease activity of RA were assessed by DAS 28. The cut off points of 5.1 of DAS 28 has been used to be indicative of high disease activity (HDA). Cognition was evaluated by Korean version of Mini-Mental State Examination (MMSE-K). CI was defined as MMSE -K scores ≤ 23. To evaluate the association of inflammation (peripheral and central) and CI, collagen induced arthritis (CIA) mice was induced in DBA/1 mice. The clinical, pathologic analyses were performed in CIA mice. The level of proinflammatory cytokines (IL-1β, TNF-α, and IL-6), and glial fibrillary acidic protein (GFAP) of joint tissue and/or hippocampus was evaluated by ELISA, qRT-PCR and western blot. Results: Cognitive impairment was observed in 16.9%. On multivariate analysis, old age (OR 3.7, 95% CI 1.9-7.3), lower education level (OR 11.9, 95% CI 4.8-29.7), and HDA (OR 2.9, 95% CI 1.3-6.2) were independently predicted CI. The concurrent presence of HDA either lower education (OR 3.1, 95% CI 1.5-6.4) or old age (OR 3.6, 95% CI 1.4-9.1) was significantly increased risk for CI than patients with lower disease activity. Patients with CI had high expression level of proinflammatory cytokines including (IL-1β, TNF-α, and IL-6). The level of proinflammatory cytokines were also higher in CIA mice compared to control. The expression of pro-inflammatory cytokines on hippocampus were increased in CIA mice compared to control by western blot. The expression level of GFAP on hippocampus also increased in CIA mice. Conclusions: High disease activity and the level of proinflammatory cytokines were relatively associated with CI in patients with RA. Thus, strict control of RA activity and inflammation might be helpful to preserve cognitive function in RA.

ICW17-1

The role of follicular helper 17 T cells in glucose-6-phosphate isomerase induced arthritis mice

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Conflict of interest: None

Objective Follicular helper T (Tfh) cells are novel T cell subset which promotes follicular B cell activation, differentiation to plasma cells, and antibody production. Recently, circulating Tfh cells have been reported to be increased in rheumatoid arthritis (RA) patients and other autoimmune diseases. Some reports have showed existence of Tfh subsets which share same characteristics as conventional helper T cell subset, but the function of these subset in RA is still unclear. The aim of this study is to elucidate the role of Tfh subsets in glucose-6-phosphate isomerase (GPI) induced arthritis (GIA) mice, which model is dependent on CD4+ T cells, B cells and IL-17. **Methods** 1) The fluctuation of Tfh numbers and subsets in draining lymph nodes from GIA mice were analyzed by flow cytometry during the course of arthritis. 2) The localization of Tfh was analyzed by immunofluorescence staining of the draining lymph nodes. 3) To analyze B cell antibody producing function, anti-GPI antibody titers of GIA mice sera were measured by ELISA. **Results** 1) Tfh cell population was increased after the immunization of GPI. The increase has started before the onset of arthritis (on day3) and peaked on day7, then gradually subsided. The subset analysis revealed the specific increase in number of Tfh17 cells at the same phase. 2) The immunofluorescence staining showed Tfh cell accumulation in the draining lymph nodes of GIA mice. 3) Anti-GPI antibody was detected from day7 of GIA mice sera, and the titer was gradually elevated over time in GIA mice sera. **Conclusion** Tfh cells, more particularly Tfh17 cells, might have a crucial role in the development of arthritis. We are now elucidating the function of Tfh17 in GIA mice.

ICW17-2

The Efficacy and Safety of Adding Low-Dose Prednisolone (PSL) Induction Therapy of Tocilizumab (TCZ) in Patients with Rheumatoid Arthritis (RA)

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Conflict of interest: None

Background: It is well known that TCZ, an anti-IL-6 receptor antibody, is an effective drug among patients in clinical trials and the real world. We investigated whether adding short-duration and low-dose PSL to induction therapy of TCZ contributes to early suppression of disease activity and bone destruction in RA. **Methods:** In a multicenter, open-label, randomized, controlled trial, 22 active biologic-naïve RA patients with moderate or high disease activity despite conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) were enrolled. The patients received either group A (TCZ 8 mg/kg div/month plus PSL; addition of PSL 5 mg/d at the start of TCZ treatment, and then reduction by 1 mg every 4 weeks) or group B treatment (TCZ 8 mg/kg div/month) for 24 weeks. The primary endpoints of this study were changes from baseline in DAS28 (ESR) and HAQ-DI score at 8 and 24 weeks. Secondary endpoint was change from baseline in van der Heijde modified total Sharp score (mTSS) which was blindly-scored at 24 weeks. **Results:** The mean DAS28 (ESR) at baseline in group A (n=10) was 6.2, and that in group B (n=12) was 5.5 (p=0.28). At 8 weeks, the mean change from baseline in the DAS28 (ESR) was significantly greater in group A than in group B (-3.4 vs -2.1, p=0.03). This difference was maintained even at 24 weeks, which was reflected in the mean change from baseline in the DAS28 (ESR) (-4.0 vs -2.6, p=0.03). At 8 weeks, the mean change from baseline in the HAQ-DI score also significantly improved in group A compared with that in group B (-0.76 vs -0.11, p=0.04). Radiographic progression (change in mTSS ≥0.5 at 24 weeks) tended to be more infrequent among group A than group B (14.2% vs 42.9%, p=0.56). An adverse event occurred in 1 patient in group B, which led to edema. **Conclusion:** We described the short-term efficacy and safety of adding low-dose PSL to induction therapy of TCZ in RA patients who showed an inadequate response to csDMARDs including methotrexate.

ICW17-3

Outcomes of modified metatarsal shortening offset osteotomy for forefoot deformity in patients with rheumatoid arthritis: Short to mid-term follow-up

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Conflict of interest: None

Objectives: Advances in drug therapy for rheumatoid arthritis (RA) have been encouraging us to preserve the matatarsopharangeal (MTP) joint in correction of forefoot deformities, and original metatarsal shortening offset osteotomy was recommended as one of the conventional surgical options for forefoot deformities in RA cases. The objective of this study was to evaluate short to mid-term outcomes of modified metatarsal shortening offset osteotomy. **Methods**: A retrospective observational study was completed for 80 RA cases who underwent modified metatarsal shortening offset osteotomy. Both lesser toe scales and RA foot ankle scales were administered using the Japanese Society for Surgery of the Foot (JSSF) standard rating system, and a postoperative self-administered foot evaluation questionnaire (SAFE-Q) at final follow-up was also checked to evaluate clinical outcomes. Radiografhiic evaluation including fore-mid-hindfoot parameters were also checked. **Results**: This procedure significantly improved clinical scores of both the JSSF [lesser toes and RA foot and ankle] scales. Of 80 feet, 24 (30%) showed recurrence of MTP joint subluxation/dislocation. Fortunately, the recurrence group showed no decrease in the postoperative JSSF and SAFE-Q scores, except for the deformity score in the JSSF [RA foot and ankle] scale. Furthermore, the feet in the recurrence group showed significant varus hindfoot. On the other hand, valgus foot in the recurrence group more frequently included midfoot bony ankyloses. **Conclusions**: Modified metatarsal shortening offset osteotomy was recommended for RA forefoot disorders as one of the joint preservation surgeries in short to mid-term follow-up. However, some modifications to avoid limitation of range of motion (ROM) in the MTP joint are required. It must be borne in mind that varus hindfoot and/or bony ankyloses in the mid-hindfoot can cause recurrence of dorsal dislocation/subluxation of the lesser toe MTP joint.

ICW17-4

Efficacy and Safety of Sarilumab in Combination With csDMARDs in Patients With Active Rheumatoid Arthritis Who Were Inadequate Responders or Intolerant of Anti–TNF-α Therapy: Results From a Phase 3 Study

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Conflict of interest: Yes

Objectives: Sarilumab is a human mAb blocking IL-6Rα. The phase 3 TARGET study (NCT01709578) evaluated addition of sarilumab to csDMARDs in patients (pts) with active RA who failed ≥1 prior anti-TNFs **Methods:** Pts were randomized to placebo (Pbo) (n=181), sarilumab 150 mg q2w (n=181), or sarilumab 200 mg q2w (n=184) subcutaneously + background csDMARD (s) for 24 wks **Results:** Baseline characteristics (N=546) were balanced among treatment groups. A significantly greater proportion of pts receiving either dose of sarilumab achieved ACR20 responses and had significantly improved HAQ-DI scores. ACR20 response rates at wk 4 were 44%, 33%, and 25% for sarilumab 200 mg, 150 mg, and placebo, respectively. Similar observations were made in the proportion of ACR50, ACR70, and HAQ-DI responders (HAQ-DI ≥0.22 units of improvement) at wk24. There was a 70% reduction from baseline in tender joint counts at wk 24 with sarilumab 200 mg compared with a 69% reduction for sarilumab 150 mg and 59% for Pbo. Similar trends were observed for reduction in swollen joint counts (73%, 72%, and 63% reductions from baseline at wk24, respectively). At wk24, there was a 52% reduction in pain VAS from baseline with sarilumab 200 mg compared with a 49% reduction for sarilumab 150 mg and a 39% reduction for Pbo. CRP levels at wk 24 were reduced from baseline by 96% with sarilumab 200 mg, 87% with sarilumab 150 mg, and 25% with Pbo. Treatment-emergent adverse events (TEAEs; safety population, N=546) were more frequent in sarilumab groups (66% and 65% for sarilumab 150 and 200 mg, respectively, vs 50% for Pbo). Infections were the most frequently reported TEAEs. Observed neutropenia was not associated with increased risk for infections. Laboratory abnormalities included decreases in neutrophils and elevations in lipids and transaminases **Conclusion:** Sarilumab demonstrated efficacy in pts with active RA who were inadequate responders or intolerant of anti-TNFs. Safety findings were consistent with prior studies

ICW17-5

Application of population-specific imputation reference panel to large-scale genome-wide association study of rheumatoid arthritis

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Conflict of interest: None

Objectives: Genome wide association study (GWAS) have identified many common variants associated with rheumatoid arthritis (RA). However, the contribution of rare variants (RVs, minor allele frequency <1%) and low-frequency variants (LFVs, minor allele frequency 1-5%) on RA risk is not yet investigated comprehensively. Imputation is a method to infer the genotypes of unobserved variants using known haplotypes in reference panels. Due to population specificity of RVs and LFVs, their imputation qualities are generally poor when we utilized current reference panels. In order to overcome this limitation, we constructed Japanese specific reference panel from whole genome sequencing data of 1,037 Japanese individuals and applied this panel to GWAS meta-analysis of RA, which has the largest sample size among the previously reported GWAS using single populations. **Methods:** We compared the imputation accuracy of Japanese specific reference panel with the reference panel from the 1000 genome project (1KG, n=2,504). GWAS samples were collected from IORRA cohort (2,352 cases and 6,260 controls) and BioBank Japan cohort (4,023 cases and 28,865 controls). After array-based genotyping and quality control, we performed imputation with Japanese specific reference panel. We evaluated the association of each variant with the risk of RA using logistic regression model. Meta-analysis was performed using the fixed-effect inverse variance method. **Results:** Japanese specific reference panel had higher imputation accuracy of RVs and LFVs than 1KG reference panel. Preliminary analysis discovered six novel associations (four common variants and two LFVs) at P-value threshold of 5.0×10^{-8}. Both of novel LFVs were East Asian specific and one of them co-localized with an enhancer region of regulatory T-cells. **Conclusions:** Although we are in the preliminary stage, we identified novel risk alleles of RA which were hard to discover in other populations.

ICW18-1

Exosomes derived from HTLV-1 Infected cell Enhances IFN-γ Induced Expression of CXCL10 in Rheumatoid Arthritis Synovial Fibroblasts

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Conflict of interest: None

Objectives: Human T-lymphotropic virus Type 1 (HTLV-1) positive

rheumatoid arthritis (RA) patients show severe inflammatory state and resistance to anti-rheumatic therapy including biologic agents. However it is still not clear the worsening mechanisms of RA by HTLV-1 infection. We investigated the role of HTLV-1 infected cell derived exosomes in the pathogenesis of RA. **Methods:** Exosomes were isolated and purified from cultured medium of HTLV-1 infected cell line (MT2). RASF was cultured with MT2 derived exosomes with or without IFN-gamma for 24hours. Total RNA was extracted using TRIZOL methods. The expression of RIG-I, Tax, HBZ, IL-6, CXCL10, and CCL5 mRNA in RASF was measured using real-time quantitative PCR. The expression of pattern recognition receptor, RIG-I was determined by immune blotting. BMS345541 (BMS) was use as inhibitor of the activity of NF-kB. Silencing of RIG-I in RASF was performed by transfection of siRNA against RIG-I. **Results:** MT2 derived exosome contain nucleic acids such as Tax, HBZ and GAPDH mRNAs. MT2 derived exosome increase the expression of IL-6, CXCL10, and CCL5 mRNA in RA synovial fibroblasts (SFs). IFN-gamma is well known as one of important cytokine to consider the pathogenesis of HTLV-1 associated inflammatory diseases. IFN-gamma increases the expression of RIG-I protein in RASFs, dose dependent manner. IFN-gamma also induced the expression of IL-6, CCL5, and CXCL10 mRNA in RASFs. MT2 derived exosome significantly enhances the expression of CXCL10 mRNA, but not IL-6 and CCL5, in RASFs activated by IFN-gamma. BMS inhibits the expression of CXCL10 induced by exosome, but not IFN-gamma. Finally, silencing of RIG-I suppressed the expression of CXCL10 in RASFs induced by co-stimulation of both exosome and IFN-gamma. **Conclusion:** It is possible that exosomes derived HTLV-1 infected cell enhance IFN-gamma induced expression of CXCL10 in RASFs via pattern recognition receptor, RIG-I.

ICW18-2

Myocardial Abnormalities are Associated with Corrected QT Interval in Patients with Rheumatoid Arthritis without Cardiac Symptoms Assessed Using Cardiac Magnetic Resonance Imaging

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Conflict of interest: None

Objective. Patients (pts) with rheumatoid arthritis (RA) have a 2 fold higher risk of sudden death than the general population, possibly due to systemic inflammation affecting ventricular repolarization. We hypothesized that myocardial abnormalities are associated with QTc interval in RA. This study aimed to prospectively investigate the association of myocardial abnormalities assessed using cardiac magnetic resonance imaging (CMR) with QTc interval in RA pts without cardiac symptoms. **Methods**. Consecutive RA pts and control subjects were enrolled. RA pts were administered synthetic or biologic disease-modifying antirheumatic drugs (sDMARDs, bDMARDs). Images were assessed for myocardial late gadolinium enhancement (LGE) and T2-weighted imaging (T2WI). We investigated the association of CMR abnormalities with QTc interval. **Results.** We enrolled 70 pts. LGE and T2WI abnormalities were seen in 20 and 7 pts. Simplified disease activity index scores in the LGE (+) group were significantly higher than in the LGE (-) group (p=0.011). All RA pts showed normal QTc interval (412.0±20.5 ms). However, the QTc interval in the LGE (+) group was significant higher than in the LGE (-) group (p=0.001). Myocardial abnormalities were associated with QTc interval (p=0.014). Considering normal QTc interval of RA pts using 420-ms cut-off value, the sensitivity and specificity for detecting myocardial abnormalities were 91% and 70%. **Conclusion.** QTc interval may contribute to myocardial abnormalities. We should consider the possibility of subclinical cardiac involvements in RA cases even in those with normal QTc interval.

ICW18-3

Strong age-dependent effects on migration of synovial fibroblasts obtained from patients with rheumatoid arthritis or osteoarthritis under dopamine receptor stimulation

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Conflict of interest: None

Objectives: Preventing synovial fibroblasts (SF) from migrating into the adjacent cartilage is a desirable therapeutic target in rheumatoid arthritis (RA) in order to avoid joint destruction and disability. As previous studies suggest a high impact of the dopamine pathway in RASF on joint inflammation (*Capellino S et al, A&R 2014*), we aim to further investigate a possible dopamine-mediated impact on joint invasion and destruction in RA. **Methods:** SF from RA and osteoarthritis (OA) patients were obtained from patients undergoing knee joint replacement surgery (mean age: 74.3 ±11.3yrs at OA and 73.7 ± 10.3 yrs at RA patients). To investigate dopamine receptor (DR)-distribution within the RA synovium and in the invasion zone, immunohistochemistry was performed for all five DR-subtypes. Migration- and motility-assays and ELISAs for MMP3 and proMMP1 levels were performed under D1-like (D1DR and D5DR) and D2-like (D2DR, D3DR and D4DR) receptor stimulation. **Results:** D1DR, D4DR and D5DR are higher expressed on SF nearby the invasion zone and also more SF are positive for the respective DR. Migration of RASF and OASF is significantly correlated with patients' age at surgery. Younger patients (≤ 75years) show an increase in migration up to 78% whereas older ones (≥ 75years) show a reduced migration up to 50%(p=0.0009; r=0.69, OA n=8; RA n=7). No difference could be observed between RA and OA patients and between D1-like and D2-like receptor stimulation. The same trend could be observed in the motility assay (OA n=5; RA n=6). MMP3 and proMMP1 level are altered under DR activation (OA n=3; RA n=3). **Conclusion:** DR are strongly expressed in the invasion zone of the RA synovium, suggesting a direct role for dopamine on fibroblast aggressive phenotype, as confirmed in the in vitro assays. RASF migration is significantly altered under DR activation and therefore a potential therapeutic target of RA.

ICW18-4

A comparison of upper extremity and lower extremity or trunk function in mHAQ for rheumatoid arthritis patient

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Conflict of interest: None

[Objective] Modified health assessment questionnaire (mHAQ) is essential factor for the treatment of rheumatoid arthritis (RA). In this study, mHAQ was separately evaluated for upper extremity and lower extremity, and statistically compared. [Methods] 300 RA patients who are treated for more than 4 years, were enrolled. Patient was classified for onset age. In these, EORA is no less than 65-year-old at onset, and YORA for the younger onset. Average value of mHAQ in fourth treatment year and later was calculated for each patient. mHAQ was separated for upper extremity and lower extremity, and their average values were calculated. mHAQ was classified according to value of the two parts. A type that upper extremity valued more than lower extremity is named UE, same value is named EVEN, and lower extremity more than upper extremity is named LE. mHAQ less than 0.5 is classified as remission (REM), and other is classified as failure (FAI). Distribution of each group was counted and compared with chi-square test, and their average values were compared with Mann-Whiney's U-test. Statistical significance was set within 1%. [Results] Patients in REM counted 39, 121, and 47, while in FAI 23, 11, and 58, for UE, EVEN, and LE, respectively. In REM, EVEN showed significantly more than the other types, and LE counted significantly more than UE in FAI. There showed no significant difference between EORA and YORA. Average value of UE and LE in REM demonstrated 0.129 and 0.136, 0.092 and 0.092 in REM, while 0.987 and 1.323, 0.989 and 1.264, in FAI, for EORA and YORA, respectively. EORA demonstrated significantly higher value than the other in REM, and LE demonstrated significantly higher value than UE in FAI. [Conclusions] ADL declines predominantly in lower extremity. EORA patient tends to decline more than YORA, especially in lower extremity, too. In treating RA, we

need to take care for it and should make effort to maintain lower extremity function.

ICW18-5

Dosage contribution of a non-classical HLA gene, *HLA-DOA*, to the risk of ACPA-positive rheumatoid arthritis

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Conflict of interest: None

Objectives: The major histocompatibility complex (MHC) region at 6p23 confers strong risk on a variety of immune-related diseases. However, despite the success of classical human leukocyte antigen (HLA) gene causal variant fine-mapping in the MHC region, independent localization of risk from the classical HLA genes has been challenging. **Methods:** We conducted a large-scale MHC fine-mapping analysis of rheumatoid arthritis (RA) in Japanese (6,244 RA cases and 23,731 controls). We applied the HLA imputation method, using the previously constructed Japanese reference panel (n = 903). Independent risk from the classical HLA genes was assessed by using conditional regression analysis. We further conducted a multi-ethnic validation study by referring the previous studies in east Asia and European populations (n = 7,097 and 23,149, respectively). **Results:** Our study identified a significant risk of a synonymous mutation at *HLA-DOA*, a non-classical HLA gene, on anti-citrullinated-protein-autoantibody (ACPA)-positive RA risk (conditioned odds ratio [OR] = 1.20, conditioned $P = 1.4 \times 10^{-9}$), independently from the risk classical HLA genes (*HLA-DRB1*, *HLA-DPB1*, and *HLA-B*). The *HLA-DOA* risk variant demonstrated a cis-expression quantitative trait loci (cis-eQTL) effect by decreasing *HLA-DOA* expression levels, which indicated its dosage effect on RA risk. Trans-ethnic comparison revealed different linkage disequilibrium (LD) patterns between *HLA-DOA* and *HLA-DRB1*, which explains the *HLA-DOA* variant risk heterogeneity among ethnicities (most evident in Japanese [OR = 1.20], intermediate in east Asians [OR = 1.15], but weak in Europeans [OR = 1.06]). **Conclusion:** While the previous HLA fine-mapping studies have identified risk of amino acid polymorphisms of the classical HLA genes on the immune-related diseases, our study initially identifies the dosage contribution of a non-classical HLA gene to disease risk.

ICW19-1

The functional analysis of dendritic cells developed from T-iPS cells-derived from a single CD4+ T cell of Sjögren's syndrome

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Conflict of interest: None

<Objective> Sjögren's syndrome (SS) is an autoimmune disease characterized by infiltration of lymphocytes including CD4+ T cells into salivary glands. The restricted usage of T cell receptor (TCR) repertoire has been reported, suggesting antigen-specific response. Dendritic cells (DCs), used as antigen presenting cells in the analysis of the antigen-specific CD4+ T cells, are usually differentiated from monocytes in peripheral blood mononuclear cells (PBMCs). However, the acquisition of sufficient quantity of them might not be available. We tried to obtain the functional DCs from only a single CD4+ T cell through induced pluripotent stem cells (iPSCs). <Methods> 1) CD4+ T cells from a patient with primary SS were single-cell sorted and clones were established. 2) Three CD4+ T cell clones were transduced with reprogramming factors via SeV vectors and T-iPSCs were developed. 3) The usage of TCR Vβ in original T cell clone and developed T-iPSCs was examined by PCR-sequencing method. 4) The hematopoietic cells from T-iPSCs were cultured with GM-CSF, M-CSF and IL-4 for 21 days, and OK-432 was added. 5) The cell surface markers on DCs developed from T-iPSCs (T-iPSCs-DC) were examined by flow cytometry. 6) The ability of phagocytosis was compared between TiPSCs-DCs and monocyte-derived DCs (mo-DCs) using FITC-conjugated dextran. <Results> 1) We established thirty-six CD4+ T cell clones and picked up one clone. 2) Some T-iPSCs colonies were formed. They were ES-like morphology. 3) The TCR Vβ sequences among T cell clone and T-iPSCs was the identical (TRBV4.3*04-D2*02-J2.7*01). 4) TiPSCs-DCs with dendritic-cells like morphology were established. 5) TiPSCs-DCs expressed HLA-ABC and CD11c. In CD11c gated cells, co-stimulatory molecules such as CD80, CD86, and also HLA-DR were expressed. 6) The ability of phagocytosis between TiPSCs-DCs and mo-DCs was comparable. <Conclusion> We successfully obtained an adequate amount of functional DCs from a single CD4+ T cell by way of iPSCs.

ICW19-2

Functional Analysis of Macrophages in Behçet's Disease: C-C Chemokine Receptor Type 1 (CCR1) and IL-10 are Implicated in Pathogenesis of the Disease

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Conflict of interest: None

Background/Purpose: The recent GWAS and subsequent studies have identified susceptible genes such as *CCR1* and *IL10* genes, suggesting pathological roles of macrophages in Behçet's disease (BD). The purpose of this study is to compare features of *in vitro* differentiated M1 and M2 macrophages from peripheral blood between BD and healthy controls (HC). Methods: Differentiations into M1 or M2 macrophages were induced *in vitro* from peripheral monocytes in presence of GM-CSF or M-CSF, respectively. Expressions of CD68, CD163, and CCR1 were determined by realtime PCR and flow cytometric analyses. For the macrophages that were treated with LPS for 24 hours, the supernatants were analyzed for cytokine profiles using beads assay. Results: Differentiated M1 macrophage produced higher amounts of IL-6 whereas, M2 macrophage secreted higher volume of IL-10. M2 macrophage has increased expression of CD163 protein and mRNA compared to M1 macrophage. CCR1 expression was increased in M2 macrophage compared to M1 macrophage. Cell surface CCR1 protein expression in M1 macrophage was significantly higher in BD patients compared to HC. BD associated SNP (rs1518111) allele T is risk for decreased expression of *IL10* mRNA in HC M2 macrophage. Conclusion: The data suggest that both susceptible *CCR1* and *IL10* genes are implicated in pathogenesis of BD. Further experiments including functional analyses are required to elucidate mechanisms how M1 or M2 macrophages are involved in pathogenesis of BD.

ICW19-3

The relevance of IFN-γ to pathogenesis of Dermatomyositis (DM) with Rapidly Progressive Interstitial Lung Disease (RP-ILD)

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Conflict of interest: None

Objectives; Although RP-ILD in DM is fatal, effective therapy has not been established. We assessed the relevance of serum markers to RP-ILD in DM. **Methods;** We retrospectively investigated patients with 12 DM, 12 Rheumatoid arthritis (RA) and 13 ANCA-associated vasculitis

(AAV) with RP-ILD, who were admitted in our hospital since 2006 until 2015. We assessed the association of serum marker such as cytokines (IFN-γ, IL-1β, IL-6, IL-12, TNF-α) with CT scores (fibrosis score=F-score, GGO (ground grass opacity) score=G-score) in patients with 9 DM, 6 RA, 5 AAV, in addition, 10 DM, 10 RA, 10 AAV without RP-ILD patients and 19 healthy donors (HD) as control groups. **Results;** Baseline characteristics [DM/RA/AAV] were: gender (M:F) [1:11/9:3/6:7], age (y.o.) [67.7/70.3/70.8], disease duration (months) [17.8/97.6/28.0], LDH (mg/dl) [566.6/356.4/465.8], KL-6 (U/ml) [1507.2/1117.6/593.7], F-score [1.4/2.0/1.6], G-score [2.2/2.7/2.2](max 3), survival rate at 90 days (%) [0.0/33.3/30.8]. Unlike RA and DM patients, serum KL-6 levels were significantly correlated with CT score (both F and G-score) in AAV with RP-ILD (F-score; r^2=0.71, p<0.01, G-score; r^2=0.91, p<0.01). Since there are outliers in serum titer of cytokines, it was not only quantitatively but also qualitatively evaluated. Serum level of IL-6 was non-specifically and significantly elevated in all 3 diseases with or without RP-ILD as compared to HD (ANOVA, p<0.01). In contrast, IFN-γ was specifically elevated in only DM patients with RP-ILD compared to other groups (ANOVA, p<0.01). Interestingly, the serum level of IFN-γ in DM with RP-ILD was positively correlated with G-score (Spearman, ρ=0.71, p=0.02). **Conclusion;** The serum level of IFN-γ was a characteristically elevated in DM with RP-ILD patients and closely related with G-score, the marker of interstitial pneumonia. These results suggest that IFN-γ might play a pivotal role in RP-ILD in DM and is considered as a novel prognostic factor for the disease.

ICW19-4

Utility of Monocyte Counts in Diagnosing and Predicting Pneumocystis Jirovecii Pneumonitis in Patients with Autoimmune Diseases

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Conflict of interest: None

Objectives This multi-center, retrospective study was conducted to identify the characteristic features of pneumocystis pneumonia (PcP) in patients with autoimmune diseases. **Methods** We enrolled 11 patients with PcP and 29 patients with bacterial pneumonia in this study. All patients diagnosed with autoimmune diseases had been undergoing immunosuppressive therapy and were hospitalized due to pneumonia. Pneumonia was defined on the basis of clinical symptoms and radiological findings. The diagnosis of PcP was confirmed by positive β-D-glucan test results and microbiological identification of fungus existence. Patients with bacterial pneumonia were treated using antibiotics only. Whole white blood cell (WBC) counts, fractions of WBC, and lactate dehydrogenase and C-reactive protein (CRP) levels were measured and compared between the groups. Furthermore, monocyte counts were recorded 100 days before clinical onset of the disease. **Results** Monocyte and basophil counts in patients with PcP were significantly lower than those in patients with bacterial pneumonia {monocytes: 188/μL [95% confidence interval (CI): 77–299/μL] vs 499/μL (95% CI: 344–653/μL), P = 0.003; basophils: 20/μL (95% CI: 12–28/μL) vs 37/μL (95% CI: 27–47), P = 0.047}. There were no significant differences between the two groups regarding the whole WBC count, other cell counts of fraction of WBC, and CRP. If we set the cutoff value of monocyte count as 140/μL, the sensitivity and specificity were 63% and 96%, respectively. Monocyte counts in 10 of 11 patients with PcP continued to decrease up to 2 months before clinical onset of the disease but not in patients with bacterial pneumonia. **Conclusion** Monocyte count may be useful not only in differentiating PcP from bacterial pneumonia but also in predicting the occurrence of PcP infection several weeks before clinical onset of the disease.

ICW19-5

Role of IL-21 in the pathogenesis of autoimmune myositis

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Conflict of interest: None

Objective: IL-21 has been shown to be involved in the development of various autoimmune diseases; however, the role of IL-21 in autoimmune myositis remains unknown. We here examined the roles of IL-21 in the development of autoimmune myositis. **Methods:** We measured serum levels of IL-21 in patients with inflammatory myopathies and healthy donors. We also investigated the roles of IL-21 in the development of experimental autoimmune myositis (EAM) by using IL-21-deficient (IL-21$^{-/-}$) mice. **Results:** Serum levels of IL-21 were significantly increased in patients with inflammatory myopathies as compared to those in healthy donors. Upon the induction of EAM, muscle weakness and muscle inflammation were less obvious in IL-21$^{-/-}$ mice as compared to those in wild-type (WT) mice. While the numbers of CD4$^+$ T cells, CD8$^+$ T cells, and B cells in the affected muscles were similar between EAM-induced IL-21$^{-/-}$ mice and WT mice, the numbers of CD11b$^+$ cells and neutrophils in the muscles were significantly decreased in EAM-induced IL-21$^{-/-}$ mice. Comprehensive analyses of inflammatory cytokines revealed that GM-CSF production from draining lymph node cells was significantly decreased in EAM-induced IL-21$^{-/-}$ mice. We found that the main producer of GM-CSF in draining lymph nodes of EAM-induced mice was γδT cells and that GM-CSF-producing γδT cells in the draining lymph nodes and affected muscles were significantly decreased in EAM-induced IL-21$^{-/-}$ mice as compared to those in EAM-induced WT mice. Finally, we found that γδT cell deficiency or neutralization of GM-CSF improved muscle weakness of EAM-induced mice. **Conclusion:** IL-21 is involved in the development of autoimmune myositis presumably by inducing the production of GM-CSF in γδT cells.

ICW19-6

The significance of anti-phosphatidylserine-prothrombin complex antibodies in patients with anti-neutrophil cytoplasmic autoantibody-associated vasculitis

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Conflict of interest: None

Objectives: Anti-phosphatidylserine-prothrombin complex antibody (aPS/PT-Ab) is one of the common antiphospholipid antibodies. Recently, elevation of the aPS/PT-Ab level has been reported in patients with polyarteritis nodosa, indicating a possible correlation between aPS/PT-Ab and the development of vasculitis. We examined the significance of aPS/PT-Ab in patients with anti-neutrophil cytoplasmic antibody (ANCA)-associated small vessel vasculitis (AAV). *Methods:* Forty-nine patients who had been referred to Niigata University Hospital and diagnosed as having AAV between 2009 and 2015 were recruited for this study. Serum aPS/PT-Ab was measured by enzyme-linked immunosorbent assay (ELISA) using a commercially available kit (Medical and Biological Laboratories, Nagoya, Japan). Other laboratory findings were also examined and the disease activity was assessed in accordance with the Birmingham Vasculitis Activity Score (BVAS). Patients were divided into two groups according to the level of aPS/PT-Ab, and the data were compared between the groups using Student's *t* test and Fisher's exact test. Correlations between the titer of aPS/PT-Ab and each variable were also analyzed using Pearson's correlation coefficient and stepwise multiple regression analysis. *Results:* Five patients had a aPS/PT-Ab level above the cutoff value (aPS/PT (+) group). The mean white blood cell count was significantly elevated and kidney function was significantly impaired in the aPS/PT (+) group relative to the aPT/PS (-) group. Pearson's correlation coefficient analysis showed that white blood cell count, serum creatinine level, and serum PR3-ANCA level were positively associated with the aPS/PT-Ab level. Stepwise multiple regression analysis also selected these 3 factors as positive independent variables associated with aPS/PT-Ab. *Conclusion:* The positive correlation between aPS/PT-Ab and PR3-ANCA indicates that common mechanisms are involved in the production of these autoantibodies in AAV.

ICW20-1

Soluble interleukin-2 receptor reflects disease activity in IgG4-related disease and primary Sjögren's syndrome

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Conflict of interest: None

Objectives: Soluble interleukin-2 receptor (sIL2R) is known as an indicator for activation status of lymphocytes and could be a potential biomarker for disease activity of lymphoproliferative disorders and autoimmune diseases. The aim of this study is to examine the association of sIL2R with disease activity in patients with IgG4-related disease (IgG4-RD) and primary Sjögren's syndrome (pSS). **Methods:** Forty-four patients with active untreated IgG4-RD, 90 with pSS, 10 with sicca syndrome (patients with xerostomia with neither anti-SSA and SSB antibodies nor lymphocytic infiltration by lip biopsy) were enrolled. Disease activity of IgG4-RD and pSS was determined based on the IgG4-RD responder index (IgG4-RD RI) and the EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI). The association of sIL2R with disease activity was analyzed. **Results:** The level of sIL2R was significantly higher in IgG4-RD and pSS compared to sicca syndrome (699 vs 588 vs 275U/mL, p=0.008) and positively correlated with baseline IgG4-RD RI (ρ=0.718, p<0.0001) and ESSDAI score (ρ=0.615, p<0.0001). The number of affected organ positively correlated with sIL2R in both IgG4-RD (ρ=0.730, p<0.0001) and pSS (ρ=0.562, p<0.0001). Receiver operating characteristics analyses demonstrated that sIL2R was the most distinguishable biomarker for IgG4-RD patients with extra-dacryosialadenitis lesions from those without, compared to serum IgG4, IgG, IgE and circulating eosinophil counts with a cut-off value of 440U/mL. sIL2R also efficiently extracted patients with extra-dacryosialadenitis lesions in pSS (cut-off value of 511U/mL). sIL2R level was significantly decreased after immunosuppressive treatment in both IgG4-RD and pSS. IgG4-RD was most efficiently discriminated from pSS by serum IgG4 levels with a cut off value of 145mg/dL (AUC=0.967, p<0.0001). **Conclusion:** The level of sIL2R could be a biomarker for disease activity, especially for the extent of organ involvements in IgG4-RD and pSS.

ICW20-2

Microvascular abnormalities are significantly more prevalent in patients with anti-MDA5 or anti-TIF1γ antibodies and involved in the pathogenesis in polymyositis and dermatomyositis (PM/DM)

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Conflict of interest: None

[Objectives] Clinical usefulness of detecting microvascular abnormalities by nailfold videocapillaroscopy (NVC) in systemic sclerosis has been well established. However, the significance of microvascular abnormalities in patients with PM/DM is not well understood. The prevalence and significance of NVC abnormalities in PM/DM were examined. **[Methods]** Fifty-six patients with PM/DM (13 PM/43 DM) enrolled Apr 2014 - Oct 2016 were studied. Association of NVC findings with clinical features, myositis-specific autoantibodies and skin pathology in biopsy were analyzed. **[Results]** Of 56 patients, 55% had NVC changes, which were more common in DM (65%; 28/43) vs PM (23%; 3/13) (p=0.003) and correlated with the degree of perivascular inflammatory infiltrate in the upper dermis in skin biopsy (p=0.03). When the features of NVC changes + vs – patients were compared, the difference was not clear for clinical or laboratory findings and disease prognosis. However, in terms of the prevalence of NVC changes between patients with different myositis-specific autoantibodies, majority (86%, 13/15, p=0.02) of anti-MDA5+ patients, who are often accompanied by rapid progressive interstitial pneumonia, and anti-TIF1γ+(86%, 6/7, p=0.12) patients, who are associated with malignancy, had NVC changes. In contrast, it was found only in 28%(5/13, p=0.01) of anti-ARS + patients. Unexpectedly, of 13 patients who had NVC abnormalities and follow up NVC data after treatment, 12 (92%) had their NVC findings improved along with the improvement of muscle weakness and interstitial pneumonia. **[Conclusion]** Microvascular abnormalities were associated with anti-MDA5 antibodies and anti-TIF1γ antibodies. These vascular abnormalities were correlated with lymphocyte infiltration in rash and improved after treatment. These results suggest that capillary abnormalities reflect the different pathogenesis among the subgroups by the specific autoantibodies in patients with PM/DM.

ICW20-3

Association of myocardial abnormalities with disease characteristics, N-terminal pro-BNP, and cardiovascular inflammatory biomarkers in systemic sclerosis without cardiac symptoms as assessed using cardiac magnetic resonance imaging

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Conflict of interest: None

Objectives: To evaluate myocardial abnormalities assessed by cardiac magnetic resonance (CMR) imaging in systemic sclerosis (SSc) patients without cardiac symptoms, and to examine the association of myocardial abnormalities with disease characteristics, N-terminal pro-BNP (NT-proBNP), and cardiovascular inflammatory biomarker levels (tumor necrosis factor-α, interleukin-6, matrix metalloproteinase-9, leptin, adiponectin, pentraxin 3) in patients with SSc. Methods: Thirteen patients with SSc were studied (mean age; 56 years old). CMR was assessed for LV structure for left ventricular mass index (LVMI) and functional parameters for ejection fraction (EF). We conducted late gadolinium enhancement (LGE), and T2 weighted image (T2WI), using CMR. NT-proBNP and cardiovascular inflammatory biomarkers were measured. Results: SSc patients were detected in 11 of 13 (85%) in the LGE (+) group. SSc patients were detected in 5 of 13 (38%) in the T2WI (+) group. All SSc patients had normal EF. LVMI was not associated with the LGE (+) or T2WI (+) group. Compared to the LGE (-) group, the LGE (+) group had significantly higher NT-proBNP (p = 0.03). Cardiovascular inflammatory biomarkers were not associated with the LGE (+) or T2WI (+) group. Conclusion: Our result demonstrated the high prevalence of myocardial abnormalities with high NT-proBNP. Additionally, myocardial abnormalities were not associated with cardiovascular inflammatory biomarkers. Further studies are needed to determine whether CMR abnormalities affect prognosis or treatment strategy.

ICW20-4

Clinical usefulness of anti-M-type phospholipase-A-receptor antibodies in patients with membranous nephropathy and comparisons of three quantification methods

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Conflict of interest: None

[Objectives] Autoantibodies to M-type phospholipase A2 receptor (PLA2R) are specific markers of idiopathic membranous nephropathy (MN). It has also been suggested that anti-PLA2R antibody is associated with disease activity and prognosis but more solid evidence is needed. We aimed to establish quantitative measurement of anti-PLA2R antibodies and further investigate its clinical usefulness. We also aimed to validate the absence of anti-PLA2R antibodies in patients with systemic lupus erythematosus (SLE). **[Methods]** Using stable cell line expressing

PLA2R, we developed a quantitative cell-based enzyme-linked immunosorbent assay (ELISA) and Western blot (WB) for anti-PLA2R antibodies. The usefulness of these tests and the commercial solid phase ELISA were retrospectively studied in sera from 23 patients with biopsy-proven primary MN, and 16 patients with lupus MN. Repeated sera were also available in 9 patients with primary MN. **[Results]** Anti-PLA2R antibodies were detected in 12, 6, and 12 out of 23 patients with primary MN by the WB, the cell-based ELISA, and the commercial solid phase ELISA, respectively. Conversely, all of the samples from the lupus MN patients were negative. The levels of proteinuria were moderately correlated with titers of anti-PLA2R antibodies by the 3 methods (r=0.39 to 0.47). Anti-PLA2R antibodies were significantly associated with physicians' decision on immunosuppressive therapy without prior knowledge of anti-PLA2R antibody positivity (p<0.01). In all of the 6 patients who were treated with immunosuppressive therapy, titers of anti-PLA2R antibodies significantly declined by commercial solid-phase ELISA (p=0.03). **[Conclusion]** This study showed that anti-PLA2R antibody is clinically useful as diagnostic and surrogate biomarkers in primary MN. In addition, the 3 methods are all reliable measurement methods for anti-PLA2R antibodies but demonstrated different performance. The absence of anti-PLA2R antibodies in SLE patients was reconfirmed.

ICW20-5

Prevalence of radiographic thymic alteration and its clinico-serological association in systemic autoimmune diseases

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Conflict of interest: None

Purpose: Thymus, a primary lymphoid organ, plays a crucial role in immune system homeostasis. Several small-scale studies for association between radiographic thymus alterations and serological features have been reported in systemic autoimmune diseases (SADs). To our knowledge, there was no comprehensive reports of association between radiographic thymus alterations and clinico-serological features among SADs. **Methods**: 1025 patients who were randomly selected from all patients visited at our service and underwent chest CT scan between January 2013 and December 2015 were enrolled. Thymic enlargement and thymus attenuation score in axial image of CT scan were quantitatively interpreted. Their association to clinio-serological information was statistically analyzed. **Results**: After patients with thymoma or thymic cyst, and less than 30 year-old were excluded, 983 patients were served for assessment and analysis. 76% were women and mean age was 62.0 ± 13.6 years old. Prevalence of thymic enlargement in patients with SADs was more frequent (16.9%) as compared to undiagnosed patients (11.3%). Prevalence of granulated pattern defined as attenuation score 2 and over was more frequent (11.3%) as compared to undiagnosed controls (7%). Remarkably, in rheumatoid arthritis (RA) patients, radiographic thymic alteration especially thymus attenuation score, significantly associated with serum RF-positivity and serum anti-CCP antibodies-positivity (P=0.0045 and 0.0009, respectively). **Conclusion**: Thymic alteration was frequently observed in SADs. In RA patients, radiographic thymus alterations may reflect any abnormality in autoantibody production.

ICW21-1

Hepatitis Related to Hepatitis B Virus Reactivation in Patients with Systemic Lupus Erythematosus

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Conflict of interest: Yes

Objectives: The reactivation of hepatitis B virus (HBV) is an emerging issue in patients receiving immunosuppressive therapy. The object of this study is to determine the incidence of hepatitis related to HBV reactivation in Systemic lupus erythematosus (SLE) patients. **Methods:** From 2000 to 2012, 2,811 SLE cases were retrospectively reviewed for their HBV status and episodes of hepatitis. Hepatitis related to HBV reactivation was defined as ALT > 100 IU/mL accompanied with HBV DNA > 2000 IU/ml with baseline normal ALT. Factors associated with HBV reactivation and long-term outcome were analyzed. **Results:** Among them, 174 had available hepatitis B surface antigens (HBsAg). Twenty-five (14.4%) SLE patients were positive for HBsAg. During a mean 12.7 years of follow-up, 18 (72.0%) HBsAg-positive patients and 1 (3.4%) resolved hepatitis B case developed hepatitis related to HBV reactivation. Receiving glucocorticoid-containing immunosuppressive therapy was a risk factor for HBV reactivation in HBsAg-positive SLE patients (p = 0.005, odds ratio = 42.5, 95% confidence interval: 3.159~571.818). Fourteen HBsAg-positive patients received antiviral therapy during HBV reactivation, 4 of which (28.6%) died on liver failure; total bilirubin at the start of antiviral therapy was associated with mortality (P = 0.048). SLE patients with hepatitis related to HBV reactivation presented worse survival as compared to those without (P < 0.001). **Conclusions:** Hepatitis related to HBV reactivation is common in SLE patients and is associated with high mortality. HBV markers should be screened before immunosuppressive treatment and antiviral prophylaxis should be provided for HBsAg-positive SLE patients.

ICW21-2

Relapse rate and risk factors of recurrence shortly after remission induction therapy in Systemic Lupus Erythematosus

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Conflict of interest: None

Objective: To determine the relationship between relapse and serological fluctuation early after remission in patients with systemic lupus erythematosus (SLE). **Method:** Enrolled patients, who achieved remission after the treatment with daily prednisolone dose of >15 mg for active symptoms (defined by the British Isles Lupus Assessment Group Index ≥ B), were maintained with reduced daily prednisolone dose of 15 mg after the remission, defined as no requirement of additional treatments, and exhibited hypocomplementemia at daily prednisolone dose of 15 mg. 2nd serological evaluation was performed between one and six months after 1st evaluation. **Result:** Between 2005 and 2014, 76 patients (66 female) were enrolled. Median age was 37 years and SLE disease activity index score at active phase was 12. During a median observation period of 383 days, 36 (47.4%) patients experienced a relapse. >10% decrease in C3 levels, >0% decrease in C4 levels and/or >0% increase of anti-ds DNA antibody levels were significant cut-off points related to the relapse. For prediction of relapse, the sensitivity and negative likelihood ratio for >0% decrease of C4 level or >0% increase of anti-ds DNA antibody level were calculated 0.83 and 0.51, while the specificity and positive likelihood ratio for >0% decrease of C4 level and >0% increase of anti-ds DNA antibody level were calculated 0.90 and 3.06. **Conclusion**: Combination with fluctuations of C4 and anti-ds DNA antibody levels may be a useful predictor for relapse early after remission.

ICW21-3

Clinical characteristics of patients with systemic lupus erythematosus who meet the diagnostic criteria for TAFRO syndrome

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Conflict of interest: None

Objectives: TAFRO syndrome is a systemic inflammatory disorder

characterized by thrombocytopenia, anasarca, fever, renal insufficiency, and organomegaly. Since several autoantibodies can be detected in TAFRO syndrome, it has been recognized as sharing many of the clinical features of systemic lupus erythematosus (SLE). The aim of this study was to identify patients who met the 2015 diagnostic criteria for TAFRO syndrome among patients who were previously diagnosed as SLE. **Methods:** A total of 46 patients diagnosed as SLE were included (females, 67%). The clinical characteristics were investigated from medical records. A search of PubMed was conducted and the clinical data of 24 patients with TAFRO syndrome were obtained from previous reports. Student's t-test and Fisher's exact test were used. **Results:** Four SLE patients (8.7%) met the diagnostic criteria for TAFRO syndrome (TAFRO group). All were male and the mean age was older (67.5 ± 8.7 vs. 39.3±18.1 years, p=0.004) than non-TAFRO group. Arthritis (0/4 vs. 26/42, p=0.030) were less pronounced. CRP levels (6.3±4.5 vs. 1.5±3.4mg/dl, p=0.010) were higher, and the platelet count (4.1±1.3 vs. 17.3±9.2×10^4/ml, p<0.001), estimated glomerular filtration rate (32.8±20.1 vs. 93.5±35.9 ml/min, p=0.002) and anti-dsDNA antibody titer (35.0±58.6 vs. 149.8±160.9 U/ml, p=0.016) were lower in the TAFRO group. In the TAFRO group, thrombocytopenia tended to persist longer despite therapy. Comparing the TAFRO group to previous case reports of TAFRO syndrome, no significant differences were observed in age, serum Cr levels, CRP levels, and platelet count. **Conclusion:** Patients who met both sets of criteria for TAFRO syndrome and SLE showed several different clinical characteristics compared with typical SLE patients. TAFRO syndrome should be considered as one of the differential diagnoses of SLE, especially in older male accompanied by elevated CRP levels, severe kidney dysfunction, and intractable thrombocytopenia.

ICW21-4

Seasonal variations in disease onset and exacerbation of systemic lupus erythematosus

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Conflict of interest: None

Objective: It has been well acknowledged that both genetic and environmental factors are important in the pathogenesis of systemic lupus erythematosus (SLE). To elucidate the environmental factors associated with SLE pathogenesis, we investigated the seasonal differences in the disease onset and the exacerbation of SLE. Methods: In the present study, we retrospectively reviewed the medical records of 122 patients with SLE (88.5% female and the average age of 43 years) fulfilling the 1997 revised ACR classification criteria. The mean observation period was 7.2 years. The disease exacerbation was defined as either a new appearance of clinical manifestations of SLE or the clinical condition requiring the start or dose increment of glucocorticoids by at least 50%. Results: The disease onset was the most frequently observed in Spring (31.0%) and the least in Fall (16.1%). A total of 167 disease exacerbations were observed among 879 patient-years, and more interestingly, the disease exacerbation was significantly more frequently observed in Spring (38.3%) and significantly less frequently observed in Fall (10.8%) as compared with other seasons. It should be noted that the both disease onset (0.0%) and exacerbation (2.4%) of SLE were the least in September. Disease manifestation at the exacerbation was more frequently recorded rash and arthritis, but was similar throughout the seasons. Moreover, 60.0% of the disease exacerbation did not accompany serological activity defined by the increase in anti-DNA antibody and/or the decrease in complement activity. Conclusion: Concordant seasonal differences between the disease onset and the exacerbation implicated the role of environmental factors in the pathogenesis of SLE, possibly through the activation of innate immune systems.

ICW21-5

Soluble ST2 is increased in systemic lupus erythematous and is a potential marker of lupus nephritis

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Conflict of interest: None

Objective: To investigate the role of the interleukin (IL)-33-ST2 axis in systemic lupus erythematosus (SLE). **Methods:** Serum concentrations of IL-33 and sST2 were measured by sandwich ELISA in SLE patients (n=111) and healthy controls (n=36). The serum concentrations of IL-33 and sST2 were correlated with various clinical and biological parameters. The expressions of IL-33 and ST2 were investigated in kidney sections by immunohistochemistry in lupus nephritis patients (n=23) and controls (n=10). **Results:** Serum levels of IL-33 were significantly higher in SLE patients (11.64 ± 3.141 pg / ml) than in controls (1.043 ± 0.8526 pg / ml) (p <0.0001). Similarly, the serum concentrations of sST2 were significantly higher in SLE patients (34013± 2043 pg / ml) than in controls (25278 ± 2258 pg / ml) (p = 0.046). Moreover, only sST2 (r=0.269;p= 0.0042) and not IL-33 correlated significantly with disease activity (SLEDAI). In addition, serum levels of sST2 were significantly higher in patients with lupus nephritis (45438 ±5661 pg / ml) that in SLE patients without renal involvement (30691± 1941 pg / ml) (p = 0.016). The expression of IL-33 in renal biopsies of patients with lupus nephritis was not increased compared to controls, while the expression of ST2Lwas significantly higher in nephritis patients compared to controls. **Conclusions:** IL-33 and sST2 levels are increased in SLE but sST2 could represent a potential marker of disease activity and of lupus nephritis.

ICW21-6

Detailed characterization of immune cells differentiated from SLE patient-derived Induced Pluripotent Stem Cells

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Conflict of interest: None

Objectives: Systemic lupus erythematosus (SLE) is an autoimmune disease that develops on the basis of the certain genetic and environmental factors. Dendritic cells play pivotal roles in the pathogenesis of SLE by production of inflammatory cytokines and antigen presentation. Genetic analyses also suggested the importance of monocyte linage cells. To elucidate the influences of SLE genetic backgrounds, SLE patient-derived induced pluripotent stem (iPS) cells are thought to be a promising research tool. Methods: iPS cells were established from two SLE sisters. Two SLE and healthy donor-iPS clones were differentiated into monocyte linage cells. Cells were analyzed by FACS and next generation sequencing. Stimulated iPS derived cells and peripheral blood derived dendritic cells (Mo-DC) have been co-cultured with CFSE stained allo-T cells followed by FACS analyses. Results: In the differentiation assay, 80% of CD14+DC protocol induced cells showed CD14-positive at day 20, and more than 90% cells showed CD80, CD86 and HLA-DR-positive at day 28. Majority of CD11c+DC and CD123+DC protocol induced cells also showed CD80, CD86 and HLA-DR-positive. Gene expression patterns of iPS-CD14+HLA-DR+ cells resembled those of reported monocyte linage cells including skin CD14+DC. In the comparison of SLE and healthy donor-iPS-CD14+HLA-DR+ cells, differences of gene expression pattern were observed in TLR4 pathway and Type I IFN pathway. Deferentially expressed genes between SLE and heathy donor-iPS derived cells included *IRF5*, *TNFRSF4*, and *IL-10*. In the mixed lymphoid reaction assay, both of SLE and healthy donor-iPS cell derived cells were superior in function to induce T cell proliferation compared with Mo-DC. Conclusion: There were clear differences in gene expression pattern between SLE-iPS and heathy donor-iPS-derived monocyte lineage cells. These SLE-iPS-derived monocyte lineage cells were thought to be a promising tool for analyzing the pathogenesis of SLE and drug discovery.

ICW22-1

The correlation between erosion and bone mineral density in patients with rheumatoid arthritis treated with denosumab and biologic DMARDs: a prospective cohort study

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Conflict of interest: None

Object: We have previously reported the efficacy of denosumab combined with biological DMARDs on radiographic progression in rheumatoid arthritis (RA). The aim of this work was to reveal the relationship between the changes in structural joint damage and in bone mineral density (BMD) in patients with RA who were started on denosumab in addition to biologic DMARDs. **Methods:** We prospectively evaluated erosion (ERO) and joint space narrowing (JSN) scores by the van der Heijde-modified Sharp method and T-scores of the lumbar spine (LS) and total hip (TH) by dual energy X-ray absorptiometry scans at baseline and 12 months in the RA patients who were started on denosumab (60 mg every 6 months) for osteoporosis in addition to biologic DMARDs. We compared the 12-month change in ERO or JSN scores (ΔERO; ΔJSN) with the change in T-scores of the LS or TH (ΔLS; ΔTH). **Results:** Twenty-two patients (1 man and 21 women) at the mean±SD age of 74.4±8.1 at baseline were included in this study. The T-scores of the LS and TH at baseline were -1.38±1.57 and -2.53±0.85, respectively. ΔERO, ΔJSN, ΔLS, and ΔTH were 0.16±0.49, 0.44±0.66, 0.30±0.39, and 0.20±0.42, respectively. BMD was significantly increased from baseline to 12 months. There was a significant inverse correlation between the ΔERO and the ΔTH ($\rho = -0.473$, $P = 0.03$), while there was no correlation between the ΔERO and the ΔLS ($P = 0.98$) nor correlation between the ΔJSN and the ΔLS ($P = 0.57$) or ΔTH ($P = 0.25$). **Conclusions:** The change in erosive joint damage of hands and feet showed a significant relationship with the change in femoral BMD in patients with RA treated with denosumab and biologic DMARDs. BMD was ameliorated along with erosion by denosumab combined with biologic DMARDs, and may be an indicator for joint destruction.

ICW22-2

The Incidence and risk of Cancer in Rheumatoid Arthritis Patients treated with biologic DMARDs

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Conflict of interest: None

Objectives To estimate the incidence of cancer in rheumatoid arthritis (RA) patients and to evaluate the cancer risk of bDMARDs compared to those of non-bDMARDs. **Methods** A retrospective cohort of incident RA patients was established using Korean national claims database between Jan 2010 and Dec 2013. RA was defined by having a medical claim with diagnostic code and prescription of DMARDs. To made inception cohort, we identified RA in 2010 claims with no codes or prescription for RA during the previous 12 months and continuous treatment for RA in 2011-2013 (n=14,081). After excluding the patients with cancer history (n=1,684), patients were followed for the development of cancer or the last observational date. The incidence rate (IR) per 10,000 person year (PY) and incident rate ratio (IIR) of cancer for bDMARDs users based on non-bDMARDs users were calculated. Multivariate logistic regression was performed to evaluate the impact of bDMARDs on development of cancer. **Results** We included 12,397 RA patients without cancer history, contributing 41,599 PY. A total 725 cases had been developed any type of cancer and 21 cases had been developed hematologic cancer during follow-up. The IR for all cancer was 174.3 (81.5 in bDMARDs users, 180.1 in non-bDMARDs users), and that for hematologic cancer were 5.0 (12.2 in bDMARDs users, 4.6 in non-bDMARDs users). The cancer risk of bDMARDs users compared with those of non-bDMARDs was low for all cancer [IRR 0.45 (95% CI 0.28-0.70)], but high for hematologic cancer [IRR 2.65 (95% CI 0.55-7.76)]. On the multivariate analysis, the cancer risk was significantly reduced in bDMARDs (OR 0.42), after adjusting confounding factors. However, there was a tendency with an increased risk for hematologic cancers in bDMARDs without statistical significance (OR 1.69). **Conclusions** RA patients treated with bDMARDs are associated with a lower risk of cancer than patients treated with non-bDMARDs, but it was not for hematologic cancer.

ICW22-3

The Comprehensive Analysis for the Transcriptional Organization of Stimuli Responses in Fibroblast-like Synoviocytes from Rheumatoid Arthritis Patients

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Conflict of interest: Yes

Background Fibroblast-like synoviocytes (FLS) is suspected to contribute to RA pathogenesis through its genetic backgrounds and epigenetic modifications. The objective of this study is to investigate the transcriptional organization of stimuli responses and to clarify a character of RA-FLS. **Methods** FLS from RA (n = 20) and osteoarthritis (OA) patients (n = 18) were stimulated with cytokines (TNF-α, IL-1β, IL-6/sIL-6R, IFN-γ, IFN-α, TGF-β1 and combination of all 6 cytokines) for 24 hours. The paired-end RNA sequencing was performed using HiSeq 2500 (Illumina). **Results** The overview of transcriptomes showed the conserved differences between RA and OA-FLS. Through the weighted gene co-expression network analysis (WGCNA), some pathways related to malignant tumor progression (i.e, PI3K/AKT signaling) were revealed to be important for classification between RA and OA-FLS. Furthermore, a part of these pathways were suspected to be regulated by genetic backgrounds through Allele-specific expression (ASE) analysis. On the other hands, a transcriptional coactivator EP300 was suggested to be one of the crucial factors for inflammation amplification. **Conclusion** Through the comprehensive analysis, characteristic transcriptional organization of RA-FLS is expected to be elucidated.

ICW22-4

Achievement of Imaging Remission among Patients with Rheumatoid Arthritis in Clinical Remission and Their Characteristics

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Conflict of interest: Yes

Object: Therapeutic goal of rheumatoid arthritis (RA) is to achieve disease remission. However, several remission criteria have not always equated to the complete absence of true inflammation. Power Doppler Ultrasonography (PDUS) has been demonstrated to detect subclinical synovitis. The aim of this study was to elucidate the achievement rates of imaging remission and examine characteristics associated with achievement status among RA patients in clinical remission. Methods: This study was conducted in 90 RA patients who attained clinical remission, defined by DAS28ESR remission criteria. PDUS was performed in 16 joints and 2 tendons, including both first to third metacarpophalangeal, second and third proximal interphalangeal, radiocarpal (RC), second and third metatarsophalangeal joints and extensor carpi ulnaris tendons and graded on the basis of a dichotomous assessment (presence/absence). The clinical and laboratory data of patients with imaging remission were compared with only clinical remission. Results: Results: Achievement rate of imaging remission was 51.1% among RA patients with clinical remission. Forty four patients were PDUS positive. PD was detected most frequently in the right RC joint (n=38, 42.4%) The patients who reached imaging remission as well as clinical remission had lower evaluator global assessment score ($p<0.001$), and all clinical disease activity scores. While pa-

tients who did not reach imaging remission tend to more active joint count, higher PtGA and HAQ score. The patients with positive RF and/or higher level of anti-CCP titer were more likely to reach imaging remission. Conclusions: Only 51.1% of RA patients in clinical remission had PDUS defined imaging remission. Patients who were in imaging remission had lower disease activity and lower pain score, compared to patients with clinical remission only. RF positivity and high titer of anti-CCP were correlated with achievement of imaging remission.

ICW22-5

A Hypoxia-sensitive COMMD1 Regulates osteoclastogenesis and Pathologic Bone Resorption in Rheumatoid Arthritis

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Conflict of interest: None

Objectives: Hypoxia is a feature of skeletal conditions including rheumatoid arthritis (RA). The combination of cellular hyperproliferation and infiltration by T cell and monocytes in RA synovium increases the oxygen demand and results in hypoxia. The partial pressure of oxygen levels in RA synovium is shown to be 2-4%. Osteoclasts are the primary cells responsible for the bone resorption in RA and osteoclast differentiation is enhanced by hypoxia. However mechanism of this enhancement has not been extensively studied. Our aim is to clarify the factor involving the pathological bone resorption in hypoxia, which will lead to the specific therapy for bone resorption in RA. Methods: Using human osteoclast precursors (OCPs), RNA-seq and subsequent upstream analysis were performed. siRNAs were used to knock-down COMMD1 in human system. Myeloid deletion of Commd1 with arthritis and inflammatory osteolysis models were tested as mice model. cis-eQTL analysis for COMMD1 were performed using Japanese healthy donor and RA patients. Results: RNA-seq revealed 152 genes were upregulated both by RANKL and hypoxia. Upstream analysis identified COMMD1 was one of the most significant upstream regulators, following Hif1α and Hif2α. COMMD1 inhibited osteoclastogenesis in human and myeloid deletion of *Commd1* resulted in strikingly increased osteoclastogenesis in arthritis and inflammatory osteolysis models. Hypoxia did not change the mRNA levels of COMMD1 but regulated nuclear localization of COMMD1. Transcriptomic analysis revealed that COMMD1 broadly suppresses hypoxia-inducible genes, and NF-κB, cell-cycle and metabolic pathways. Regarding cell-cycle pathway, pRB-E2F1 pathway was important for human osteoclastogenesis. Finally, genetic and eQTL analysis linked increased *COMMD1* expression with decreased bone erosion in RA. Conclusion: COMMD1 is an important regulator for hypoxia-mediated osteoclastogenesis and bone erosion in RA.

Workshop

W1-1

Long term clinical results and durability of ceramic knee implants for rheumatoid patients: A minimum 15-year follow-up

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Conflict of interest: Yes

[Objective] Concerns have been suggested for total knee arthroplasty (TKA) with rheumatoid arthritis (RA) because of poor bone quality and excessive joint laxity. The purpose of this study was to evaluate the long term clinical outcomes and durability for rheumatoid patients and to compare the results with that for the osteoarthritis (OA) patients. [Methods] 170 knees using Bi-Surface Knee were included. Average age at surgery was significantly younger for RA patients. The Knee Society score was used to assess clinical outcomes. Kaplan-Meier survivorship was calculated to determine the cumulative survival rate. [Results] Knee score improved from 41.6 to 93.6 in RA knees. Function score also improved from 29.1 to 42.0. Preoperative and postoperative function score was lower in RA knees than in OA knees. With revision for any surgery or radiographic failure as the end point, Kaplan-Meier survivorship at 15 years was 89.4%. No significant difference was detected between RA and OA knees. [Conclusion] The survivorship of the ceramic knee implant was excellent over the 15-year follow-up. Low friction rate and unique design of this design might contribute to excellent long term clinical outcomes and durability.

W1-2

Long-term clinical results in patients with rheumatoid arthritis of more than 10 years after total knee replacement

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Conflict of interest: None

Purpose In this study, we examined the long-term results of TKA in patients with RA. **Materials and Methods** The subjects were 66 patients 96 knees, who could be observed for at least 10 years and were selected from among 213 knees that had been treated with TKA for preoperative RA. The mean age of the surgery was 61.3 years; the mean duration of the RA morbidity, 14.3 years; and the mean postoperative observation period, 13.3 years. The Japan Orthopedic Association JOA score, changes in ROM, radiographic evaluation, complications. **Results** Clinical results indicated that the preoperative JOA score of 45.8 improved to 79.2 at the final evaluation. The preoperative ROM was −11.0º extension and 112.6º flexion. It showed a general improvement to −0.3º extension and 111.7º flexion at the time of the final evaluation. Complications included one case of superficial infection, 2 cases of fracture in the implant vicinity, 1 case of impaired liver function, and 1 case of recurrent RA in the target knee that was subsequently alleviated with TCZ. Reimplantations were performed on 4knees. One of the cases was due to supracondylar femur fracture, and 2 cases were due to aseptic loosening,1 case requiring curettage of a lesion due to deep infection.

W1-3

Survival rate and causes of death after total hip arthroplasty in patients with rheumatoid arthritis

Akihisa Haraguchi[1], Yasuharu Nakashima[1], Hisaaki Miyahara[2], Yukio Esaki[2], Go Hirata[2], Satoshi Kamura[2], Koji Sakuraba[2], Kenjiro Fujimura[2]
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Conflict of interest: Yes

PURPOSE: To retrospectively evaluate the survival rate and cause of death after THA in patients with RA. METHODS: A total of 149 patients

with RA underwent initial THA during the period of 1998 to 2005. The mean patient ages at surgery and mean follow-up were 58 and 8.3 years. Using Kaplan-Meier method and Cox model, cumulative survival rates and factors associated with mortality were assessed. RESULT: A total of 64 deaths occurred during the study period. The cause of death could be identified in 48 patients. Malignancy (25%) was the leading cause, followed by pneumonia (23%) and sepsis (21%). An overall patient survivorship was 37% at 17 years. The mean time from primary THA to death was 7.2 years. Univariate analysis showed that operative time, age, height, body weight, and corticosteroid dose were significantly associated with patient mortality. In the multivariate analysis, older age at operation (HR 1.07, p<0.01) and using greater dose of concomitant corticosteroid (HR 1.11, p<0.01) were independently associated with greater mortality risk CONCLUSIONS: Survival rate after THA in patients with RA is 37% at 17 years. Older age and using greater dose of concomitant corticosteroid appears to impact on mortality of RA patients.

W1-4

Investigation and comparison of pre-surgical status and condition change over the 5-year interval in TKA and foot surgery using the NinJa database

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Conflict of interest: None

[Objectives] NinJa 2013 & 2008 were used to investigate pre-surgical status change of RA patients in TKA and foot surgery. [Methods] We identified 214 patients (189 women, 25 men) in NinJa 2013 & 2008 that underwent surgery in the next year. [Results] The mean values of the examined items of the past & recent TKA groups and the past & recent foot groups are as following: age, 63.0, 65.7, 64.0, 67.1, onset age, 47.1, 52.2, 45.2, 47.6, disease duration, 16.0, 13.6, 18.9, 19.5, CRP*, 1.9, 1.0, 1.0, 0.6, arthroplasty count*, 0.47, 0.26, 0.73, 0.52, tender joints*, 6.5, 3.7, 7.2, 5.0, swollen joints, 4.0, 2.9, 3.7, 3.4, PtPain VAS* 4.4, 3.8, 3.6, 3.4, PtGVAS* 4.6, 3.6, 3.7, 3.7, DrVAS* 3.5, 2.6, 2.7, 2.1, DAS28CRP* 3.9, 3.1, 3.3, 3.1, mHAQ* 0.96, 0.70, 0.61, 0.64, and PSL* dose 3.8, 2.2, 3.3, 2.3. In the items with*, the status were significantly better in 2013 than in 2008 with TKA while there was no significant change with foot surgery in any of the items. [Conclusion] The percent of TKA surgery decreased and control of disease activity became better in TKA patients. It is suggested that the necessity of small joint surgery did not change even after progress of medication treatment compared with that of large joint surgery.

W1-5

Change in the surgical treatment for cervical spine disorders related to Rheumatoid Arthritis during recent 15 decades

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Conflict of interest: None

Since the approval of biologics in Japan, treatment of rheumatoid arthritis (RA) had dramatically improved. Good disease control had contributed to prevent the progression of joint deformities, which resulted in the decreasing of joint prosthesis in RA patients. On the other hand, surgeries of hand and foot intended to be more functional and good appearance were increasing. However, it is unclear about the cervical spine surgery. We clarified the change in the surgical treatments for cervical spine disorder related to RA patients at our institution. From 2001 to 2015, 71 RA patients were demonstrated cervical spine surgery in our institute. The mean age was 65.4 years. According to the lesions, we classified the cervical disorder into 3 types: upper lesion such as atlantoaxial subluxation, the middle and lower lesion including subaxial subluxation, the expanded lesions containing both features. In addition, we compared the patients for 7 years after approval of biologics (from 2001 to 2007) with them for the latest 8 years (from 2008 to 2015). The number of surgeries for cervical spine disorder with RA in our institute has been remained. However, RA-related disorders have been decreasing. The expansion of RA remission may lead to reduction of the cervical spine surgeries with RA.

W1-6

Recent Trends in Orthopedic Surgery with Rheumatoid Arthritis (RA): Analysis of the Numbers of RA-related Surgeries in Our Department

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Conflict of interest: None

[Objective] The purpose of this study is to reveal the recent trends in the numbers of rheumatoid arthritis (RA)-related surgeries. **[Methods]** We investigated the number of operations for patients with RA performed in our department from 2000 to 2014, and revealed the feature of the change of them. **[Results]** The total number of operations was over 200 per year in 2000 and 2001. It peaked in 2001 and decreased to 2003, and it has remained flat since then. The number of total joint replacements peaked in 2005 and decreased gradually. The number of synovectomy was remarkably decreased. In contrast, the number of foot arthroplasty and that of spine surgery have increased. Sixty to eighty total knee replacements were performed per year until 2006, while the number of them has decreased in half after 2012. The peak number of the total hip replacements was 44 in 2001, while the number of them has been about 20 per year since 2008. The number of elbow joint replacements, shoulder joint replacements, or ankle joint replacements has all increased. **[Conclusion]** Our results suggest the number of orthopedic surgery for RA was affected by the change of drug therapy in RA.

W2-1

Investigation of perioperative complications associated with surgery with combined use of biologics listed in the AORA registry

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Conflict of interest: None

Purpose: Biological disease-modifying antirheumatic drugs (bDMARDs) suppress immunity, which leads to the risk of perioperative complications such as surgical site infection (SSI) and protracted wound healing. We investigated perioperative complications in cases of surgery with the combined use of bDMARDs listed in the Akita Orthopedic Group on Rheumatoid Arthritis (AORA) registry by 2015. **Methods**: We investigated 119 cases of bDMARDs use out of 775 surgery cases between 2000 and 2015. We examined the effect of drug discontinuation, shift of surgery, infection rate, and the protracted wound healing rate. **Results**: No cases for which bDMARDs were used exhibited worsening of disease activity due to discontinuation of drug administration and no cases were refractory to pharmacotherapy. The most common surgical procedure was total knee arthroplasty (TKA). Postoperative SSI was observed in 6 cases. Two of those cases were total hip arthroplasty (THA), one case was TKA, and three cases were ankle surgery. All six cases were treated with tocilizumab (TCZ). Postoperative protracted wound healing was observed in one case treated with etanercept (ETN). **Conclusions**:

As TCZ suppresses inflammation markers and symptoms such as fever, it should be prudently used in the perioperative period.

W2-2

The factors for troubles of healing wounds after forefoot surgery in patients with rheumatoid arthritis

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Conflict of interest: None

Objective: When patients with rheumatoid arthritis have severe deformities at their forefoot, they have operations and start to walk from next day in our hospital. But they often have troubles of healing wounds, so we explore those factors. Method: Fifty two forefoot surgeries were performed in 30 patients, there were 27 women and 3 men, between Marth 2009 and September 2016. We divided into two groups, one is good wound healing group and the other is delayed wound healing group, and several factors were analyzed. Results: The mean age was 66 years, the mean duration of the disease was 21.8 years, and the mean DAS28 was 2.2. Methotrexates were used in 37 feet, biological agencies were used in 12 feet and prednisolones were used in 6 feet. Good wound healings were recorded in 37 feet and delayed wound healings were recorded in 19 feet. The factors of delayed wound healing were the operative time and the number of toes processed. Early rehabilitation, medications, age, duration of disease and radiological evaluations didn't differ between the groups. Conclusion; Longer operative time and the number of toes processed were risk of delayed wound healing after forefoot surgery in patients with rheumatoid arthritis. Surgeons should attempt to shorten operative time.

W2-3

Mechanical prophylaxis and anti–platelet factor 4/heparin antibody After total joint surgery

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Conflict of interest: None

【Object】To investigate the refrence between mechanical prophylaxis and anti–platelet factor 4/heparin antibody after total joint surgery【Methd】We performed prospective study of 2069 patients who underwent TKA or THA. Approximately half of the patients received postoperative thromboprophylaxis with UFH, LMWH, or fondaparinux. The other half received only dynamic mechanical thromboprophylaxis (DMT:IIPC or Foot pump). We measured anti -PF4/heparin before and 10 days after surgery using an immunoassay.【Results】Multivariate analysis revealed that DMT was an independent risk factor for seroconversion (odds ratio [OR], 2.01; 95%confidence interval [CI], 1.34-3.02;P5.001), which was confirmed with propensity-score matching (OR, 1.99; 95% CI, 1.17-3.37; P 5.018). For TKA, the seroconversion rates in patients treated with DMT but no anticoagulation and in patients treated with UFH or LMWH without DMT were similar, but significantly higher than in patients treated with only stocking. The proportion of patients with ≧1.4 optical density units appeared to be higher among those treated with any anticoagulant plus DMT than among those not treated with DMT.【Conlusion】Our study suggests that DMT increases risk of an anti-PF4/heparin immune response, even without heparin exposure.

W2-4

Incidence of deep vein thrombosis after total knee arthroplasty in patients with rheumatoid arthritis －influence of ankle deformity on deep vein thrombosis－

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Conflict of interest: None

The incidence of deep vein thrombosis (DVT) after total knee arthroplasty (TKA) is high. Since DVT may cause pulmonary embolism, it needs to be prevented. Recent studies have shown that active movement of the ankle decrease the risk of DVT. However, the influence of ankle deformity on the incidence of DVT is unclear. The aim of the present study was to assess the influence of ankle deformity on the incidence of DVT after TKA in patients with rheumatoid arthritis (RA). Between June 2011 and May 2016, TKA was performed on 55 joints in 43 RA patients. Ultrasonography was performed preoperatively and postoperatively on days 2 and 14. Deformity of the ankle joint was assessed using the Larsen grading (LG) method. In 29 patients who showed ankle deformity with LG 0-II, the incidence of DVT was 25%. In 17 patients who showed ankle deformity with LG IIIand IV, it was 47.4%. A multivariate logistic regression analysis identified two independent clinical predictors for the risk of DVT; a history of DVT (odds ratio, 22.5; p=0.001), severe ankle deformity with LG III or higher (odds ratio, 4.85; p=0.044). These results indicates that severe ankle deformity with LG III or higher is a risk factor of DVT after TKA in patients with RA.

W2-5

Effects of disease activity on total ankle arthroplasty in patients with rheumatoid arthritis

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Conflict of interest: Yes

(Purpose) The purpose of the present study is to elucidate the effects of disease activity on the postoperative outcome of FINE TAA. (Methods) We examined 17 TAA was performed from April 2001 to December 2012 at our hospital. Clinical assessment was made by JSSF score, and imaging evaluation was examined pre- and postoperative standing radiographic imaging. We also examined the effect of high/moderate disease activity group (HDA/MDA group) and a low disease activity group (LDA) and implant survival rate between the groups. (Results) JSSF score significantly improved from 34.8 preoperatively to 69.4. A factor affecting JSSF score was disease activity. The implant survival rates in HDA/MDA and LDA groups were 58.3% and 100%, respectively, but no significant differences were noted. The survival rate of talar component subsidence was significantly better in LDA group than in the HDA/MDA group. Joint removal and ankle fusion surgery were performed in three HDA group, due to loosening of the artificial joint (37.5%). (Conclusion) Subsidence of talar component and reoperation were noted for the HDA / MDA group, and intraoperative disease activity appeared to affect the clinical outcome of TAA. It is important to perform TAA under strict control of disease activity.

W2-6

Knee function after total knee arthroplasty is influenced by disease activity in patients with rheumatoid arthritis

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Conflict of interest: None

Objective: This study evaluated the effect of total knee arthroplasty (TKA) with capsulosynovectomy on disease activity and knee function in patients with rheumatoid arthritis (RA). Methods: Seventy-seven patients with RA who underwent primary TKA with more than one year of follow-up were retrospectively reviewed to assess postoperative knee function and disease activity. Results: Postoperative knee function was significantly improved in Japanese Orthopaedic Association (JOA) scores one year after surgery. (48.9 vs. 86.0, p<0.01) The disease activity of RA was significantly decreased in DAS28-CRP one year after surgery. Postoperative knee function was negatively correlated with RA disease activity.

(p<0.01) Conclusion: TKA improves both knee function and disease activity in patients with RA. Based on the results, knee function after TKA is influenced with disease activity.

W3-1

Adult-onset Still's disease with atypical persistent rashes and typical evanescent rashes

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Conflict of interest: None

Case1. 19-year-old woman presented with fever, polyarthralgia, and both salmon-pink evanescent rashes and persistent rashes. Slight liver dysfunction and hyperferritinemia were detected. Case2. 56-year-old man presented with fever, lymphadenopathy, and he also had both evanescent rashes and persistent rashes. Liver dysfunction and hyperferritinemia were observed. Both cases were diagnosed as adult-onset Still's disease (AOSD), and histologically atypical rashes were characterized by individual necrotic keratinocytes. The diagnosis of AOSD can be very difficult because specific clinical and laboratory features in association with AOSD are inadequate. Typical evanescent salmon-pink rashes are universally considered as major criterion, but several atypical persistent rashes are also observed. Histologically, typical rash has no specific observations, but atypical rash shows individual necrotic keratinocytes especially in the upper epidermis. Since the appearance of clinical atypical rash and dyskeratotic cells in the epidermis could be poor prognostic factors, the skin biopsy of atypical rashes is necessary.

W3-2

The clinical features of elderly onset Adult Still's disease

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Conflict of interest: None

[Objective] Adult onset Still's disease (AOSD) is a systemic inflammatory disease characterized by fever, rash, and arthralgia. Many cases are relatively young adults, but elderly onset cases are not rare. [Method] The clinical features of patients who developed AOSD at 65 years or older were compared to those who developed AOSD before age 65. [Result] At diagnosis, fourteen patients (28%) were 65 years or older, and 36 patients (72%) were younger than 65. Skin lesion was more frequent (93% vs 81%) and pulmonary lesion such as pleuritis was more common (50% vs 3%) in elderly-onset group. On the other hand, sore throat (42% vs. 78%), arthralgia (64% vs. 89%), lymphadenopathy (21% vs 56%) and splenomegaly (36% vs 56%) was relatively infrequent in elderly onset group. The steroid pulse therapy was more frequently given in elderly onset group (64% vs 28%), but the usage of immunosuppressive drugs were similar between two groups. There was no difference in the frequency of relapse, but more complications during treatment were observed in elderly onset group (50% vs 25%). [Discussion] In elderly onset AOSD, some characteristic clinical features were revealed, and treatment related complications were more frequent.

W3-3

Is 2016 classification criteria for macrophage activation syndrome (MAS) in systemic juvenile idiopathic arthritis useful for the diagnosis of MAS in adult-onset Still's disease?

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Conflict of interest: None

[Objective] To evaluate the usefulness and problems of 2016 MAS classification criteria in systemic juvenile idiopathic arthritis (SJIA), for the diagnosis of MAS in adult-onset Still's disease (AOSD). [Methods] Laboratory data from 44 patients with active AOSD (including four patients with MAS) were applied to the MAS classification criteria. [Results] Serum ferritin of all patients with MAS and that of 88% of patients without MAS (MAS-negative) were higher than reference value (684 ng/ml). Percentages of MAS-negative patients that showed positive for the criteria items were as follows: 23% for platelet count ≤181x109/L, 53% for AST >48 U/L, 15% for triglyceride (TG) >156 mg/dl, 14% for fibrinogen (FNG) ≤360 mg/dl. When these data were applied, all patients with MAS and 33% of MAS-negative patients fulfilled the criteria. The reference values that showed the highest likelihood ratio were as follows: platelet count ≤95x109/L, AST >147 U/L, TG >205 mg/dl, and FNG ≤297 mg/dl. [Conclusion] The new MAS criteria are unsuitable for the diagnosis of MAS in AOSD. It may be necessary to change the reference values of criteria items in case this is applied to AOSD.

W3-4

An autopsy case of severe TAFRO syndrome refractory to the intensive immunosuppressive therapy

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Conflict of interest: None

A 69-year-old man was admitted to our hospital due to abdomen distension at the beginning of May, 2016. Upon admission, he was febrile (37.7℃) and the laboratory data revealed thrombocytopenia, mild renal failure, and elevation of CRP and FDP. A whole-body CT showed abdominal paraaortic lymph nodes, hepatosplenomegaly, pleural and peritoneal effusion. No infection was shown in repeated blood, ascites, and urine cultural samples. Anti-nuclear antibody and other autoantibodies were all negative. Bone marrow aspiration and random skin biopsy showed no malignancy. As a result, we diagnosed TAFRO syndrome. Followed by methylprednisolone pulse therapy (500 mg for 3 days), after the initial intensive therapy with prednisolone (60 mg/day) and cyclosporine (100 mg/day), we added tocilizumab (8mg/kg intravenously). The inflammation gradually ameriorated but thrombocytopenia deteriorated and persisted. He died of septic shock at the end of July, 2016. Autopsy was performed and macrophages with phagocytosis were often observed in lymph nodes. <clinical significance> TAFRO syndrome is characterized by Thrombocytopenia, Anasarca, Fever, Renal insufficiency, and Organomegaly. The mechanism and treatment of TAFRO syndrome are still uncertain. Autopsy cases of TAFRO syndrome are rare.

W3-5

Two cases of relapsing polychondritis with preceding Vokt-Koyanagi Harada disease-like symptoms

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Conflict of interest: None

We report two relapsing polychondritis (RP) cases with preceding Vogt-Koyanagi-Harada disease (VKH disease)-like symptoms.【Case 1】A 68-year-old man presented with polyarthritis, bilateral loss of vision, hearing loss of right ear, and cerebellar ataxia. CSF study showed pleocytosis. Bacterial culture was negative. These findings led to suspicion of VKH disease. He was treated with steroid therapy. Three years later, polyarthritis, bilateral swelling of ears, and bilateral epicleritis developed, and he was admitted to our hospital. CT scan and MRI showed the inflammation of ascending aorta and aortic arch. Biopsy of the right ear revealed cartilage with inflammatory cell infiltration. He was treated with high dose oral prednisolone and methotrexate, and his symptoms and aortitis went into remission.【Case 2】A 82-year-old man presented with visual loss of right eye. An ophthalmic evaluation revealed serous retinal detachment in right eye and choroidal folds in left eye. He was diagnosed as VKD disease and treated with steroid therapy. One year later, he was admitted to our hospital with antibiotics-resistant swelling of right ear. Biopsy of right ear showed inflammatory cell infiltration in cartilage. Oral prednisolone was administrated and the symptom of ear was improved.

W3-6

A case of the parvovirus B19 infectious disease that presented various immunological response

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Conflict of interest: None

Parvovirus B19 infection is known to provoke various immunological responses. We presents an interesting parvovirus B19 infection case which mimicked syphilis and SLE.【Case】Thirty seven-year-old woman who was healthy until 5 days prior to admission, when fever, loss of appetite and bilateral coxalgia developed. On the admission day, her family brought her to our hospital because altered mental status appeared. The temperature was 37.7 degrees Celsius and jolt accentuation but no focal neurological deficits were observed. Because blood examination showed positive RPR and TPHA, a neurosyphilis was suspected and 1500mg of AMPC were started. On the admission day 2, erythema of cheek and limbs and polyarthralgia appeared. Blood tests revealed thrombocytopenia, hypocomplimentemia and positive Lupus anticoagulant and, therefore, definite SLE was diagnosed according to 2012 SLICC classification criteria. Focused medical interview clarified her son had suffered the erythema infectiosum 10days prior to her admission, and an additional serological test demonstrated positive parvovirus B19 IgM antibody. All her symptoms were gradually resolved in self-limiting manner within a week and all laboratory abnormalities including RPR, TPHA, hypocomplimentemia and LAC also disappeared.

W4-1

Persistent pruritic skin lesions with dyskeratotic cells in upper layer of epidermis are specific and associated with high levels of serum IL-18 in adult-onset Still's disease

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Conflict of interest: None

Objectives: The aim of this study is to assess the clinical significance of dyskeratotic cells (DC) in skin lesions of Japanese patients with adult-onset Still's disease (AOSD). Methods: We retrospectively assessed clinical and histological findings of skin lesions in Japanese patients with AOSD (n=12). Moreover, we compared histological finding of AOSD with that of dermatomyositis (DM) (n=6), drug eruptions (DE) (n=6), and Graft versus Host disease (GVHD) (n=6). Results: AOSD with persistent pruritic skin lesions (n=7) histologically showed DC only in upper layer of epidermis and horny layer without intraepidermal infiltrations of inflammatory cells. DC were positive by TUNEL and ssDNA stainings, suggesting apoptosis. AOSD with evanescent rash (n=5) histologically showed no DC. DM (n=6), DE (n=6) and GVHD (n=6) histologically had DC in all layers of epidermis with inflammatory cells' infiltrations. Notably, AOSD with DC (n=7) had significant higher levels of serum IL-18 than without DC (n=5). Conclusions: AOSD with persistent pruritic skin lesions is characterized and specific by prominent epidermal apoptosis, which might be related to high levels of serum IL-18. Therefore, it could play a pivotal role to recognize the atypical skin lesions of AOSD for correct early diagnosis.

W4-2

Analysis of lymphocyte subsets in peripheral blood mononuclear cells (PBMCs) from patients with adult onset Still's disease (AOSD)

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Conflict of interest: Yes

【Background】AOSD is a rare systemic inflammatory disease that presents as fever of unknown origin accompanied by systemic manifestations. Although involvement of some viral infections and inflammatory cytokines in its pathogenesis has been reported, the precise etiology remains unknown. We are investigating the etiology of AOSD through lymphocyte subset flowcytometry analysis followed by next-generation sequencing (NGS) analysis.【Methods】We recruited 17 AOSD patients (Mean: 50±14.3 years old) who fully fulfilled the Yamaguchi's criteria. 30 healthy controls were picked up (Mean: 50.5±14.4 years old). Each lymphocyte subset was identified by FACS and sorted for NGS analysis.【Results】In lymphocyte population, percentages of NK cells, CD19+ B cells, and CD4+ T cells were significantly lower in AOSD patients. Treg cells and follicular helper T cells in T cell subsets also showed significant decrease.【Conclusion】NK cytotoxicity dysfunction in AOSD patients was previously reported. We have found the decrease in NK cells and Treg cells, which is compatible with previous reports. However, the lymphocyte percentage difference alone cannot tell us specific lymphocyte subset importance in the pathogenesis of AOSD. Further RNA-seq analysis of each subset is awaited.

W4-3

Efficacy of secukinumab for relapsing polychondritis with psoriasis vulgaris: A case report

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Conflict of interest: None

We described a 39-year-old man presenting relapsing polychondritis (RP) with a 7-year history of psoriasis vulgaris who were successfully treated with secukinumab. He was suffering from high fever for 2 months and auricular swelling, arthritis and expanding scaly erythema for 1 month before admission. Auricular cartilage biopsy revealed inflammatory cell infiltration and cartilage denaturation. The patient was diagnosed with RP in consideration of chondritis, high CRP levels (4.62mg/dL), and high fever. Psoriasis vulgaris is a chronic skin disease caused by the excessive secretion of inflammatory cytokines such as interleukin-17 (IL-17). This case experienced deterioration of psoriasis vulgaris at the time of RP onset, suggesting the possibility that IL-17 could be involved in the disease onset of RP as well as the disease activity of psoriasis vulgaris. Therefore, we treated the patient with subcutaneous injection of anti-IL-17A antibody (secukinumab) 300 mg/week for 5 consecutive weeks and all the clinical features were significantly improved. To our knowledge, anti-IL-17 biological agent therapy has never been applied for RP. Secukinumab might be useful for the treatment of RP.

W4-4

Two cases of muscular sarcoidosis with different clinical courses

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Conflict of interest: None

[Case 1] A 78-year-old man was referred to our hospital because of nodular muscle swelling in his right upper arm. The serum levels of muscle enzymes were normal. MRI showed evidence of inflammatory muscle disease. Biopsy of affected muscle revealed noncaseating epithelioid cell granulomas, compatible with muscular sarcoidosis. Three months after

admission, the size of the muscle nodules reduced without therapy. [Case 2] The patient was an 82-year old-woman with a past medical history of sarcoidosis. Twelve years prior to the admission, she was diagnosed with sarcoidosis using lung and skin biopsy at another hospital and had a follow-up examination but no therapy. Five months prior to the admission, she experienced lower extremity muscle weakness. As she had difficulty walking, she was admitted to our hospital. The serum myoglobin was elevated. MRI showed muscle atrophy. Biopsy of affected muscle revealed noncaseating epithelioid cell granulomas, compatible with muscular sarcoidosis. Prednisolone (30 mg per day) was started, but muscle strength was not recovered. [Discussion] Muscular sarcoidosis is classified as a mass type and a myopathy type. While the mass type may often resolve spontaneously, the myopathy type may progress to muscular atrophy in the absence of therapy.

W4-5

Development of SAPHO syndrome after tocilizumab therapy in a patient of rheumatoid arthritis

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Conflict of interest: None

We report a 67-year-old woman with rheumatoid arthritis who developed SAPHO syndrome during tocilizumab (TCZ) therapy. She first developed RA at the 66 years and treated with MTX. After 2 month later, she came to our hospital because of exacerbation of the arthralgia. The treatment was changed from MTX to FK506 because of interstitial pneumonia. Three months after the treatment, although she was administered etanercept, she stopped due to itching papulars on her limbs. Then TCZ therapy was started and her arthralgia was gradually improved. However, five months after first TCZ therapy, the patients presented with exacerbation of anterior chest pain and papulars on her palms, plantas, and hips. Skin biopsy diagnosed with pustulosis palmaris et plantaris. Bone scintigraph showed increased tracer uptake in the sternoclavicular joints and sternum. Therefore, she was diagnosed with SAPHO syndrome and switched to adalimumab. The arthralgia and skin lesion was gradually improved. Moreover, serum levels of IL-6 were markedly higher at the diagnosis of SAPHO syndrome than after adalimumab. [Clinical significance] We report the development of SAPHO syndrome during TCZ therapy in a patient of rheumatoid arthritis. The treatment of TCZ may induce to the pathophysiology of SAPHO syndrome.

W4-6

Clinical considerations of 23 cases of syndrome of Remitting Seronegative Symmetrical Synovitis with Pitting Edema

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Conflict of interest: None

Remitting Seronegative Symmetrical Synovitis with Pitting Edema (RS3PE) syndrome is, reported by Dr. McCarty DJ in 1985, good prognostic, acute onset, a symmetrical synovitis with pitting edema at dorsum of hand and foot, and is the connective tissue disease which responds to the treatment with a small amount of prednisolone (PSL) over the age of 70. In this time, we present, with bibliographic consideration, 23 cases of RS3PE syndrome which ten patients cured. Twenty-three cases of the disease in our department from April 2007 are clinically analyzed. The average age of onset is 77.6, the ratio of males to females is 1.9:1. All patients internally got PSL therapy, maximally 20 mg (average 13.9 mg, 13.0 mg in cured cases and 14.6 mg in non-cured) per day. Ten patients (43.5%) had a relapse in the course, and 10 cured during mean period of 23.1 months. Five got cancer including two of malignant lymphoma and one of myelodysplastic syndromes, despite the screening at the onset of treatment. In our 23 cases, 10 patients cured. Five patients, including three of hematologic malignancy, got cancer, and it is necessary for the patients to get periodic examinations.

W5-1

Correlation between salivary epidermal growth factor levels and refractory intraoral manifestations in patients with Sjogren's syndrome: Influences of administration of sialogogues and corticosteroid

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Conflict of interest: None

[Object] To assess influences of administration of sialogogues and corticosteroid on changes of salivary epidermal growth factor (EGF) levels and the severity of intraoral manifestations in Sjögren's syndrome (SS). [Methods] 23 SS patients, followed up for three consecutive years, were enrolled. Salivary EGF concentration was measured using an enzyme-linked immunosorbent assay, and intraoral manifestations were evaluated using a short version of the Oral Health Impact Profile (OHIP-14). The changes of salivary flow rate, EGF levels, and the severity of intraoral manifestations were analyzed by prescription contents. [Results] In SS, the OHIP-14 score was significantly increased and total salivary EGF output was significantly decreased after three years follow-up (10.2 vs 12.6, p=0.040, 10158.4 vs 8352.8 pg/10 min, p=0.032). Significant decreases in salivary flow rate and total EGF output were showed in SS patients with administration of sialogogues. In SS patients without administration of corticosteroid, the OHIP-14 score and total salivary EGF output significantly deteriorated (9.1 vs 11.8; p=0.047, 11040.3 vs 8810.3 pg/10 min.; p=0.021) [Conclusions] Corticosteroid may retard the development of refractory intraoral manifestations and deterioration in saliva quality.

W5-2

The Breakthrough of the Pathogenesis of Anti-centromere antibody positive Sjögren's Syndrome by Measuring the MicroRNA Analysis from the Minor Salivary Gland

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Conflict of interest: None

MicroRNAs (miRNAs) are small conserved non-coding RNA molecules that post-transcriptionally regulate gene expression by targeting the 3′ untranslated region of specific messenger RNAs for degradation or translational repression. MiRNAs also play an important role in innate immunity and acquired immunity. Anti-centromere antibody is one of the specific autoantibodies of systemic sclerosis. Sometimes it is also recognized in patients with Sjögren's syndrome (SS). Anti-Ro/SSA and anti-La/SSB antibodies are also recognized in SS. 【Objective】To elucidate the pathogenesis of SS due to different autoantibodies between anti-centromere antibody, and anti-Ro/SSA antibody and anti-La/SSB antibody, we investigated miRNAs from the minor salivary gland (MSG). 【Patients and method】We analyzed 12 female patients with primary SS: 7 patients have anti-centromere antibody and 5 patients have anti- Ro/SSA antibody. We measured miRNAs in MSG using the 3D-Gene™ from Toray Industries. 【Results】Four microRNAs including miR-133b expression levels in patients with anti-centromere antibody elevated more than anti-Ro/SSA antibody. On the other hand, seven microRNAs including miR155-5p expression levels decreased in patients with anti-centromere antibody more than anti-Ro/SSA antibody.

W5-3

Detection of human T lymphotropic virus type-I bZIP factor and tax in the salivary glands of Sjögren' s syndrome patients

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Conflict of interest: None

Objective: To detect human T lymphotropic virus type-I (HTLV-I) bZIP factor (HBZ), tax and related molecules in labial salivary glands (LSGs) from patients with Sjögren's syndrome (SS). **Methods:** Expression of HBZ and tax in LSGs from HTLV-I+ and -SS patients were analyzed by in situ hybridization (ISH). Expression of Foxp3 and NF-kB in IHC was quantified. **Results:** In HTLV-I+ SS, especially in ATL and HAMSS, both HBZ and tax were detected by ISH in mononuclear cells (MNCs) and ducts, although HBZ and tax highly expressed in MNCs of ATL and HAM-SS, respectively. HBZ and low frequency of tax was found in HTLV-I asymptomatic carrier (AC)SS, although no expression of these molecules was found in HTLV-I- SS. Although expression of Foxp3 was found in MNCs of all SS patients, frequency of ATL was greater than that of ACSS and HTLV-I- SS ($p<0.01$). Frequency of Foxp3 was similar in an ATL and HAMSS, although there was significance between HAMSS and ACSS. NF-kB was expressed in nucleus of MNCs from all SS patients without significance. In HTLV-I+ SS, MNCs co-expressed Foxp3 and NF-kB. Expression of Foxp3 and NF-kB in ducts was different according to infection. **Conclusion:** These results suggest that HBZ-mediated Foxp3 expression is specifically associated with pathogenesis of HTLV-I+ SS.

W5-4

Comparison of performance of the new 2016 American College of Rheumatology (ACR) - European League Against Rheumatism (EULAR) classification criteria for primary Sjögren's syndrome with former three sets of criteria in Japanese patients

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Conflict of interest: None

<Objectives> To compare the performance of the new 2016 ACR-EULAR classification criteria for primary Sjögren's syndrome (SS) with 1999 revised Japanese Ministry of Health criteria for SS (JPN), 2002 American-European Consensus Group classification criteria for SS (AECG), and 2012 ACR classification criteria for SS in Japanese patients. <Methods> 499 patients with primary SS (pSS) or suspected pSS who were followed-up in June 2012 at 10 hospitals in Japan, had been examined for all four items of JPN (pathology, oral, ocular, anti-SS-A/B) were enrolled. We assessed 1) clinical diagnosis by the physician in charge which was set as the "gold standard", 2) sensitivities, 3) specificities, and 4) accuracies of four sets of criteria. <Results> 1) pSS was diagnosed in 302 patients and ruled out in 197. 2) The sensitivity of ACR-EULAR criteria (95%) was higher than those of JPN, AECG, and ACR criteria (82%, 83%, and 79%, respectively). 3) The specificity of ACR-EULAR (72%) was lower than those of other three sets (91%, 91%, and 85%, respectively). 4) The accuracy was comparable among the four sets (86%, 86%, 86%, and 81%, respectively). <Conclusion> 2016 ACR-EULAR criteria had higher sensitivity, lower specificity, and similar accuracy compared with former three sets of criteria.

W5-5

Expresssion and function of toll-like receptor 7-9 in the salivary glands of Sjogren's syndrome patients

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Conflict of interest: None

[Objectives] The aim of this study was to clarify the expression and function of toll-like receptor (TLR) 7-9 in labial salivary glands (LSGs) from patients with Sjogren's syndrome (SS). [Methods] Expression of TLR7-9 in LSGs from SS patients and healthy controls werewas analyzed by immunohistochemistry. Co-expression of TLR7 and cell phenotype in LSG from SS patients and healthy controls was analyzed by immunofluorescence. Expression of downstream molecules of TLR7 was analyzed by immunofluorescence in cultured primary salivary gland epithelial cells (SGECs) obtained from SS patients. [Results] In SS, TLR7 was detected by immunohistochemistry in mononuclear cells (MNCs) and ducts, whereas low frequency of TLR9 was found in MNCs of SS patients. TLR7 was detected by immunofluorescence in CD20 positive cells, plasma cells and dendritic cells. Additionally, downstream molecules of TLR7 were detected in dendritic cells. Stimulation of SGECs with a TLR7 ligand, loxoribine for ten minutes induced the translocation of interferon regulatory factor-7 and the expression of tumor necrosis factor receptor-associated factor-6. [Conclusions] These results suggest TLR7 activation is associated with pathogenesis of SS.

W5-6

Evaluation of clinical features and activity of pediatric primary Sjögren's syndrome using ESSDAI

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Conflict of interest: None

Objectives: The aim of this study is to clarify the clinical features and evaluate the activities of pediatric primary Sjögren's syndrome (SS) using ESSDAI. Methods: We retrospectively reviewed available medical records or clinical summaries of patients who have been diagnosed as having SS before 16-year-old from April 1986 to March 2016 at KKR Medical Center and Hokkaido University Hospital. Results: Twenty-five patients (2 male and 23 female) were enrolled. Chief complaints at the diagnosis were fever (68%) and arthralgia (48%) followed by recurrent parotid swelling (44%). Only 4 patients initially had mild dry mouth. Frequencies of positive ANA (≥1:160), RF, anti-SSA and anti-SSB antibodies were 92%, 84%, 80%, and 64%, respectively. Mean score of the 25 patients was 14.92 (ranging from 3 to 38). Twenty-two patients scored 5 or higher. The frequency of each domain was: constitutional 68%, lymphadenopathy 16%, glandular 60%, articular 48%, cutaneous 28%, renal 12%, muscular 8%, peripheral nervous system 4%, central nervous system 20%, hematological 4%, and biological 96%. Conclusion: Because sicca symptoms are rare in pediatric SS, only patients with extraglandular manifestations could be diagnosed as having SS and be accordingly active as judged from high scores of ESSDAI.

W6-1

The use of EULAR Sjögren's Syndrome Disease Activity Index in primary Sjögren's syndrome in childhood: a multicenter study

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Conflict of interest: None

Background: There are few data about EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) of primary Sjögren's Syndrome (pSS) in childhood. **Objectives:** The ESSDAI scores of pSS in childhood at onset were investigated at institutions in which members of the SS working group had been working. **Methods:** 40 patients (5 male, 35 female, mean age of onset 9.1±3.6) with pSS in childhood who had visited seven institutions were examined. **Results:** The mean ESSDAI score was 8.8±6.7. Ten cases scored more than 14 points, 19 cases ranged between 5 to 13 points, and 6 cases scored less than 5 points. The number of active patients (low~high activity level) was 20 cases in the constitutional domain and 22 cases in the biological domain. In this investigation, there was no patient with active disease in lung and muscle domain. In five patients diagnosed as systemic lupus erythematosus, the mean ESSDAI score was 6.0 ± 3.7. **Conclusion:** The proportion of patients with active disease above 5 points evidenced high ratios (72.5%, 29 cases). Pediatric onset pSS patients have few dry symptoms, but more systemic symptoms. So it is possible that ESSDAI can evaluate the disease activity more accurately than other methods for evaluation of dry symptoms.

W6-2

Clinical significance of lip biopsy among 145 patients with sicca symptoms and various immune disorders

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Conflict of interest: None

Purpose and Methods: Clinical significance of lip biopsy among patients with various immune disorders are not certain. We evaluated patients who underwent lip biopsy between Jan. 2015 and Oct.2016. Those patients also met at least two of the following criteria. 1) sicca symptoms, 2) positive SSA antibody, 3) ANA>x40, 4) IgG>=1700 mg/dl, 5) WBC<4000 /μl, Neu<1500 /μl, Ly<1000 /μl or Plt<100000 /μl, 6) C3<80 mg/dl, 7) interstitial pneumonia, 8) cryoglobulin, 9) TgAb>=28.0 IU/ml or TPOAb>=16.0 IU/ml, 10) arthralgia. Results:Lip biopsy was performed for 145 cases, including 96 patients of unknown diagnoses, 21 RA, 8 SLE, 4 SSc and 16 patients with other diagnoses. In this study, we defined that the sialadenitis was positive if more than 50 lymphocytes were infiltrated aroud capillary ducts. Overall positive ratio was 86.9%(126/145). Positive ratios of patients with unknown diagonosis, RA, SLE, SSc and other diagnoses were 87.5%(84/96), 85.7%(18/21), 87.5%(7/8), 100%(4/4), 81.3%(13/16), respectively. Patients with SSA antibody and ANA>x40 had the highest positive ratio of lip biopsy. Conclusion: Positive ratio of lip biopsy among patients with above mentioned criteria was high (86.9%). Subclinical SjS might be popular even in patients with immune disorders without sicca symptoms.

W6-3

Investigation of factors related to recurrence and new development of organ involvement in IgG4-related disease

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Conflict of interest: None

[Objectives] This study aimed to clarify differences between risk factors of recurrence and those of new development of organ involvement (OI) in IgG4-related disease (IgG4-RD). **[Methods]** We retrospectively investigated factors related to recurrence and new development of OI in 86 IgG4-RD patients whose follow-up period was more than 12 months. **[Results]** The patients comprised 57 men and 29 women (mean age 65.9 years). Mean follow-up period was 63.1 months (range 14-150). At diagnosis, their mean serum IgG4 level was 718 mg/dL. Seventy-one patients were treated with glucocorticoid (GC). Recurrence of OI was detected in 20 patients, and new development of OI in 15. Four of 20 patients did not receive GC at the time of recurrence, whereas 8 of 15 patients did not at the time of new development of OI. In multivariate Cox regression analysis, blood eosinophil counts (per 100/μL, HR 1.072) and continuation of GC (vs discontinuation or observation without GC, HR 0.245) had a significant impact on the time to new development of OI, whereas age (per year, HR 0.942) and ANA positivity (vs negativity, HR 6.632) had a significant impact on the time to recurrence of OI. **[Conclusions]** Our data suggests that risk factors of recurrence and new development of OI are different in IgG4-RD.

W6-4

Association of serum levels of fibrosis-related biomarkers with pathogenesis in IgG_4-related disease

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Conflict of interest: None

Objectives. We evaluated the association of serum levels of fibrosis-related biomarkers with pathogenesis in IgG4-related disease (IgG4-RD). *Methods.* Serum levels of GDF-15, MCP-1 (CCL2), TIMP-1, hyaluronic acid (HA), P3NP and sIL-2R were examined by ELISA in 72 patients with IgG4-RD and 20 healthy controls. We calculated the enhanced liver fibrosis (ELF) score. Additionally, we analyzed the association between serum biomarkers and organ involvements in patients with IgG4-RD. *Results.* In IgG4-RD patients, age (median) was 66 years, and serum levels of IgG4 (median) 457 mg/dl. Serum levels of all above biomarkers were significantly higher than health controls. Each GDF-15, MCP-1, TIMP-1, HA, IgG4, sIL-2R and ELF score were significantly positively correlated. Serum levels of GDF-15, MCP-1, TIMP-1, and HA were significantly higher in patients complicated with retroperitoneal fibrosis among organ involvements. *Conclusion.* Serum levels of GDF-15, MCP-1, TIMP-1 and HA correlated with degree of fibrosis in patients with IgG4-RD.

W6-5

Clinical characteristics of IgG4-related kidney disease accompanied with hypocomplementemia

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Conflict of interest: None

Objective. This study aimed to clarify clinical features of IgG4-RKD patients with hypocomplementemia compared with those without it. **Methods.** We extracted 24 patients with IgG4-RKD between September 2005 and October 2016 in our hospital. Based on the presence/absence of hypocomplemetemia at diagnosis, we divided them into hypocomplementemia group (n=11) and normal complement group (n=13), and retrospectively analyzed clinical features during the clinical course in the two groups. **Results.** The patients comprised 17 men and 7 women with an average age of 67.9 years. Age, serum IgG levels, gaps between serum IgG and IgG4 level, serum IgG1 levels, and the number of involved or-

gans were significantly different between the two groups, while serum IgG4 levels were not. At relapse of renal lesions, although both groups showed serum IgG4 elevation, hypocomplementemia group showed exacerbation of hypocomplementemia and expansion of gaps between serum IgG and IgG4 level, while normal complement group did not. **Conclusion.** Hypocomplementemia may be associated with multiple organ involvement and elevation of other IgG subclasses than IgG4 including IgG1 in IgG4-RKD.

W6-6

Analysis of CD180-negative plasmablasts in IgG4-related disease

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Conflict of interest: None

Large population of plasmablasts are found in patients with IgG4-related disease (IgG4-RD) and may take part in pathophysiology of the disease. However, the features of the plasmablasts in IgG4-RD have not been fully elucidated yet. We have studied clinical significance of CD180 (RP105)-negative B cells including plasmablasts in IgG4-RD. The CD180 molecules expressed on mature B cells is one of the Toll-like receptor (TLR) associated molecules. RP105 is deeply associated with B cell function. We also analyzed the 5 sub-populations of plasmablasts in the diseases. Increased CD180-negative B cells in IgG4-RD is very high levels like as seen in SLE. The distribution of sub-population in IgG4-RD was predominantly earlier subsets of plasmablasts. The differential expression antigens including CXCR5 was found in CD180-negative plasmablasts between IgG4-RD and SLE. Especially, persistent expression in the later subset in IgG4-RD was prominent. Plasmablasts may be profoundly associated with pathophysiology in this disorders.

W7-1

Assessing the importance of pathologically confirming a lymph node biopsy for lymph node swelling developing in RA patients

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Conflict of interest: None

The purpose of this study is to evaluate the importance of pathologically confirming the biopsy findings of lymph node swelling developing in RA patients. It is well known that RA patients develop LPD at a frequency two to four times higher than that in the general population. In addition, RA patients also tend to develop MTX-LPD. This disease seldom shows a spontaneous regression after the withdrawal of MTX medication. Meanwhile, lymphadenopathy has been reported to occur in from 41 to 82% of RA patients, while histologically showing either reactive lymphoid hyperplasia or cortical hyperplasia. We assessed RA patients by performing a lymph node biopsy from April 2012 to October 2016 at Osaka-Minami Medical Center. A total of twenty-nine cases were examined. Sixteen cases (55.2%) were diagnosed with LPD, while eleven cases (37.9%) were diagnosed with reactive lymphadenopathies. One patient was diagnosed to have fibrotic lesions scattered mature lymphocytes and one patient demonstrated massive necrosis. In conclusion, when evaluating potential spontaneous regression of MTX-LPD without pathological confirmation, it is important to understand that about one-third of all such patients have reactive hyperplasia, and not MTX-LPD.

W7-2

Presepsin as a diagnostic marker for distinguishing between bacterial pneumonia and exacerbation of interstitial pneumonia in patients with connective tissue disease

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Conflict of interest: None

【Objective】To assess the usefulness of presepsin for distinguishing between bacterial pneumonia (BP) and exacerbation of interstitial pneumonia (E-IP) in patients with connective tissue disease.【Method】We retrospectively analyzed 35 patients with connective tissue disease who were clinically suspected with pneumonia between June 2014 and October 2016. Pneumonia was diagnosed based on clinical symptoms and via radiographic methods. BP was diagnosed based on a good response to antibiotics. E-IP was diagnosed based on a good response to immunosuppressants. Concentrations of plasma presepsin, serum procalcitonin, and C-reactive protein, and white blood cell counts were measured and compared.【Results】Seventeen patients were included in the BP group and 18 in the E-IP group. Plasma presepsin levels in the BP group were significantly higher than in the E-IP group (mean, 95% confidence interval: 558 (269-847) pg/mL vs. 231 (139-325) pg/mL; p=0.00124). According to receiver operating characteristic curve analysis, presepsin had a higher diagnostic accuracy for infection than other tested components, with the area under the curve as 0.81.【Conclusion】Measuring presepsin levels can help in distinguishing between BP and E-IP in patients with connective tissue disease.

W7-3

Evaluation of oxidative stress markers in patients with rheumatoid arthritis treated with tocilizumab: the 52-week analysis

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Conflict of interest: Yes

< Objective > Treatment with biologics improves the joint prognosis of patients with rheumatoid arthritis (RA), however their impacts on cardiovascular (CV) events related to long-term prognosis remain elusive. Oxidative stress is involved in the process of atherosclerosis. In this study we have sought to determine the effect of tocilizumab (TCZ) treatment on the levels of oxidative stress markers in RA patients. < Methods > Levels of 8-OHdG and 8-iso-PGF2a in urine of RA patients treated with TCZ were evaluated by enzyme immunoassay and enzyme-linked immunosorbent assay, respectively, at baseline and 52 weeks. < Results > 32 out of 82 patients with RA (mean age 60.6 years old; mean disease duration 8.7 years; concomitant MTX 56.3%) were evaluated. The rate of DAS28 (ESR) and CDAI remission at 52 weeks was 79.3% and 33.3%, respectively. In all patients levels of 8-OHdG in urine were decreased, while levels of 8-iso-PGF2a in urine were not altered. The subgroup analysis shows that levels of urinary 8-OHdG were statistically decreased in patients with short disease duration (< 2 years) and low BMI (< 25). < Conclusions > These findings suggest that treatment with TCZ improves the long-term prognosis of patients with RA by lowering the risk

of CV events.

W7-4

New disease activity biomarkers under tocilizumab therapy for rheumatoid arthritis

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Conflict of interest: None

[Background] Tocilizumab (TCZ) is essential biologics in the treatment with rheumatoid arthritis (RA). DAS28 and SDAI are often underestimated because CRP and ESR are considerably decreased under TCZ treatment. We need the new disease activity biomarkers alternative to conventional inflammatory markers. [Objectives] To extract and identify the new biomarkers from patients with RA treated with TCZ. [Method] We collected serum from patients with RA under TCZ therapy at baseline, 4 weeks and 1 year. We conducted the differential analysis by using BLOTCHIP-MS technology. Thereafter, we determined the prospective biomarker peptide after structural analysis. We verified the interconnectedness of those peptide and CDAI. [Result] We investigated 14 cases that we completed peptide analysis. We detected 64 candidate peptide in consequence of the differential analysis for 7 patients who had completed CDAI remission. Furthermore, we determined the 8 amino acid sequences (sensitivity 71.4~100%, specificity 42.9~85.7%). We validated for 14 cases by using multi biomarker, combination of those peptide biomarker, 4 multi biomarkers were related to CDAI (Spearman rank correlation coefficient > 0.6). [Conclusion] We detected new disease activity marker alternative to CDAI under TCZ treatment.

W7-5

IL-6 blockade with tocilizumab suppresses CD154 expression on CD4 positive T cells in patients with rheumatoid arthritis

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Conflict of interest: Yes

[Objective] CD154 (CD40L) -CD40 interaction pathologically contributes to RA by stimulating release of cytokines, MMPs, and others. We hypothesized that IL-6 blockade with TCZ would decrease CD154 expression on T cells in RA patients. **[Methods]** PBMCs were isolated from 14 RA patients at baseline, 24 and 48 weeks of TCZ treatment. The proportion of CD154+CD4+ T cells was analyzed with FACS. **[Results]** DAS28-ESR and CDAI were significantly reduced at 24 and 48 weeks compared with those at baseline. Also, the serum levels of MMP-3 were significantly decreased at 48 weeks (245.0±299.1 ng/mL at baseline; 83.5±78.8 ng/mL at 24 weeks *p=0.053*; 55.5±27.0 ng/mL at 48 weeks, *p=0.033*). The proportion of CD4+ cells was significantly increased at 24 and 48 weeks compared with those at baseline. However, the proportion of CD154+CD4+ cells in CD4+ cells was significantly decreased at 24 weeks compared with that of baseline (4.3±2.8% at baseline; 2.6±1.7% at 24 weeks *p=0.031*; 2.9±1.9% at 48 weeks, *p=0.163*). **[Conclusion]** The IL-6 blockade decreases disease activities in RA patients. It also reduces the proportion of CD154+CD4+ in CD4+ T cells in RA patients. A decrease in CD154 expression in CD4+ T cells might lead to a decrease in disease activities in RA patients during TCZ treatments.

W7-6

Evaluations of the clinical efficacy, and the efficacy prediction factors at baseline in rheumatoid arthritis patients treated with tocilizumab

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Conflict of interest: None

【Methods】Participants comprised 31patients who met the 2010 ACR / EULAR classification criteria. At baseline and at weeks 24 and 52 of TCZ treatment, clinical results were obtained from clinical records and evaluations were made using the DAS28ESR, CDAI and SDAI. Peripheral blood was obtained at the same time and serum concentrations of cytokines (IL-6, IL17-A, TNF-α) and MMP-3 were analyzed.【Results】28 patients received followup, and 3 patients ceased TCZ therapy because of side effects or other reasons. DAS28ESR scores decreased from 5.09 at baseline, to 2.60 in Week 52. 16 patients were in remission state (DAS-28ESR) at week 56. Mean concentration of serum (serum) MMP-3 decreased from 254.1ng/ml at baseline, to 75.3 ng/ml at week 52. Serum IL-6 was 24.9 pg/ml at baseline, 59.4 pg/ml at week 24, and 40.1 pg/ml at week 56. Serum IL-17A was increased at week 24 than that of baseline, then decreased at week 52. Serum TNF-α was decreased from baseline to week 52. According to multivariate analysis, the baseline scores of CDAI, SDAI and serum IL-6 have been correlated with DAS28ESR score at week 52.【Conclusion】The clinical effectiveness of TCZ therapy was confirmed. The serum concentration of IL-6 at baseline might be a prediction factor.

W8-1

Clinical significance of serum levels of ROM (reactive oxygen metabolities) at 12 weeks during treatment with biologic agents as a predictor for the 52-week remission

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Conflict of interest: None

【Background】We have shown that serum levels of reactive oxygen metabolities (ROM) at 12 weeks during treatment with biologic agents (BAs) are predictive for the 52-week remission by DAS28. However, it is unknown whether ROM is also a predictor for other clinical remission such as CDAI, SDAI and Boolean.【Methods】Fifty-four biologic-naïve RA patients (mean age: 59.8±13.6 y.o., disease duration: 7.26±10.8 y) were included in this study. Association between serum levels of ROM and clinical parameters at 12 weeks during treatment with BAs and the remission by DAS28, CDAI, SDAI and Boolean at 52 weeks was investigated.【Results】Remission rates at 52-week for DAS, CDAI, SDAI and Boolean was 69, 54, 57 and 56%, respectively. A multivariate logistic regression analysis revealed that ROM at 12 weeks was associated with the 52-week remission by SDAI and Boolean (OR: 0.989, 95%CI: 0.978-1.000). Furthermore, ROC curves demonstrated their AUC was 0.746 and the cut-off value was 389.5 (sensitivity: 55.0%, specificity: 92.3%).【Conclusion】ROM at 12 weeks during treatment with BAs was a predictor for the 52-week remission by SDAI and Boolean, although its sensitivity was low. Serum levels of ROM could be a useful biomarker in the treatment strategy aiming at the early remission of RA.

W8-2

An influence of fracture on disease activity of rheumatoid arthritis

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Conflict of interest: None

Introduction The patients with rheumatoid arthritis (RA) seems to have higher risk of fracture because of osteoporosis and poor nutrition. However, there are few reports about disease activity of RA at pre and

post fracture event. The purpose of this study is to evaluate the effect of fracture event on disease activity. **Materials and methods** Eighteen (4 males and 10 females) RA patients who had fracture were treated in our hospital. Average age was 68 years old (40-89) and average disease duration of RA was 15 years (3-50). In this study, we evaluated fracture parts, treatment methods (conservative or operative) and disease activity of RA (DAS28) at pre and post 6months fracture events. **Results** Fracture parts were divided into three group such as upper extremity, lower extremity and trunk. As a result, there were 3 fractures in upper extremities, 5 fractures in lower extremities and 10 fractures in trunks. Eight fractures were treated surgically and 10 fractures were treated conservatively. Average disease activity of RA was higher at post 6months fracture events than at pre fracture events. **Conclusions** Our current study supposed that fracture events might make disease activity of RA worse. Treatments of osteoporosis and nutrition are important to prevent fracture in RA patients.

W8-3

Reduction of Anti-cyclic citrullinated glucose-6-phosphate isomerase peptide antibodies by 3 kinds of biologics treatments in rheumatoid arthritis

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Conflict of interest: None

Objective: To investigate the fluctuation of several ACPAs by 3 kinds of biologics treatments (infliximab;IFX, tocilizumab;TCZ, and abatacept;ABT). Methods: After informed consent was obtained, plasma samples were obtained from 132 ACPA-positive RA patients. The levels of anti-CCG (cyclic citrullinated GPI peptide)-7, anti-CCG-2 and anti-CEP-1 antibodies (Abs) were measured by ELISA before and after 6 month treatment with IFX (n=46), TCZ (n=45) and ABT (n=41). Data were analyzed using the paired t-test. Results: Anti-CCG-7 Abs were significantly decreased with treatment of IFX, TCZ, and ABT (optical density [OD] mean: 0.68 to 0.43, P=0.001, OD mean: 0.55 to 0.42, P=0.002, OD mean: 0.97 to 0.82, P=0.048, respectively). Anti-CCG-2 Abs were significantly decreased with IFX treatment (OD mean: 1.13 to 0.97, P=0.003). However, anti-CCG-2 Abs were not decreased with TCZ and ABT treatment. These treatments had no effect on the levels of anti-CEP-1 Abs. In each group, the mean value of the DAS-28 CRP decreased significantly after the treatment. Conclusion: These findings suggest that the change of Ab level is different for each ACPA and anti-CCG-7 Abs are a possible biomarker for the treatment effectiveness of biologics in RA.

W8-4

Radiographic Progression Is Less Significant in Anti-Carbamylated Antibody-Positive Patients with Rheumatoid Arthritis (RA)

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Conflict of interest: None

Purpose: We previously found in162 patients with RA who were clinically active and thus under treatment with biological DMARDs that radiographic progression was less significant when anti-carbamylated protein antibody (aCaPAb) was positive. We here studied aCaPAb in 268 patients with RA whose sera were measured on their first visit to our hospital. **Methods:** aCaPAb was measured by ELISA. The change in van der Heijde-modified total Sharp score per year ΔTSS was assessed using cumulative probability plots. Statistical tests were performed using Mann-Whitney U test. **Results:** In sera of 268 RA patients measured on their first visit, the extent of radiographic progression (cumulative probability plot of ΔTSS) was similar between aCaPAb+ACPA+(n=80) and aCaPAb-ACPA+(n=188) patients. Radiographic progression was less significant in aCaPAb+ACPA+ patients as compared with aCaPAb-ACPA+ patients when 95 percentile of mostly radiologically-progressive patients were selectively compared: meanΔTSS was 7.28 vs 17.01, meanΔESS (erosive score) was 4.49 vs 12.81. **Conclusion:** Radiographic progression seems less significant in aCaPAb-positive RA patients when they are basically progressive with higher ΔTSS. Study is a co-work with Drs. Verheul MK, Trouw LA, Leiden University, Netherlands.

W8-5

A novel scoring system based on common laboratory tests predicts the efficacy of IL-6 inhibitor in patients with rheumatoid arthritis

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Conflict of interest: None

Objectives. To develop a scoring system to supply helpful information on selecting either an IL-6 or a TNF inhibitor (TNF-i). **Methods.** 98 cases treated with tocilizumab (TCZ) or a TNF-i were retrospectively analyzed to develop a scoring system. Then, the validity of the scoring system was verified in an additional 228 cases. **Results.** The analysis of 98 patients revealed a significant correlation between TCZ efficacy and the values of platelet count, hemoglobin, AST, and ALT; in contrast, there was no similar correlation in the TNF-i group. The cut-off values were defined by receiver operating characteristic (ROC) analysis to develop a scoring system (1 point/item, maximum of 4 points). A good TCZ response was predicted if the score was 2 or more; in contrast, a TNF-i seemed to be preferable if the score was 1 or less. Similar results were obtained in a validation study of an additional 228 cases. These differences became more remarkable in cases with 3 or more points; for these cases, the good responder probabilities of TCZ/TNF-i were 75.0%/37.9%($p<0.01$) and the non-responder probabilities were 3.1%/27.6%($p<0.01$), respectively. **Conclusions.** The score appears useful for identifying a better treatment at the time of selecting either an IL-6 or a TNF inhibitor.

W9-1

Efficacy of HRT for menopausal arthralgia

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Conflict of interest: None

[Object] Post-menopausal women complaining of MS and joint pain visited the hospital at division of Rheumatology. Most cases showed no evidence of abnormality in blood test and joint swelling except for joint pain. We present clinical practice for these patients. [Methods] 119 post-menopausal women visiting the clinic from 2013 to 2015 were enrolled. Blood exam included serum CRP, RA, ANA, anti-SS-A, E2 and FSH. Assessment of joint pain recorded by patient VAS, E2 and FSH were obtained at 0, 2, or 6 month. These patients received HRT without NSAID. [Results] E2:79.8±78.3 pg/ml after treatment is higher than E2:25.6±26.0 before, FHS: 43.2±22.9 mIU/ml after is lower than FSH: 75.9±29.6 before. P-VAS: 23±23 after is lower than P-VAS:100 before. These results are statistically significant. $P<0.0001$. MS and joint pains were disappeared within 2~6 months. In case of presenting RF or ANA, they have continue taking them to prevent RA or SjS. [Conclusions] We came

across many female patients with post- menopausal arthralgia, in contrast to Europe or other developed country. HRT is very effective in such disease condition and may be recommended more.

W9-2

An autopsy case of immune thrombocytopenic purpura (ITP) complicated by thrombotic thrombocytopenic purpura (TTP), autoimmune hemolytic anemia (AIHA) and anti-phospholipid syndrome (APS)

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Conflict of interest: None

A 21-year-old male patient with mild mental retardation was diagnosed with ITP 7 years ago, and treated with PSL. His serum LDH level increased and platelet counts decreased about 2 months ago. Direct Coombs-positive hemolytic anemia and kidney dysfunction were detected 13 days ago. When he came to the hospital for follow-up, his blood pressure decreased to shock vital. Deterioration of Evans syndrome (ITP+AIHA) was suspected, and introduction of apheresis therapy was needed. After receiving platelet transfusion, his vital sign further fell down and he died. Later, severe decrease of ADAMTS-13 activity, ADAMTS-13 inhibitor, and β2GPI-dependent antiphospholipid antibodies (APLA) were detected. Autopsy revealed systemic organ microinfarctions via platelet thrombosis. These findings suggest that this patient was complicated by TTP, AIHA and APS. It is reported that APLA-positive rate in ITP patients ranges from 30 to 73%, and that the incidence of thrombotic events is significantly high in these patients. This case might have underlying disease such as SLE or genetic disorder. [Clinical significance] We have to pay attention to the possibility of deterioration of systemic condition in ITP patients, which was complicated by various autoimmune diseases.

W9-3

2 cases of TAFRO syndrome

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Conflict of interest: None

TAFRO syndrome is a disease defined by thrombocytopenia, anasarca, fever, reticulin myelofibrosis or renal insufficiency, and organomegaly. case 1:A 46-year-old woman was admitted because of back pain and fever. Her symptoms suggested pyelonephritis, but antibiotics were no effect. During the hospital stay, thrombocytopenia and anasarca appeared. After she was transferred to our hospital, bone-marrow biopsy revealed fibrotic bone marrow and computed tomography showed organomegaly. Then, we diagnosed TAFRO syndrome. One course of high-dose methylprednisolone therapy, prednisolone 30mg/day and cyclosporine improved her symptoms. case 2:A 61-year-old woman had fever and thrombocytopenia. After antibiotic therapy was failure, she came to our hospital. Fever improved gradually, but blood platelet count decreased. We thought she had idiopathic thrombocytopenic purpura, because megakaryocyte in bone-marrow aspirate increased. Prednisolone 30mg/day was started, but anasarca occurred around the same time. Fibrotic bone marrow was revealed by biopsy. Then, we diagnosed TAFRO syndrome. She got better with an escalating dose of prednisolone and cyclosporine. We report two cases of TAFRO syndrome, it took several weeks after admission for diagnosis because the symptoms gradually appeared.

W9-4

A case of TAFRO syndrome introduced our hospital with suspicion of systemic lupus erythematosus (SLE)

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Conflict of interest: None

A 66-year-old woman was referred to us with thrombocytopenia. Bone marrow biopsy showed normal formation. Though she was diagnosed as idiopathic thrombocytopenic purpura and got follow-up, a fever and the facial edema appeared after the day. Laboratory tests showed thrombocytopenia, renal dysfunction, hypoalbuminemia, occult hematuria and urinary protein. Whole body computed tomography demonstrated anasarca, multiple lymphadenopathy. She was admitted to our hospital with suspected of SLE from these findings. Physical exam revealed a slight fever and the swelling of supraclavicular node and edema of the face and the lower limbs. Both of anti-nuclear antibody and anti-double stranded DNA antibody were negative. Lymph node biopsy revealed reactive lymphoid hyperplasia. These findings did not suggest multicentric Castleman's disease or SLE. Her clinical features were diagnosed as TAFRO (thrombocytopenia, anasarca, fever, renal dysfunction, and lymphadenopathy) syndrome. She was successfully treated with prednisolone 55 mg/day, after that thrombocytopenia and renal dysfunction gradually improved. TAFRO syndrome is a rare disease and its clinical features often like to SLE, so rheumatologist must pay attention to this disease.

W9-5

Two cases of rheumatoid arthritis in forefoot symptoms diagnosed with other diseases

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Conflict of interest: None

[Background] Rheumatoid arthritis (RA) could develop from forefoot symptoms. We need to distinguish from other diseases. We report two cases of RA in forefoot symptoms diagnosed with other diseases. [Case 1] A 47-year-old woman had a swelling, pain and the mass of about 3cm in right 3rd toe MTP joint. MRI showed soft tissue tumor. We operated the mass which continued with MTP joint and was synovial-like tissue. It had a lymphocyte and a plasma cell-based diffuse inflammatory cell to a synovial tissue by pathology. ESR 25 mm/h and RF 24 IU/ml were increased. And we diagnosed RA. We attain remission with methotrexate (MTX) and etanercept in start of therapy 9.5 years. [Case 2] A 65-year-old woman had a pain, swelling and tenderness in right 3rd toe. X-ray and MRI showed normal. The symptom was improved by nerve block. And we diagnosed Morton's neuroma. She had a pain and swelling in right hallux and 5th toe MTP joint after 3.5 years. MRI showed synovitis. RF 32 IU/ml and ACPA 28.6 U/ml were increased. As a result, we diagnosed RA and administered MTX. In start of therapy 6 months, the symptom is improved. [Conclusions] There were reports that RA developed later diagnosed Morton's neuroma. It is important that we distinguish forefoot pain or soft tissue tumor in forefoot from RA.

W9-6

A case with refractory adult onset Still's disease, for which azathioprine was considered effective

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Conflict of interest: None

A 65-year-old-woman was admitted to our hospital because of fever,

sore throat, arthralgia and liver dysfunction. Skin rash also appeared. Laboratory examination showed WBC16260/μl, CRP18.61mg/dl, serum ferritin6153.1ng/ml, and negative for anti-nuclear antibody and rheumatoid factor. As adult onset Still's disease, 40mg of prednisolone was administered daily. She got better, however, WBC, CRP and serum ferritin level increased again, liver function grew worse, and therefore, steroid pulse therapy was performed and followed by 60mg of prednisolone daily. She got afebrile, but serum ferritin rose to 72900ng/ml, she had DIC and HPS. The treatment with thrombomodulin and plasmapheresis caused better condition, and cyclosporine A was administered. When prednisolone was gradually reduced, WBC and platelet decreased and serum ferritin level increased again, so steroid pulse therapy, change of cyclosporine A to tacrolimus and addition of dexamethasone palmitate were performed. Although serum ferritin level increased and liver function grew worse, with the reduction of prednisolone, the administration of azathioprine brought her into improved condition. Finally, dexamethasone palmitate discontinued, and she was discharged from the hospital.

W10-1

Therapeutic effect of anti IL7R antibody for ANCA associated glomerulonephritis

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Conflict of interest: None

【Object】ANCA associated glomerulonephritis (GN) presents a rapidly progressive GN, and it may lead to the end-stage renal failure. After cytotoxic T cells recognize and destruct foreign substances, a portion of the T cells remains as memory T cells. IL7 binds to IL7 receptor which expresses on CD8 positive memory T cells, and activates various pathways. We studied whether an exhaustion of CD8 positive memory T cells causing by an administration of anti IL7R antibody for model mice of ANCA associated GN improves GN.【Methods】I injected 20μg recombinant MPO for the immunization at day0 and for booster at day7. Then, I injected 1.5mg anti GBM antibody for trigger at day16. In the process, I injected anti IL7R antibody at day15, 17 and 19, total 1.5mg/mouse, then, I culled mice at day20. I measured urinary albumin by ELISA, and infiltrations of macrophages, neutrophils, and CD4 and CD8 positive T cells of kidney tissue by immunostaining. Also I measured various cytokine/chemokine of kidney tissue by RT-PCR. I discussed the changes of CD8 positive memory T cells of kidney and spleen by FACS.【Results】In the treatment group, urinary albumin, infiltration cells and cytokine/chemokine were decreased【Conclusion】It suggests that anti IL7R antibody improves ANCA associated GN.

W10-2

Neutrophil extracellular traps (NETs) from neutrophils cultured with glomerular endothelial cells cause endothelial cell damage

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Conflict of interest: None

Objective: Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis often causes necrotizing glomerulonephritis. It has been demonstrated that NETs are related to the pathogenesis of ANCA-associated vasculitis. In this study we investigated the relationship between NETs and glomerular endothelial cell damage. Methods: Polymorphonuclear neutrophils (PMN) isolated from healthy donors and ANCA-associated vasculitis patients were cultured with BrdU-labelled glomerular endothelial cells in the presence or absence of phorbol myristate acetate (PMA). The amount of glomerular endothelial cell damage was estimated by analysis of BrdU-labelled DNA fragments in the supernatants. Isolated PMN were treated with PMA or PMA plus anti-myeloperoxidase antibody, and the amount of NETs induction was evaluated. Results: The amount of glomerular endothelial cell damage in the presence of PMA was associated with the amount of NETs induction. Endothelial cell damage in the absence of PMA was practically undetected. In patients of ANCA-associated vasculitis, the amount of NETs induction and glomerular endothelial cell damage decreased after immunosuppressive therapy. Conclusion: It is possible that NETs are associated with glomerular endothelial cell damage in ANCA-associated vasculitis.

W10-3

Property of anti-NETs autoantibodies (Anti-NETs) in patients with ANCA-associated vasculitis (AAV)

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Conflict of interest: None

OBJECTIVES: To clarify the property of Anti-NETs in AAV. **METHODS:**(1) We experienced a patient with hydralazine-induced AAV, which was improved by discontinuing the drug, but relapsed later. In the serum at relapse, Anti-NETs was detected by indirect immunofluorescence (IIF). We assessed the abilities for NET induction/degradation of the sera at disease onset (A; ANCA/Anti-NETs: +/-), relapse (B; +/+), immediately after therapy (C; -/+) and on remission (D; -/-). (2) We explored the prevalence of Anti-NETs in 11 AAV patients by IIF and assessed the relationship between the presence and the abilities for NET induction/degradation. **RESULTS:**(1) NET degradation ability was low in A-D, while the ability for NET induction was high in A, B and C. (2) Anti-NETs was present in 6 (56%). NET induction/degradation abilities were not different between the Anti-NETs+ and Anti-NETs- sera. Although NET degradation ability in the sera without Anti-NETs was increased by addition of DNase I, the increase was not observed in some sera with Anti-NETs. In addition, NET degradation ability in some sera with Anti-NETs was markedly increased by depletion of IgG. **CONCLUSIONS:** Our study suggested that Anti-NETs, found in some patients with AAV, would have diverse properties in the pathophysiology of AAV.

W10-4

Differential expression in interferon signature genes between microscopic polyangiitis and systemic lupus erythematosus

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Conflict of interest: None

Objective: In systemic lupus erythematosus (SLE), interferon (IFN) signature in peripheral blood has been established by transcriptome analyses. On the other hand, IFN signature has not been reported in ANCA-associated vasculitis (AAV). In this study, we examined whether IFN signature is also observed in AAV. Methods: Expression of IFN signature genes in whole blood was analyzed in 8 SLE and 6 microscopic polyangiitis (MPA) patients and 14 healthy controls using the Agilent microarray. Differences in IFN signature gene expression were tested by Welch's t-test. Results: Among 392 IFN signature gene probes, 68 (17.3%) were significantly increased in MPA, showing enrichment of IFN signature probes when compared with 1514 (7.6%) in total 20052 probes (P=9.6E-11). In SLE, 159 (40.6%) out of 392 IFN signature probes were upregulated, confirming the IFN signature. Cluster analysis and principal component analysis showed differential expression patterns in IFN signature probes between SLE and MPA. When expression was compared between SLE and MPA, 115 probes were upregulated in SLE, while 45

were down regulated. Conclusions: IFN signature was observed in MPA. Expression patterns of IFN signature genes are different between MPA and SLE.

W10-5

Circulating biomarkers of disease activity and organ damages in ANCA-associated vasculitis

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Conflict of interest: None

[Objectives] To identify novel biomarkers which reflect disease activity and organ damages in AAV with targeted proteomics approach. [Methods] The following serum samples were obtained from our hospital and cohort study (RemIT-JAV-RPGN): 105 with MPA; 36 with GPA; 25 with EGPA; and 3 with unclassifiable disease. Of these, the 79 patients were obtained paired sera before and month 6 after treatment. Biomarker candidates were selected with targeted proteomics approach using selected reaction monitoring (SRM) and validated by ELISA. [Results] The following five proteins were identified as a biomarker to distinguish between highly active AAV and remission (AUC>0.85): TIMP-1, CRP, LRG1, TNC, and S100A8/S100A9. Of these, only TIMP-1 was a biomarker to distinguish between non-remission (mildly active AAV) and remission at month 6 after treatment. The serum levels of CD93 and TKT were higher in patients with active renal disease than in those without renal disease. TNC level was elevated in patients with lung infiltration. [Conclusion] We identified the following best-performing markers: TIMP-1 as disease activity; CD93 and TKT as renal damage; and TNC as lung infiltration.

W10-6

Relationship between moesin and progression cutaneous arteritis to systemic polyarteritis nodosa

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Conflict of interest: None

[Objectives] We examined serum anti-moesin antibody levels in severe cutaneous arteritis (CA), most likely polyarteritis nodosa (PAN). We investigated moesin mRNA expression in formalin-fixed and paraffin-embedded skin biopsy specimen of patients with PAN, CA, and superficial venous thrombosis. [Methods] Moesin mRNA copy numbers were measured in the cutaneous affected tissue specimens using a quantitative real time reverse transcription-polymerase chain reaction assay. [Results] Elevated serum anti-moesin antibodies were significantly found in treatment-resistant PAN. Copy numbers of moesin mRNA differed significantly between PAN patients and CA patients. Similarly, moesin mRNA copy numbers in patients with PAN were significantly higher than in superficial venous thrombosis. We found a significantly positive correlation between moesin mRNA copy numbers and BVAS in patients with PAN and CA. [Conclusions] Elevated serum anti-moesin antibodies could play some role in the exacerbation of symptoms in patients with PAN. We propose that moesin mRNA level in affected skin tissue could be used as a marker for activity of PAN progress.

W11-1

Characterization of lymphoproliferative disorders occurring in 17 rheumatoid arthritis patients

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Conflict of interest: None

[Objectives] Rheumatoid arthritis (RA) is a risk factor for development of malignant lymphoma. Treatment with methotrexate (MTX) increases risk of lymphoproliferative disorders (LPD). [Methods] We analyzed 17 RA patients who developed LPD from January 2010 to October 2016. [Results] Fifteen patients had been administered with MTX and 5 patients had received biological DMARDs. The mean age was 67±8, mean disease duration of RA 16±10 years, and mean duration of MTX treatment 4.4±2.3 years. Diagnosis was as follows: nine diffuse large B cell lymphomas, one follicular lymphoma, one Hodgkin lymphoma, one T cell-rich large B-cell lymphoma and one plasmablastic lymphoma. EB virus infection was detected in tumor tissues in 4 of 12 patients analyzed. Eleven patients received chemotherapy, while 6 patients were cured after discontinuation of MTX. After treatment of LPD, RA relapsed within mean 11±8 months in 9 patients, and LPD recurred within mean 37±12 months in 3 patients. The death due to LPD was not observed. [Conclusion] We analyzed the character of LPD occurring in RA patients. It is necessary to be careful about recurrence of both RA and LPD.

W11-2

A retrospective analysis of methotrexate-associated lymphoproliferative disorders

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Conflict of interest: None

[Object] Methotrexate-associated lymphoproliferative disorders (MTX-LPD) have been reported recently. However, characteristics of MTX-LPD remain unclear. Then, we analyzed clinical characteristics of MTX-LPD in our department. [Methods] Of patients in our department from April 2003 to August 2016, 21 patients complicated by MTX-LPD were selected and analyzed. [Results] 20 rheumatoid arthritis patients and one psoriatic arthritis were included. The median MTX dosage and total amount of MTX were 7.2mg/week and 2504mg, respectively. The median MTX duration was 8 years. 16 patients (76%) had complete remission with only cessation of MTX. 5 patients (24%) had chemotherapy. In pathological findings, most of them (33%) showed polymorphic LPD. So, we divided MTX-LPD patients with pathological diagnosis into two groups, polymorphic LPD and others. Time from onset to biopsy in polymorphic LPD group was significantly shorter than others (p=0.01). Time to complete remission in polymorphic LPD was significantly shorter than others (p=0.02). [Conclusions] Polymorphic LPD was most frequently showed in our department. Most of polymorphic LPD group had complete remission without chemotherapy and shorter time to complete remission.

W11-3

Methotrexate associated lymphoproliferative disorders (MTX-LPD) in rheumatoid arthritis: Efficacy of PET/CT as a predictor for spontaneous regression of LPD

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Conflict of interest: None

Object: Recently methotrexate associated lymphoproliferative disorders (MTX-LPD) in rheumatoid arthritis (RA) are common as the iatrogenic immunodeficiency-associated LPDs. Some MTX-LPD regress after MTX withdrawal, but the mechanism is not still unclear. We investigated predictors for spontaneous regression of LPD. **Methods**: We analyzed the clinical features, characteristics, and outcomes in 26 patients of MTX-LPD from 2004 to 2015, retrospectively. **Results**: The spontaneous regression after cessation of MTX was detected 13 of 26 cases (50%). Maximum standardized uptake value (SUVmax) of F-fluorodeoxyglucose

(FDG) uptake in positron emission tomography/computed tomography (PET/CT) was significantly lower and the maximum size of LPD was significantly smaller in the spontaneous regression patients (p=0.02, p=0.002, respectively). Both SUVmax and size of tumor were related to the prognosis (p=0.04, p=0.006, respectively). The spontaneous regression cases never relapse during follow-up period, despite the usage of several anti-rheumatoid arthritis drugs including biological agents. **Conclusion**: Evaluation by PET/CT can obtain good predicators for the spontaneous regression and prognosis. Early detection of LPDs and early cessation of MTX are important for management of RA patients.

W11-4

Study of the predictive factor about spontaneous regression of MTX-LPD in RA patients

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Conflict of interest: None

Background: Lymphoproliferative disorders (LPD) that develop patients treated with MTX is known as MTX-LPD. We have some cases of MTX-LPD to regress for the treatment with MTX withdrawal. Although some reports presented about predictive factor about spontaneous regression of LPD, there is not enough evidence. Objectives: We investigate the predictive factor for spontaneous regression of MTX-LPD. Methods: We enrolled RA patients who developed MTX-LPD. In addition, they were divided into patients who were followed-up after the discontinuation of MTX alone (withdrawal group) and patients who were performed chemotherapy after one month or more of the MTX withdrawal (CTx group), and we weighed these two group. Results: We enrolled 24 patients in the withdrawal group and 9 patients in the CTx group. In withdrawal group, the peripheral lymphocyte counts significantly elevated after MTX discontinuation. As for subset of lymphocyte with specimen from a lesion, CD8 positive lymphocyte increased in CTx group than withdrawal group significantly. Conclusions: Our results suggest that the elevation of peripheral lymphocyte after the MTX withdrawal and the degree of CD8 positive lymphocyte in affected region may become a predictive factor for MTX-LPD treatment.

W11-5

Trends in the occurrence of malignancy in Japanese patients with rheumatoid arthritis based on the Institute of Rheumatology, Rheumatoid Arthritis (IORRA) cohort during a 14-year observation period

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Conflict of interest: None

[Object] To investigate the trends in the occurrence of malignancy in Japanese patients with RA. [Methods] Among patients with RA enrolled in the IORRA, all malignancies occurring from April 2000 to September 2013 were extracted from self-reported information and confirmed by medical records. For malignancies overall and at frequently involved sites, the SIRs and 95% CIs during 3 periods (pre-biologics, 2000-2003; early biologics, 2004-2007; and late biologics, 2008-2011) were calculated and trends were analyzed using a Poisson regression model. [Results] Among 11,106 patients with RA (68,483 person-years), 507 overall malignancies were confirmed. The SIRs (95% CIs) of overall malignancies were 0.96 (0.80-1.14) in pre-biologics, 0.95 (0.80-1.11) in early biologics and 0.91 (0.79-1.05) in late biologics, respectively (P = 0.43). The SIRs (95% CIs) of lung cancer were 1.68 (1.07-2.53), 0.60 (0.29-1.10) and 0.97 (0.60-1.48), respectively (P = 0.36). The incidence of malignant lymphoma remained markedly increased, with SIRs (95% CIs) of 4.53 (2.59-7.35), 4.06 (2.36-6.50) and 4.59 (3.00-6.72), respectively (P = 0.63). [Conclusions] Trends in the occurrence of malignancy in Japanese patients with RA have not changed dramatically in these 14 years.

W11-6

The Frequency of HTLV-1 Infection and Adult T-cell leukemia in Rheumatoid Arthritis Patients in an Endemic Area

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Conflict of interest: None

Objectives:Tree cases of RA developed adult T-cell leukemia (ATL) at our hospital. To clarify the clinical characteristics of RA patients infected with HTLV-1 and the risk factors for development of ATL. Methods: Sera from 986 patients with RA were screened for HTLV-1 antibodies using CLIA methods. Results:78patients (7.9%)were positive for HTLV-1 ab. The ages of HTLV-1-positive patients were significantly older than those of HTLV-1-negative patients (71±11vs64±14 years old). The ages in RA onset were also older in positive patients than negative patients (61±14vs54±16 years old, p<0.001). There were no differences in the frequencies of ANA, RF and ACPA between the HTLV-1-positive and -negative RA patients. The frequencies of HCVantibodies-positive and HBV resolved infections were higher in HTLV-1-positive RA patients than those of negative patients (9.5%vs2.2%,33%vs23%, respectively). There were no differences in administered DMARDs including PSL, MTX, bDMARDs between HTLV-1-positive and negative RA patients. Tree cases of HTLV-1-positive patients (3.8%)developed ATL. Conclusions:The findings strongly suggest that HTLV-1 is involved in the pathogenesis of diseases in a subset of patients with RA in endemic area, and RA treatments may be a risk factor of ATL in RA patients.

W12-1

Two-year clinical outcome of denosumab treatment alone and in combination with teriparatide in Japanese treatment-naive postmenopausal osteoporotic women

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Conflict of interest: None

[Object] This randomized, prospective study aimed to evaluate the clinical outcome of denosumab treatment alone and in combination with teriparatide in treatment-naive, postmenopausal Japanese female patients with osteoporosis. [Methods] Thirty patients were assigned into 2 groups: denosumab group (denosumab alone, n = 13); or combination group (denosumab + teriparatide, n = 17). Bone turnover markers and L1–4 lumbar vertebrae BMD (L-BMD) and bilateral total hip BMD (H-BMD) were determined at various time points up to 24 months post-treatment. [Results] Percent changes of TRACP-5b and urinary NTX were equally suppressed in both groups, with slight increases at 12, 18, and 24 months. L-BMD was significantly increased at the majority of time points in both groups, and at 24 months a significant difference was observed between combination groups and the denosumab (17.2% increase versus 9.6% increase, respectively; $P < 0.05$). There was no significant difference in H-BMD between the groups, although levels tended to be higher in the combination group than the denosumab group (9.5% increase versus increase 5.6%, respectively). [Conclusions] These findings suggest that combination therapy may represent an important treatment for primary osteoporotic patients.

W12-2

Glucocorticoid Osteoporosis Case series switch to denosumab from once-weekly teriparatide inadequate response to bisphosphonates

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Conflict of interest: None

[Objective] To clarify the efficacy and difference from primary osteoporosis, in the setting of glucocorticoid-induced osteoporosis (GIOP) switching once weekly teriparatide (TPTD) to denosumab. [Method] We investigated GIOP patients inadequate to bisphosphonates who received denosumab for 1.5 years switching from once-weekly TPTD. We analyzed bone density (lumbar and femoral neck), bone metabolic markers (serum NTx and BAP) and fracture events. [Result] We investigated 6 cases. Only one fracture event within 3 years. Lumbar bone density (YAM) change ratio was increased during TPTD and denosumab treatments (TPTD 1.5Y 0.63±3.20%, denosumab 1.5Y 4.09±3.14%). In contrast, femoral bone density (YAM) change ratio was decreased for 3 years (TPTD 1.5Y -7.37±5.43%, denosumab 1.5Y -6.93±8.16%). The change ratio of serum NTx level was increased (10.6±39.8%, 33.1±86.1%), but the BAP was decreased only after denosumab therapy (12.5±39.0%, -20.8±38.5%). [Conclusion] Switching from once-weekly TPTD to denosumab demonstrated quite different from previous study, that was intended for primary osteoporosis treated with daily TPTD and denosumab, in bone density and bone metabolic marker with patient with GIOP.

W12-3

Anti-resorptive agent-related osteonecrosis of the jaw in 7 patients with rheumatic disease

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Conflict of interest: None

Objectives: Anti-resorptive agent-related osteonecrosis of the jaw (ARONJ) is a rare adverse effect of various drugs. RA has been reported to be a risk factor for ONJ. We aimed to clarify clinical problems associated with ARONJ based on our cases.. Methods: retrospective data analysis of ARONJ cases in our division. Results: Seven female patients with a mean age 70.0 (range, 61-83) years were assessed: RA 5 cases, MPA 1, and PMR 1. Suspected drugs: bisphosphonate, 4 cases and denosumab, 3. Osteoporosis complications were in 3 denosumab-administered cases. Concomitant drug: steroid, 5 cases, MTX, 3, tacrolimus, 2, and tocilizumab, 1. All cases received either immunosuppressant. ARONJ onset followed tooth extraction in 3 cases, dental treatment 2 cases, periodontal disease 1 case, and infection 1 case. One patient developed ONJ due to dental treatment for MTX-LPD. One patient formed an abscess on the cheek. The other patient was administered the 4th denosumab for good progress after tooth extraction and ARONJ developed after 1 month. Conclusions: Attention should be paid to ARONJ onset during dental treatment with immunosuppressants and anti-resorptive agents. There is a need for informed consent for the risk of ARONJ in patients beginning bone-resorption inhibitor administration.

W12-4

Medication-related osteonecrosis of the jaw with rheumatoid arthritis

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Conflict of interest: None

Objectives: Medication-related osteonecrosis of the jaw (MRONJ) is a rare adverse effect of drugs. Rheumatoid arthritis (RA) is a risk factor for ONJ. We aimed to clarify clinical problems associated with RA secondary to MRONJ based on the Japanese Adverse Drug Event Report (JADER) database. Methods: We extracted ONJ cases from JADER of the PMDA, and compared clinical characteristics of RA and non-RA groups. Cases with malignancy were excluded. Results: 500 MRONJ cases were extracted (RA group, 113; non-RA group, 387). Women predominated with no difference between two groups ($p = 0.1052$). Age at MRONJ onset was younger in the RA group (>60 years old, RA vs non-RA, 80.5% vs 98.1%, $p < 0.0001$); osteoporosis complications were less in the RA group (60.1% vs 90.4%, $p < 0.0001$). Incidence of diabetes mellitus, renal disease and bone fracture did not differ in the two groups ($p = 0.4448$, 0.1451, 0.1631). In the RA group, concomitant drugs were steroids in 93 cases, MTX in 52 cases, and bisphosphonates (BP) in 104 cases. MRONJ developed in 5 patients administered MTX without steroid and BP. Conclusions: RA patients who developed MRONJ were cases with steroid administration. In MRONJ with RA, BP might have had been partly administered for the prevention of steroid-induced osteoporosis.

W12-5

Research of muscle quality and muscle mass by using Body Composition Analyzer on patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] The patients with rheumatoid arthritis (RA) are lower muscle mass and higher rate of sarcopenia than healthy individuals. Muscle quality has been evaluated by score. We examined the relationship between muscles quality, muscle mass, disease activity and quality of life of RA patients. [Methods] 51 RA patients were measured by body composition analyzer RD-501 (TANITA). The average age was 63.6 years old, mean disease duration was 8.2 years. We evaluated muscle quality score, muscle mass, disease activity (DAS28-ESR), RF, ACPA, CRP, MMP-3, mHAQ, disease duration, Steinbrocker stage, and class. [Results] DAS28-ESR was 3.45 ± 1.04, muscle quality score was 47.1 ± 15.4 points and muscle mass was 35.2kg (33.0-39.3). There was no significantly correlation in muscle quality and muscle mass ($r=-0.13$, $p=0.36$). Muscle quality was significantly lower in older age ($r=-0.48$, $p<0.05$). Muscle mass and age had weakly negative correlation ($r=-0.24$, $p=0.09$). DAS28-ESR and muscle quality had significantly negative correlation ($r=-0.32$, $p=0.03$), but there was no correlation in DAS28-ESR and muscle mass ($r=-0.13$, $p=0.38$). [Conclusions] There was significantly negative correlation in muscle quality and disease activity. The patients of higher disease activity had low muscle quality.

W12-6

The effect of BCAA supplementation on glucocorticoid (GC)-induced myopathy in patients with rheumatic disorders – variable effect of BCAA for flexor and extensor muscles, and normal and reduced radiation attenuation muscles

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Conflict of interest: None

[Object] Recently, we confirmed that supplementation of BCAA would be effective on GC-induced myopathy in patients with rheumatic disorders. To more precisely evaluate the effect of BCAA on skeletal muscle mass and quality, we analyzed the differential effects of BCAA on musculus rectus femoris and biceps femoris by CT. [Methods] We defined HU ranges of CT from -29 to +150 HU to demarcate muscle tissue. Moreover, since intramuscular lipid content affects skeletal muscle radiation attenuation, we separately measured cross sectional area (CSA) of

thigh muscle defined by -29 to +29 HU (reduced) and +30 to +150 (normal) HU. [Results] Each CSA of rectus femoris was not changed in both BCAA (-) and (+) groups in each range of HU. Although CSA of biceps femoris defined by -29 to +150 HU was significantly increased in both groups, those defined by +30 to +150 HU was significantly increased in BCAA (+) group but not in BCAA (-) group. Moreover, the differences and ratios of CSA of biceps femoris either defined by -29 to +150 HU or +30 to +150 HU between before and after trial were significantly increased in BCAA (+) group compared with BCAA (-) group. [Conclusions] These results indicate that sensitivity of BCAA might be different in muscle type and/or intramuscular lipid contents.

W13-1

Long-term Safety of Baricitinib (Bari), an Oral JAK 1/JAK 2 Inhibitor, in Patients (pts) including Japanese (JP) with Moderate to Severe Active Rheumatoid Arthritis (RA): an Integrated Analysis

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Conflict of interest: Yes

Objectives: To evaluate the long-term safety of Bari in pts with moderate-to-severe active RA including JP. **Methods:** Incidence rate of adverse events (AEs) was calculated using data in RA pts receiving Bari, placebo (PBO) or active comparators, and pooled from completed phase 1 to 3 studies and an ongoing long-term extension study of Bari in RA pts. **Results:** 3464 pts (510 JP) were exposed to Bari (max 1631 days) as of Aug 2015. In controlled periods, no increases in deaths, AEs leading to study drug discontinuation, malignancies, major adverse cardiac events, or serious infections were seen for Bari vs PBO/active treatment. Herpes zoster (HZ) was more frequent for Bari vs PBO. In all pts receiving Bari, all tuberculosis cases occurred in endemic areas; none in Japan. No confirmed opportunistic infections associated with Bari were reported. No increased risks were found over time for the above events with longer exposure to Bari. In JP, treatment-emergent AEs of HZ and those related to hepatic function were more frequent than overall pts, but most of them were mild and no notable difference was found in abnormal hepatic tests from overall pts. **Conclusion:** Bari had an acceptable safety profile in pts with active RA. In JP, the safety of Bari did not notably differ from overall pts.

W13-2

Efficacy of sarilumab, human anti–IL-6 receptor monoclonal antibody in KAKEHASI study, Phase 3 trial for Japanese rheumatoid arthritis patients

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Conflict of interest: Yes

Object: To demonstrate 24-week efficacy of sarilumab, a human monoclonal antibody blocking IL-6Rα, in a randomized double-blind placebo-controlled multicenter study (KAKEHASI study). Sarilumab was added to methotrexate (MTX) in Japanese patients with moderately to severely active rheumatoid arthritis (RA) who were inadequate responders to MTX. Methods: Patients received subcutaneous sarilumab 150 mg q2w + MTX (S150), 200 mg q2w + MTX (S200), or placebo + MTX (P). Primary efficacy endpoint was ACR20 at 24 weeks. Result: Mean age of 243 RA patients (81/S150; 80/S200; 82/P) was 54.9 years. Ratio of women was 77.8% and mean disease duration was 7.84 years. Mean DAS28-CRP at baseline was 5.6/S150, 5.4/S200, and 5.2/P. At Week 24, ACR20 was achieved by 67.9% and 57.5% of patients treated with S150 and S200, respectively, compared with 14.8% treated with P ($p<0.0001$ for both comparisons). ACR50 ($p<0.0001$) and ACR70 ($p<0.05$) at 24 weeks were also improved significantly compared to P. Improvement in HAQ-DI at 16 weeks was significantly larger in both S150 and S200 than in P ($p<0.0001$). Sarilumab was generally well-tolerated in each group. Conclusion:The efficacy and tolerability of sarilumab added to MTX was demonstrated in RA patients who were inadequate responders to MTX. (NCT02293902)

W13-3

Safety of Sarilumab, a novel human anti–IL-6 receptor monoclonal antibody: Safety outcome at 24 weeks in placebo-controlled double-blind study for Japanese Rheumatoid Arthritis patients (KAKEHASI study)

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Conflict of interest: Yes

Object: To assess sarilumab, a human mAb blocking IL-6Rα, added to methotrexate (MTX) in Japanese patients with moderately to severely active rheumatoid arthritis (RA) who are inadequate responders to MTX. Methods: Patients were randomized to subcutaneous sarilumab 150 mg q2w + MTX (S150), 200 mg q2w + MTX (S200), or placebo + MTX (P). Result: Of the 243 RA patients (81/S150; 80/S200; 82/P) 21.8% were age ≥ 65 years. Patient characteristics at baseline are similar among groups. Over 85% of patients completed study treatment up to Week 24. AE were the most frequent reason for permanent treatment discontinuation [6 (7.4%) in S150, 8 (10.0%) in S200 and 5 (6.1%) in placebo]. The number of patients with serious adverse events was similar in S150 (n = 4), S200 (n = 4), and P (n = 6). No deaths occurred. Neutropenia was reported for 7 patients in S150, 9 patients in S200, and no patients in P. Of 4 patients with serious infections, 3 (2 in S150, 1 in P) had ANC prior to onset ≥ LLN (ANC was 1.74 Giga/L, 2.8 Giga/L, 4.34 Giga/L in S150, and 3.03 Giga/L in P, respectively). Conclusion:Sarilumab added to MTX in Japanese RA patients was clinically tolerated during 24 weeks and associated with laboratory changes consistent with IL-6 signaling blockade. (NCT02293902)

W13-4

Efficacy and safety of abatacept in elderly rheumatoid arthritis patients

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Conflict of interest: Yes

[Objectives] Abatacept has been considered to be relatively safe based on the results of the PMS data. Sometimes, abatacept is quite easily used in the elderly patients. We studied the efficacy and safety of abatacept in the Japanese elderly patients in this study. [Methods] Participants were consecutive 508 RA patients treated with abatacept who were registered in the TBC Registry system. We compared DAS28-CRP score, EULAR response rate, and 4-year discontinuation rate due to adverse events (AEs) between three groups: Elderly (>72 years), meddle (62-72 years), and young (<62 years). [Results] DAS28 score and EULAR response rate were comparable between groups throughout 52 weeks. Discontinuation rate due to AEs were different between groups:(15.9, 9.9, and 3.4%, respectively). However, there was no significant difference between groups within the patients using concomitant methotrexate. [Conclusion] We found relatively low discontinuation rate due to AEs even in the elderly group. Interestingly, the elderly group demonstrated the comparable rate with young group within the patients using methotrexate concomitantly with abatacept. We have to pay great attention to the adverse events when we use abatacept in the elderly patients without using methotrexate.

W13-5

Effectiveness of interferon-free antiviral therapy for chronic hepatitis C virus infection in patients with autoimmune diseases

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Conflict of interest: None

[Background] Hepatitis C virus (HCV) infection in patients with autoimmune diseases cause clinical problems, such as chronic stimuli to the immune system induced by HCV itself, exacerbation of autoimmunity by interferon (IFN) therapy, and limitation of immunosuppressant. Recently, several interferon-free direct acting antivirals (DAAs) for HCV have been approved. [Objectives] To evaluate effectiveness of DAAs for HCV in patients with autoimmune diseases. [Methods] We analyzed retrospectively 13 consecutive patients (7 RA, 2 SLE, 1 APS, 2 dermatomyositis, 1 EGPA) treated with DAAs for HCV from July 2014 to October 2016. [Results] All 13 patients showed undetectable HCV RNA soon after starting the DAAs. In 7 RA patients, 5 had no change in RA treatment, and 2 were started methotrexate after elimination of HCV. The mean ΔSDAI (0-24w) was -3.1 in the former, and -16.4 in the latter. In the other cases, improvement of complement and disappearance of autoantibodies were observed after DAAs therapy. No adverse events during therapy were noted, however 1 case of liver cancer, 1 case of zoster and 2 cases of tuberculosis occurred after completion of DAAs. [Conclusion] We report the safety and effectiveness of DAAs for HCV in patients with autoimmune diseases based on literature review.

W13-6

Herpes Zoster (HZ) in Patients (pts) Including Japanese (JP) with Moderate to Severe Active Rheumatoid Arthritis (RA) Treated with Baricitinib (Bari), an Oral JAK 1/JAK 2 Inhibitor

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Conflict of interest: Yes

Objectives: To evaluate HZ in pts with moderate to severe active RA including JP treated with Bari. **Methods:** Incidence rate (IR) per 100 pt-years of HZ was calculated using data in RA pts receiving Bari, placebo (PBO) or active comparators, and pooled from completed phase 1 to 3 studies and an ongoing long-term extension study of Bari. **Results:** HZ was reported in 170 of 3492 pts (514 JP) exposed to Bari (IR=3.3) as of Jan 2016. In the controlled periods, HZ rate for Bari 4 mg was higher than PBO (IR: 4.4 for Bari 4 mg, 1.0 for PBO), but comparable to adalimumab (ADA) in RA-BEAM (IR: 3.3 for Bari 4 mg, 2.8 for ADA, 1.0 for PBO). Most HZ were mild or moderate for Bari; few were disseminated or complicated (no visceral events). HZ rate for Bari appeared higher in pts with advancing age, but not with longer RA duration or corticosteroid use, and did not increase with prolonged exposure to Bari. In JP, HZ rate for Bari appeared higher than overall pts (43 pts, IR=6.5). **Conclusion:** In pts with RA, Bari was associated with an increased risk of HZ compared to PBO. HZ rate did not increase with prolonged exposure. HZ rate for Bari appeared higher in JP. Due to a small number of JP with HZ, further evaluation of predisposing factors is needed.

W14-1

The correlation between achievement of physical activity amount goal and characteristics in patients with rheumatoid arthritis

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Conflict of interest: None

Objectives: We aimed to identify the relationship between achievement of a physical activity goal and the characteristics of patients with rheumatoid arthritis (RA). **Methods:** Overall, 137 patients with RA who performed physical activity were enrolled. Statistical analysis was performed to examine correlations between patient characteristics and their achievement of physical activity goals by Spearman's rank correlation analysis and by the receiver operating characteristic method. **Results:** Characteristics that were highly correlated with achievement of physical activity goals were the Health Assessment Questionnaire Disability Index (HAQ-DI) (correlation coefficient −0.503, $p < 0.001$), global visual analog scale (VAS) (correlation coefficient −0.459, $p < 0.001$), and disease activity score in 28 joints (DAS28-CRP) (correlation coefficient −0.451, $p < 0.001$). The cutoff values for achievement of a physical activity goal were 0.30 for HAQ-DI (sens 50.0%, speci 89.8%), 28.0 for global VAS (sens 62.8%, speci 79.7%), and 1.79 for DAS28-CRP (sens 73.1%, speci 69.5%). **Conclusions**: We aim to preserve activities of daily living for patients with RA. To achieve physical activity goals in these patients, the values of HAQ-DI, global VAS, and DAS28-CRP should be kept very low.

W14-2

Comprehensive assessment for the deformities in rheumatoid hand using cluster analysis

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Conflict of interest: None

[Objective] The fingers are affected in more than 90% in rheumatoid hand. Whereas assessment for finger deformity and functional disorder of a patient is important, comprehensive assessment as a hand unit is difficult because the deformity of each finger is related complicatedly. The purpose of this study is to establish a comprehensive rating system by the presence and degree of deformity. [Methods] We started observational cohort in 2004 and followed-up in every five years. We put the subjects at each evaluation point together then analyzed 156 cases 297 hands. The subjects were divided into groups using cluster analysis and the finger function of each group was compared. The finger function was evaluated using three methods; one is for mobility and others are for ADL of upper limb. [Results] The nonhierarchical cluster analysis using the K-means method was performed, and we classified the subjects into 7 clusters. Finger mobility was kept in the 1st and the 2nd cluster, but score turned worse in the clusters except it that deformity was mixed. In ADL evaluation, the 5th cluster which had highly damaged thumb was the worst. [Conclusion] From the results of the cluster analysis, hand function got worse in cases with highly damaged thumb deformity or combined deformities.

W14-3

Prognosis prediction with joint index vector: A multicenter observational study based on the *NinJa* (National database of rheumatic diseases by IR-Net in JAPAN)

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Conflict of interest: None

Background: Joint index (JI) vector, Vji (x, y, z) was calculated as $x=JI_{UL}+JI_{US}$, $y=JI_{LL}+JI_{LS}$, and $z=JI_{UL}+JI_{LL}-JI_{US}-JI_{LS}$, where JI of upper/large (UL), upper/small (US), lower/large (LL), and lower/small (LS) was determined previously[1]. **Aim:** To examine the clinical features of subgroup of RA patients classified by Vji and to predict the next-year group. **Methods:** Patients were classified by $|V|=\sqrt{(x^2+y^2)}$ and z (G1:$|V|\leqq 0.1$, G2:$|V|>0.1$ & $|z|\leqq 0.2$, G3:$|V|>0.1$ & $z<-0.2$, G4:$|V|>0.1$ & $z>0.2$). A transformation matrix was generated from mean vectors of G2, G3, G4, which were derived from 10,206 data with serial registration in 2013 and 2014 *Ninja*. Serial registered 10,760 data in 2014 and 2015 were used for validation. **Results:** Patients in G4 had the highest HAQ-DI. About a half of patients were predicted correctly, and 87.6% patients hit whether they went G4 or not. G4-hit patients had shorter disease duration, lower RF levels, higher frequency of MTX use, and lower disease activity. Rate of G4 prediction elevated to 90% using a transformation matrix under the adjustment of RF, disease duration, and MTX use. **Conclusion:** Prediction using joint index vector hit around 90% of patients who went into the high HAQ-DI group. **Reference:** 1. Nishiyama S, et al. Rheumatol Int. 2012:32;2569-71

W14-4

An analysis of predictive factors for response to biological DMARDs (bDMARDs) in patients with rheumatoid arthritis

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Conflict of interest: None

【Objective】The effects of genetic, serological, and environmental (e.g. periodontitis) factors have been suggested on rheumatoid arthritis (RA). We determined whether these factors may predict response to bDMARDs therapy.【Methods】We evaluated rheumatologic and periodontal parameters, and serum levels of CRP, RF, anti-CCP antibodies in 54 patients with RA who received medication with inhibitors of TNF and IL-6 receptor at baseline, and 3 and 6 months later. Serum levels of peptidylarginine deiminase 4 (PAD4), *Porphyromonas gingivalis* PAD (PPAD) titer, and frequencies of genotypes of PADI_4, PTPN22, IL-1A, IL-1B, IL-6, TNFA, STAT3 were also determined at baseline.【Results】A significant improvement was observed in all rheumatologic parameters and periodontal inflammation after bDMARD therapy at 3 and 6 months. Twelve patients with EULAR no response showed significantly lower baseline DAS28-CRP, TJC, and SJC, and higher baseline anti-PPAD titer and frequencies of risk genotypes of PADI_4 94 and 104, than 42 patients with the response. A significant association was further obtained between baseline anti-PPAD titer and EULAR response at 6 months.【Conclusions】These results suggest a causative effect of baseline anti-PPAD titer on bDMARDs response in patients with RA.

W14-5

The factors associated with remission induction for patients with rheumatoid arthritis

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Conflict of interest: None

【Objective】The aim of this study was to assess the factors associated with remission in Japanese patients with rheumatoid arthritis (RA).【Methods】A total of 305 patients with RA were enrolled in this study. All the patients met 1987 ACR and/or 2010 ACR/EULAR classification criteria, and visited our center between May 2014 and March 2015. Their medical records were reviewed for tender, swollen, painful and stiff joint counts, physician's global assessment (MDGA), patient's global assessment (PtGA), patient's pain visual analog scale (Pain VAS), HAQ-DI, treatments, and laboratory data.【Results】The remission rates by SDAI were 49.5%. The patients achieving SDAI remission were younger, less positive for rheumatoid factor and less treated with biological DMARDs. SDAI remission was significantly less achieved in elderly (age ≥65, n=201) patients than non-elderly (age <65, n=104) patients (44.8% versus 58.7%, P=0.022). Subjective joint counts and CRP was not significantly different, but PtGA was significantly worse in elderly patients than non-elderly patients (23.5 versus 15.4).【Conclusion】The composite measure of RA disease activity and remission criteria should be prudently applied in daily clinical practice for elderly patients.

W14-6

Validation of index of activity speed (Time Up and Go test) for outcome measure of patients with long-standing rheumatoid arthritis: multicenter prospective cohort study for evaluation of joint surgery on physical function

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Conflict of interest: None

Objectives: The purpose of this study is to validate index of activity speed [Time Up and Go (TUG)] in long-standing RA using multicenter prospective cohort to set treatment goal for joint surgery and rehabilitation. **Methods:** We started the prospective cohort study for RA patients who were performed elective joint surgery. In this study, we collected baseline (preoperation) data as follows; age, sex, disease duration, drug therapies, and disease activity, functional evaluations [TUG, HAQ-DI, joint ROM], and patient-reported outcome [EQ-5D (QOL) and BDI-II (depression)]. Correlation between TUG and other variables were determined. cut-off values of TUG for HAQ remission were determined using ROC curve. **Results:** 435 surgical patients were registered. Mean values for age, disease duration, and sex were 64.2 years, 17.1 years, and 89% female, respectively. We confirmed the significant correlation ($r>0.3$) between TUG and Age, HAQ-DI, EQ-5D and range of motion (hip, knee, shoulder). Cut-off value of TUG for HAQ remission (<0.5) was 8.6 seconds (sensitivity 64%, specificity 65%). **Conclusions:** The cut-off values of TUG (~9 seconds) should be important for assessment of disability in patients with long-standing RA and could provide target of surgical procedure and rehabilitation program.

W15-1

The efficacy and safety of rituximab in patient with ANCA associated vasculitis

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Conflict of interest: None

[Object] Purpose is to reveal the efficacy and safety of rituximab (RTX) in patients with ANCA associated vasculitis (AAV). [Methods] We investigated the medical records of 148 AAV patients had visited our hospital from June 2005 until October 2016. [Results] Fifteen (6 MPA and 9 GPA) were treated with RTX. Seven were treated as the first remis-

sion induction, 5 as the re-induction, and 3 as the maintenance. Observation period was 25 months (median; range 2-155). BVAS score was 12.1. Fourteen cases achieved remission (BVAS:0). The mean PSL dose was 27.6 (mg/day) at baseline (=start of RTX), then 11.5 at 3 months and 7.3 at 6 months. The adverse events were as follows, (first induction): PCP 1 (dead), CMV 1, *Mycobacterium avium* 1 and malignancy 1, (re-induction and maintenance): CMV 1, HBV reactivation 1, and upper respiratory tract infection 3. The risk factor of the whole infection was PSL dose at baseline (P=0.0439) and that of severe infection was RPGN (P=0.0067). As glucocorticoid-related complications, 7 hypertension, 6 diabetes, and 10 hyperlipidemia were newly diagnosed or worsened. [Conclusions] RTX was effective for AAV, but infection rate was higher as compared to the result of RemiT-JAV cohort. Infection rates between the first induction and the re-induction were similar.

W15-2

Low-dose Rituximab as induction therapy for Japanese patients with ANCA-associated vasculitis

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Conflict of interest: None

[Objectives] Four times of once-weekly doses of 375 mg/m^2 rituximab (RTX) are frequently used in remission induction therapy for ANCA-associated vasculitis (AAV). Here, we investigated the efficacy and safety issue of low dose RTX for Japanese patients with AAV. [Methods] We retrospectively examined AAV patients who met the 2012 Chapel Hill classification from 2006 to 2016. We divided them into 2 groups, those treated with high-dose (HD) and low-dose (LD) RTX. HD RTX was the original regimen and LD RTX consisted of twice of one-weekly dose of 375 mg/m^2. We evaluated cumulative complete remission (CR) rate and relapse rate for 1.5 years. CR was defined as BVAS=0 and relapse was defined as BVAS≧1. [Results] We evaluated 17 patients with HD and 8 patients with LD RTX. Higher percentage of elderly patients was observed in LD group ($p<0.01$). No significant difference was found in cumulative remission rate ($p=0.8$), relapse rate ($p=0.6$), B cells counts and serious adverse events. We found patients with nasal involvement and pulmonary nodule/cavity formation had higher relapse rate in LD group than those with HD group ($p=0.05$, and $p=0.09$ respectively). [Conclusions] LD regimen of RTX, especially in elderly patients, might be effective in remission induction therapy in AAV.

W15-3

Case reports of ANCA-associated vasculitis with Rituximab

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Conflict of interest: None

OBJECTIVES: We performed case study to validate the efficacy and safety of Rituximab (RTX) therapy for ANCA-associated vasculitis (AAV) in our hospital. METHODS: We selected 5 AAV patients treated with RTX (treatment protocol: 375 mg/m^2 once a week, 4 times, iv) who admitted to our hospital for treatment between 2014 and 2016, then analyzed their clinical record. RESULTS: Of the 5 AAV patients (3 females), 4 were new-onset and 1 was recurrent, 4 diagnosed as MPA and 1 as GPA. Serum levels of MPO- and PR3- ANCA were 252-1460 U/mL and 3.0->350 U/mL and, BVAS was 3-27. PSL was used in all patients. After RXT therapy, serum levels of MPO- and PR3-ANCA reduced by 20.0-84.8% and 33.3-100%. BVAS reduced by 33.4-100%. Exacerbation of proteinurea and multiple-mononeuropathy was shown in each patient. Adverse events included 3 CMV infection, 1 hypotension, and 1 pancytopenia. Treatment protocol was completed in 3 patients, but not in 2 patients (hypotension and CMV infection). CONCLUSION: In this study, although improvement of ANCA value was confirmed in all cases, examples in which some exacerbations of clinical symptoms were confirmed were also confirmed. Also, as an adverse event, many infections, particularly CMV infections, were found.

W15-4

The efficacy of rituximab on refractory or recurrent otitis media with ANCA-associated vasculitis in our hospital

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Conflict of interest: None

【Objectives】To evaluate the efficacy of Rituximab (RTX) in patients with refractory or recurrent otitis media with ANCA-associated vasculitis (OMAAV) in our hospital.【Methods】Of the 23 OMAAV patients, six patients were administrated with RTX.【Results】We recruited 5 refractory and 1 recurrent OMAAV cases (3 males and 3 females). The average age was 72-years old. They were consisted of 4 MPA probable, 1 GPA probable and 1 GPA. Both hypertrophic pachymeningitis and facial palsy were observed in 4 cases. Otitis media was involved in bilateral ears in 5 cases. All patients were treated with methlyprednisolone pulse therapy and intravenous cyclophosphamide, following with corticosteroid (mean prednisolone 0.76mg/kg/day) and azathioprine. RTX was used from 2 to 4 times. 4 patients with twice RTX administration achieved complete remission. At month 10 after the therapy, one patient had a relapse and re-complete remission with additional RTX. Of 2 patients treated with 4 times RTX administration, one achieved complete remission, and the other patient died due to the progressed disease and infection.【Conclusion】RTX could be effective for the remission induction in the refractory or recurrent OMAAV cases. Further study on strategy for safety and efficacy is needed.

W15-5

Diffuse Alveolar hemorrhage is a new poor prognostic factor

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Conflict of interest: None

[Objective] AAV with DAH has been recognised as a severe state, but this condition has not been defined as a poor prognostic factor. [Methods] We retrospectively analysed the clinical features of 179 patients with AAV who were treated at our hospital From January, 2005 to June, 2016. [Results] The study included 136 patients with MPA and 43 patients with GPA. The mean age at onset of MPA and GPA was 70.6±14.2 and 62.5±17.0 years old, respectively. Observation period was 5.4±5.0 years. Renal involvement was found in 111 cases (MPA 93, GPA 18), and DAH was in 20 cases (MPA 17, GPA 3). All patients with DAH experienced renal involvement. Among the poor prognostic factors of FFS 2009, older age was the most common factor (70%), followed by renal insufficiency (41%), CNS involvement (4%), and GI signs (2%). Forty eight patients (41 patients with MPA and 7 with GPA) were died during the observation period. Among the 48 deaths, 27 patients were died within the first year of diagnosis. The major causes of death within the first year of diagnosis were infection (59.3%), and uncontrolled vasculitis (33.3%). Survival rate was significantly lower in patients with DAH than in those without DAH at 1, 3, and 12 months post diagnosis ($p<0.001$). [Conclusion] DAH in AAV was a poor prognostic factor.

W15-6

Clinical study of granulomatosis with polyangiitis with respiratory tract involvement

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Conflict of interest: None

[Objective] To evaluate the clinical characteristics of granulomatosis with polyangiitis (GPA) with respiratory tract involvement in Japan. [Methods] This study comprised 7 cases of GPA with respiratory tract involvement, who were admitted to the department of rheumatology in our hospitals and have had induction treatment from September 2006 to July 2016. Clinical characteristics, HRCT findings, treatments and prognosis were retrospectively assessed. Lung fields were devided into 3 sections: upper, middle, lower, by 2 levels (carina tracheae and 2 cm head side from diaphragm). [Results] Six GPA patients were female, and the mean age was 66.7 years old. The median BVAS was 21, and 3 patients were positive for MPO-ANCA, 4 for PR3-ANCA. Nodule or mass were the most frequent lung leision. All patients had lung leision in upper section, 6 in middle, 3 in lower. All patients were treated immunosuppressant: 6 by AZP, one by MTX, 6 by IVCY, one by RTX. All cases got remission, but three cases relapsed. [Conclution] It is suggested that the lung involvement of GPA in Japan is majorly nodule and mass, and is not many in lower section.

W16-1

Behçet's disease could be categorized with clinical symptoms

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Conflict of interest: None

[Object] Patients with Behçet's disease (BD) presents heterogeneous clinical symptoms, with different disease outcomes. We here performed subgrouping analysis in an attempt to predict treatment and prognosis of the BD. [Methods] We performed the principal component analysis (PCA) of 625 BD most of them fulfilling the Japanese Ministry of Health, Labor and Welfare criteria (360 males and 265 females) in 7 hospitals. We analyzed patient's background and clinical symptom (including special type of BD) as variables. [Results] PCA extracted 2 major components; Group A (male patients having ocular and neurological lesions) and Group B (patients having vascular and intestinal lesions). The 2 groups were compared with Group C (No ocular and serious organ involvement). Frequency of HLA-B51 were 52.4% in Group A, 22.2% in Group B and 34.9% in Group C. TNF inhibitors were given to 19.2%, 23.0% and 0% of Group A, B, and C, respectively. [Conclusions] Our data suggested BD patients could be subcategorized into several distinct clinical subgroups including 2 groups as shown here. The subgrouping may be helpful for establishment of precision medicine.

W16-2

The efficacy and the safety of anti-TNF agents in Behçet's disease patients

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Conflict of interest: None

<OBJECTIVE>To evaluate the clinical features of the patients with Behçet's disease (BD) treated with anti-TNF agents. <METHODS>We retrospectively evaluated 1)clinical characteristics, 2)efficacy, 3)persistence, and 4)safety of anti-TNF therapy (infliximab;IFX, adalimumab;ADA) in BD patients in University of Tsukuba hospital. <RESULTS>1)All of the 9 ocular BD (OBD) patients were treated with IFX. In intestinal BD (IBD) patients, four received IFX, and three received ADA as first line therapy. 2)Improvement of uveitis was recorded in 8 of the 9 OBD patients. In IBD, clinical improvement was shown in 1 of the 4 patients in IFX, and in all 3 patients in ADA. Two IBD patients were refractory to first line therapy (IFX 1, ADA 1) and switched for second line agents, however, they did not respond. 3)IFX was continued in 7 of the 9 OBD patients. In IBD, anti-TNF therapy was continued in 2 of the 5 patients in IFX and 2 of the 4 patients in ADA. The mean duration of therapy were 4.5±3.0 years in OBD, 16±25 months and 16±7 months in IBD in IFX and ADA, respectively. 4)Severe complications were 2 infections in OBD, and 2 infections, 1 intestinal perforation and 1 intestinal obstruction in IBD. <CONCLUSION>IFX was efficient in OBD, while anti-TNF therapy was less effective in IBD.

W16-3

Revision of Guidelines for the Management of Neuro-Behçet Disease

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Conflict of interest: None

[Objective] With the goal of revision of the first edition, we are currently reviewing the previous guidelines and literature on NBD to prepare new clinical questions (CQs) and a flow chart of diagnosis and treatment of NBD. [Methods] CQs on NBD were extracted, and draft CQs and a flow chart were prepared. Then, corrections were made based on opinions of an expert panel of 7 rheumatologists and 4 neurologists (one specialized in both fields). The rate of agreement on CQs was then determined by voting. [Results] The grade of each recommendation was established based on the evidence level and opinions of the experts. After this, items with an agreement rate of 4 or higher in a 5-step grading system were retained as CQs. The CQs on NBD comprised one general question, 7 questions on acute NBD, and 5 questions on chronic progressive NBD. A new flow chart was prepared based on the revised guidelines and CQs. [Conclusion] The revised edition of the Japanese 'Guidelines for the Management of Neuro- Behçet Disease' prepared in this study are mainly based on expert opinions and the results of open and observational studies. Guidelines that can be used for international studies are needed, for which verification by multiple institutions in Japan and other countries would be desirable.

W16-4

Anticoagulant therapy is not prohibited for deep vein thrombosis in patients with Behcet's disease

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Conflict of interest: None

【Objects】Anticoagulant therapy is not recommended for deep vein thrombosis (DVT) in patients with Behcet's disease (BD) in accordance with 2008 EULAR recommendations because of no evidence of the efficacy and risk of pulmonary hemorrhage. The present study investigated usage of anticoagulants for BD with DVT in the real world.【Methods】Usage of anticoagulants for DVT was analyzed in 105 vasculo-BD patients at 5 institutes of Japan and reports from foreign countries.【Results】Warfarin, aspirin and other antiplatelets were given to 70%, 57%, and 17% of 69 BD patients with DVT. Mild bleeding complications were found in 4 patients (6%). Warfarin was used more than 80% in reports from UK, French, and China except one paper from Turkey (6%). No reports referred to serious bleeding as a complication.【Discussions】Although there is no evidence of clinical efficacy of anticoagulant therapy for BD with DVT, the present study as well as previous reports from several countries showed that warfarin was frequently used as standard therapy in the real world. Nonetheless, serious bleeding complication such as pulmonary hemorrhage was not documented.【Conclusion】Anticoagulant therapy is not generally prohibited for BD with DVP.

W16-5

Emergency hospitalisation of Behcet disease patients

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Conflict of interest: None

Objectives: Behcet disease (BD) has a relatively good prognosis. However, the cause for emergency hospitalization of BD patients is unknown. Therefore we studied the clinical conditions for emergency hospitalisation in BD patients. Methods: Between 2005 and 2016, 205 patients meeting BD's diagnostic criteria of 1980 were came in our hospital. Investigation of the conditions causing hospitalisation was performed by their clinical records or by phone. In emergency hospitalization, the patients who did not require emergency treatment were excluded from this investigation. Results: Of the 205 BD patients analysed in this study, 29 (14%) were brought to hospital by ambulance and underwent emergency treatment. Eleven of 29 patients were hospitalized due to neural, intestinal or vascular lesion of BD. Eleven cases were diagnosed with intestinal type, 7 cases with neural type, and 2 cases with vascular type (one duplication). No significant difference in the clinical examinations was found between before and after hospitalisation. Eighteen cases was hospitalized several times during this period. Conclusion: In the emergency hospitalisation of BD patients, the frequency of neural, intestinal or vascular lesion is high.

W16-6

Analysis of the pathophysiology of Neuro-Behçet's disease related with cyclosporine-A

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Conflict of interest: None

[Object] Behçet's disease (BD) is a rare immune-mediated inflammatory disease. Previous studies showed that cyclosporine-A (CyA) was effective for the ocular complication of BD. Other studies demonstrated that CyA had been linked with higher risk of Neuro-Behçet's disease (NBD) development. The current study was undertaken to clarify the complicated pathophysiology of NBD. [Methods] Peripheral blood mononuclear cells (PBMCs) were obtained from 2 healthy adult volunteers. HLA-B51 was positive in one volunteer, and HLA-A26 was positive in the other. PBMCs were cultured with or without CyA (100 ng/ml). After 2 hours, IgG purified from different RA patients or BD patients was added to the culture medium. After additional 48 hours of incubation, the supernatants were assayed for IL-6. Data are expressed as the ratio of IL-6 levels of supernatants with CyA to those without CyA. [Results] In 2 different experiments, the ratio of IL-6 with BD-IgG was significantly higher than that with RA-IgG (0.928±0.009 vs 1.729±0.329, p=0.0396, 0.836±0.044 vs 1.088±0.078, p=0.0139). [Conclusion] These results indicate that the IgG from BD patients plays a pivotal role in the pathogenesis of NBD.

W17-1

The clinical features of 223 Behcet's disease (BD) patients

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Conflict of interest: None

Objectives We evaluate the clinical features of BD in Japan. Methods We extracted 223 patients (108 males and 115 females) who fulfilled BD criteria of Ministry of Health, Labour and Welfare in Japan from January, 2006 until May, 2015. We examined sex, onset age, disease type, clinical symptoms, laboratory data and medications. Results The onset age was 36.0±12.8 years old. Gastrointestinal manifestations (25%), neurogenic diseases (9%), and vascular involvements (8%) were found in BD. HLA-B51 and A26 was positive in 41% and 24%, respectively. The frequency of acneiform lesions, ocular involvements and HLA-B51 was significantly higher in male, while erythema nodosum, genital ulceration and arthritis were significantly lower. Patients with ocular involvements showed a higher assosiation rate with neurogenic diseases and HLA-B51, and lower wih gastrointestinal manifestations. Biologics were used for 66 cases (30%), and it could be continued for 1 year in 91%, and for 2 years in 83%. Conclusion A higher incidence of gastrointestinal manifestations was observed in patients with BD. Patients with ocular involvements showed a higher assosiation rate with neurogenic diseases, and lower wih gastrointestinal manifestation. Most patients could continue biologics safty and effectively.

W17-2

A case of pregnancy and delivery after achievement of remission by infliximab therapy in young women with vascular Behcet's disease

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Conflict of interest: None

A twenty-seven year old woman visited a general hospital complaining cough, hemoptysis, chest pain, and exertional dyspnea. By that time, she had been suspected to have Behcet's disease (BD) because of thrombophlebitis and multiple stomatitis. Blood test showed the inflammation and the computed tomography revealed the left pulmonary arterial aneurysm. She was referred to our hospital and diagnosed as having vascular BD by the presence of recurrent oral aphthous ulcers, thrombophlebitis, folliculitis-like rashes, pudendal ulcer and the vascular lesion, based on the diagnostic criteria. Although the case was considered as an indication of the strong immunosuppressive therapy, the patients refused the use of corticosteroids and cyclophosphamide. In these regards, infliximab therapy (5mg/kg) was initiated. After the first administration of infliximab, the respiratory and mucocutaneous symptoms resolved completely. The diameter of the left pulmonary arterial aneurysm reduced (22 to 15 mm) at 14 weeks after the initiation of the therapy. She became pregnant twenty months later after the diagnosis. Continuing infliximab therapy, she gave birth safely by Caesarean section. The importance of the novel therapy for this very rare case will be discussed.

W17-3

Multidisciplinary therapy for intestinal Behcet's disease with MDS: A case report

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Conflict of interest: None

A 46 year-old woman presented with right lower abdominal pain. She was diagnosed as myelodysplastic syndrome (MDS) 16 years ago. Two years later, she was diagnosed as Behcet's disease according to recurrent oral and genital ulcerations and cutaneous lesions. Six years later, she was diagnosed as intestinal Behcet's disease with right lower abdominal pain and erosion at the terminal ileum. Treatment with prednisolone (PSL) and tacrolimus was started. Although these medications were used, her abdominal pain could not be controlled. Colonoscopic examination revealed deep punched-out ulcer. Treatment with Infliximab (IFX) at a dose of 5mg/kg was initiated, and improvement of abdominal symptoms was temporarily observed. The third dose of administration of IFX, the patients developed right lower abdominal pain. Although she was switched to adalimumab, her symptoms continued to worsen. She was treated with PSL, IFX at a dose of 10mg/kg in addition to sulfasalazine, methotrexate and antibiotics therapies. Abdominal symptoms subsided, and there was a striking improvement in her CRP levels. Here we report a case of intestinal Behcet's disease with MDS needed multidisciplinary therapy.

W17-4

Efficacy of Adalimumab (ADA) for interstitial pneumonia (IP) complicated with intestinal and vascular type Behçet's disease (BD)

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Conflict of interest: None

Case: 48-year-old female She had oral and vulvar ulcer and was diagnosed with BD at 26 y/o. Predonisolone 5 mg was started. At 29 y/o external jugular vein obstruction and IP was developed. Cyclosporine 150 mg was started. At 48 y/o, she was hospitalized due to exertional dyspnea and hematochezia. Lab data showed CRP 5.29mg/dl, ESR 102mm/h, LDH 302U/l, KL-6 2101U/ml, and HRCT showed traction bronchiectasis and GGO in both lungs indicating exacerbation of IP. BALF cell count was 1462/ml (neutrophil 75%) and bacterial culture was negative. Histopathology showed neutrophilic and histiocytic colonization in alveoli, and the fibrous and thickened alveolar septum infiltrated with neutrophils without a bacterial phagocytosis indicating neutrophilic inflammation of BD. As multiple ulcers were detected in terminal ileum, ADA was started. Hematochezia was relieved, and the chest X-ray also showed improvement. Discussion: Neutrophil activation plays a major role in pathophysiology of BD, and TNF-α is one of the neutrophil activating factors. The abacterial neutrophilic inflammation in both pulmonary parenchyma and interstitium suggested that BD associated with the etiology of IP. The improvement of chest image after ADA administration suggested control of neutrophil had an efficacy for IP.

W17-5

A case of relapsing polychondritis complicated with vasculo-Behçet's disease

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Conflict of interest: None

We report a 51-year-old female of relapsing polychondritis (RP) who developed vasculo-Behçet's disease (BD). She was admitted to our hospital with dyspnea, cough and arthralgia in February 20XX-3. Chest CT revealed tracheal narrowing and peritracheal inflammatory changes. Arthritis, bilateral scleritis and left conjunctivitis were also detected, and she was diagnosed with RP. She was successfully treated with corticosteroids. In June 20XX, she was admitted again because of pulmonary actinomycosis. This lesion tended to improve with antibiotics, but high fever persisted. She also presented with erythema nodosum, thrombophlebitis and retinochoroiditis. Pathergy test was positive and the genotype testing was also positive for HLA-B51. FDG-PET/CT showed high FDG uptake in left femoral vein. After 2 weeks, contrast enhanced CT revealed a deep vein thrombus there, and she was diagnosed with vasculo-BD. Since treatment with infliximab, colchicine and anticoagulant under treatment with PSL 17.5mg/day did not respond sufficiently, we increased PSL to 30mg and added MTX. She has been in remission since then. A case of RP complicated with vasculo-BD is a rare condition; however, clinicians should be aware of this.

W17-6

A case of Behcet's disease with coronary artery aneurism developed fifteen-years after the abdominal aortic aneurysm

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Conflict of interest: None

59 years-old man diagnosed of Behcet's disease at 20 years old, was referred to our hospital because of chest pain for two days. He had history of operations for intestinal perforation followed by panperitonitis at 25 years old and for abdominal aortic aneurysm at 45 years old, however, he was not recently noticed the laboratory abnormalities by the medical check. On admission, he revealed normal vital signs, and the laboratory findings revealed negative for ESR, CRP, CK and troponin T, but inferior wall myocardial infarction was diagnosed by electrocardiogram and ultrasonography. The complete obstruction of RCA #4PD was confirmed by the catheterization and PCI was enforced. In addition, saccular aneurysm of LMT and diffuse sclerotic dilatation of three main arterial vessels were observed. CABG was enforced later and HLA-B51 was negative. It is reported that abdominal aortic aneurysm and the coronary artery aneurysm were present in several percent each in Behcet's disease. This case was clinically characterized by development of aneurysms in different time and region though the inflammatory markers seemed negative. The treatment considering the vascular involvement in Behcet's disease should be needed despite systemic inflammatory markers.

W18-1

Possible predicting factors of Barthel index (BI) ADL scores at the end of medical rehabilitation in patients with rheumatoid arthritis

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Conflict of interest: None

[Background] Accumulated evidence points that rehabilitation plays important role in treatment for RA patients. However, the disease activity may affect on the effect. [Methods] From October 2014 to September 2015, 49 consecutive RA patients received rehabilitation in our university hospital. The medical records were reviewed, and statistical analysis was performed to assess possible predicting factors of the Barthel index (BI, ADL score), at the end of rehabilitation. [Results] There were 38 female and 11 male, and the mean age was 69.1 years old. Mean length of rehabilitation in the hospital was 37.9 days. Tender joint count (TJC) showed statistically significant negative correlation with the BI ($P<0.05$), while the Visual Analogue Scale (VAS) for pain had a positive tendency. Previ-

ous steroid treatments correlated to the fragility fractures (P<0.05), but not to the BI. [Conclusions] Among several factors on the disease activity, TJC and VAS may affect the BI ADL scores.

W18-2

Does hindfoot arthrodesis deteriorate walking ability in patients with rheumatoid arthritis? - a cross-sectional study using a large cohort -

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Conflict of interest: Yes

Objective: To evaluate the effects of hindfoot surgeries on walking ability of patients with RA by using a large cohort of RA. Patients and methods: A total of 418 patients were evaluated. The averages of age, duration of disease and disease activity were 62 years old, 12.5 years and 2.83 in DAS-28. The ratios of patients who used oral steroid, MTX and bDMARD were 35%, 66%, and 38%. Among 418 patients, 36.4%, 3.6%, 0.7% and 9.8% of patients underwent any of orthopedic surgery, hindfoot arthrodesis, total ankle arthroplasty, or forefoot surgery, respectively. Walking ability was evaluated by walking speed and others. Results: Patients who underwent any of orthopedic surgery were lower in walking speed, the distance of steps. Patients who received hindfoot surgery were lower in walking speed and the distance of steps. Any differences were not found in those measures between patients who received hindfoot arthrodesis and forefoot surgeries. Conclusions: Orthopaedic surgeries in the lower extremity can prevent the deterioration of walking ability in patients with RA. The hindfoot arthrodesis has similar effects on walking ability compared with forefoot surgeries.

W18-3

Association between changes of subcutaneous deep temperature in knee joint and knee motion after total knee arthroplasty

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Conflict of interest: None

[Object] Inflammation after total knee arthroplasty (TKA) may disturb rehabilitation and knee function recovery. This study was aimed to clarify association between subcutaneous knee temperature, an indicator of inflammation, and knee motion after TKA. **[Methods]** TKA was performed via medial parapatellar approach for 30 knees with osteoarthritis. Each patient received routine rehabilitation without cryotherapy. Pre- and postoperative knee temperatures were measured at the point 6 cm medial to the superior patellar pole and at the depth of 1 cm. Knee motion was assessed at baseline and day 14 after TKA. **[Results]** The temperature in both knees showed no difference at baseline, peaked at day 1 and thereafter decreased with time. The temperature in knees with TKA was still higher at day 14 whereas contralateral knee declined to baseline levels at day 3. We calculated the differences in temperature between baseline and the highest temperature after TKA, and in range of motion between baseline and day 14. A significant inverse correlation was found in the differences between the temperature and each of knee extension, flexion, and total range of motion. **[Conclusions]** A rise in subcutaneous knee temperature could cause adverse effects on knee motion recovery after TKA.

W18-4

The new joint weighted scoring system which predicts the modified health assessment questionnaires scores in rheumatoid arthritis patients: validation studies using the National Database of Rheumatic Diseases by iR-net in Japan in 2009 and 2014

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Conflict of interest: None

[Background] We reported the impact of each joint disease on the MHAQ by using 2011 NinJa (the National Database of Rheumatic Diseases by iR-net in Japan) data. The MHAQ score was significantly affected almost all joints disease tended to aggravate physical ability. We also developed a joint weighted scoring system from the results of the odds ratio. An integer score was assigned to each bilateral and unilateral joint disease, respectively, as follows: shoulder, 4 and 2; elbow, 3 and 2; wrist, 2 and 2; hip, 0 and 3; knee, 3 and 2; ankle, 2 and 2; finger, 1 and 1. We acquired 3 points as the cut-off value of this system through statistical analysis (Mod Rheumatol, 2016). [Objectives] To validate this scoring system by applying to NinJa in 2009 and 2014. [Methods] 7,189 and 13,459 subjects from NinJa in 2009 and 2014 were analyzed. The presence or absence of disease (swelling and/or tenderness) in each joint were investigated. ROC curve analysis was performed to each patient with total score of the scoring system. [Results] DAS28CRP were 2.9 and 2.4. ROC analysis' results were cut-off value, 3 points; AUC, 0.72, 0.68. [Conclusions] This scoring system was validated and suggested to be useful to predict of functional disability of RA patients instead of changing of disease activity.

W18-5

A Preliminary Study on Pain Symptoms, Functional Impairment, and Psychophysiological Problems of Rheumatoid Arthritis Patients Using Biologic Drugs at Home: The Utility of a Close Psychosocial Evaluation

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Conflict of interest: None

[Introduction] Catastrophic thinking, which is believed to affect patients even if they are taking BIO, is a factor leading to pessimism, passive behavior, and depression among patients, which is also said to affect the therapeutic effect of treatments. This study examined and compared the pain symptoms, functional impairment, and psychophysiological problems of RA patients taking biologic drugs, as well as the relationships among these factors. [Methodology] The subjects were 14 female patients with RA (59.71±4.61 years). Items evaluated: Disease activity was measured using SDAI; pain intensity using VAS; and functional impairment using PDAS, HAQ, and Locomo25. Psychophysiological state was evaluated using PCS, HADS, TSK, PSEQ, GSES and EQ-5D. [Results and Discussion] Even among those who were taking BIO, some patients were tormented by catastrophizing, feelings of powerlessness, anxiety, and kinesophobia. Self-efficacy in confronting helplessness and pain was more strongly related to functional impairment than to disease activity or pain intensity. RA patients at home, it is important to adequately consider not only the disease activity and pain with functional impairment and, but it is also necessary to factor in the effects on psychosocial pain such as catastrophizing.

W18-6

A study of correlation between psychological resilience and physical activity in patients with rheumatoid arthritis

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Conflict of interest: Yes

[Objectives] Psychological stress is one of the possible factors to cause or worse rheumatoid arthritis (RA). Meanwhile, psychological resilience is defined as an individual's ability to successfully adapt to life tasks in the face of social disadvantage or highly adverse conditions. In this study, we investigated the correlations between psychological resilience, psychological stress, and physical activity in patients with RA. **[Methods]** A survey with self-completed questionnaires using the Frenchay Activities Index for physical activity, Stress Response Scale-18 (SRS-18) for psychological stress, and Adolescent Resilience Scale (ARS) for psychological resilience was conducted. Patients' stresses and coping techniques were also questioned. **[Results]** Two hundred nine (34 males and 175 female) patients with RA participated this survey. The average scores were as follows; SR-FAI: 28.24, SRS-18: 9.15, and ARS: 3.39. Multiple regression analyses revealed that physical activity and psychological resilience were positively correlated and that psychological stress and psychological resilience were negatively correlated conversely. **[Conclusion]** Psychological resilience is correlated with physical activity in patients with RA and suggested to contribute to reduce psychological stress.

W19-1

Genetic analysis of 27 patients in whom tumor necrosis factor receptor-associated periodic syndrome (TRAPS) was suspected

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Conflict of interest: None

Introduction: Tumor necrosis factor receptor-associated periodic syndrome (TRAPS) is a rare autoinflammatory disease caused by mutations of the *TNFRSF1A*. Methods: We conducted genetic tests on 27 patients in whom TRAPS was suspected; these patients had been referred to our study for genetic diagnosis of TRAPS from May 2013 to October 2016. Results: The V2A and C70G variants were found in 1 patient each. The V2A variant was novel. The father, old brother, and nephew of the patient with the C70G variant had previously been described as having TRAPS with the C70G variant. The patient with C70G variant was only 1 patient who had a family history of TRAPS-like symptoms. When the patient had a family history of TRAPS-like symptom, the sensitivity was 50% and the specificity was 100% for the probability of carrying *TNFRSF1A* variants. When the patient had 2 or more of positive family history of TRAPS-like symptoms, age at disease onset =<20 years and inflammatory attacks lasting >=5 days on average, the sensitivity was 100% and the specificity was 60%. Conclusion: The *TNFRSF1A* variant was identified only in a minority of patients having TRAPS-like symptoms. Functional analysis of variant TNF receptor and accumulation of cases will clarify the pathogenic significance of the V2A variant.

W19-2

The contribution of SAA1 polymorphisms to Familial Mediterranean fever susceptibility in the Japanese population

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Conflict of interest: None

[Background] In view of the inflammatory nature of FMF, we investigated whether serum amyloid A (SAA) gene polymorphisms may affect the susceptibility of Japanese patients with FMF. [Methods] The genotypes of the -13C/T SNP in the 5'-flanking region of the SAA1 gene and the two SNPs within exon 3 of SAA1 (2995C/T and 3010C/T polymorphisms) were determined in 83 Japanese patients with FMF and 200 healthy controls. [Results] The frequencies of SAA1.1 allele were significantly lower (21.7% versus 34.0%), and inversely the frequencies of SAA1.3 allele were higher (48.8% versus 37.5%) in FMF patients compared with healthy subjects. The frequency of -13T alleles, associated with the SAA1.3 allele in the Japanese population, was significantly higher (56.0% versus 41.0%, p=0.001) in FMF patients compared with healthy subjects. [Conclusions] Our data indicate that SAA1 gene polymorphisms, consisting of -13T/C SNP in the 5'-flanking region and SNPs within exon 3 (2995C/T and 3010C/T polymorphisms) of SAA1 gene, are associated with susceptibility to FMF in the Japanese population.

W19-3

Clinical characteristics of 7 cases developing palindromic rheumatism and intermittent hydrathrosis with gene polymorphism associated with autoinflammatory syndromes

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Conflict of interest: None

Objective and methods: Palindromic rheumatism (PR) is characterized by recurrent arthritis or periarthritis without residual joint destruction. Autoinflammatory syndromes are known as differential diagnoses of intermittent hydrathrosis. We evaluated the clinical feature of patients diagnosed as PR with polymorphisms of the genes responsible for auto-inflammatory diseases. **Results:** Seven patients (2 males and 5 females, median age of disease onset 20 years, median disease duration 12 years) were enrolled in the study. All patients manifested intermittent hydrathrosis. RF and Anti-CCP were not detected in all patients and findings of articular X-ray and ultrasonography were normal. Polymorphisms of the genes were identified as following; *MEFV*(n=5, all non-exon10), *CIAS1*(n=1) and *TNFRSF1A*(n=1). Although csDMARDs were not effective in all cases, colchicine applied to 5 with *MEFV* polymorphism was effective in four. TNF inhibitors was effective in one of two. During observation, no patients developed RA and one patients was complicated with Bechet's disease. **Conclusions:** Association of polymorphisms of the genes responsible for auto-inflammatory diseases should be considered in cases manifesting PR, especially hydrathrosis, though systemic manifestations were not noted.

W19-4

The first case of canakinumab administration during pregnancy for cryopyrin associated periodic syndrome

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Conflict of interest: None

Cryopyrin-associated periodic syndrome (CAPS) is a rare autoinflammatory condition caused by overproduction of interleukin-1β(IL-1β), and canakinumab, a human anti-IL 1β monoclonal antibody that selectively blocks IL-1β has been licensed in Japan since 2011 for CAPS. But there is no report of its efficacy and safety during pregnancy. So we report here the clinical course of a Muckle-Wells syndrome (MWS) patient administered canakinumab during pregnancy. The patient was a 32-year-old Japanese woman in her first pregnancy. She was diagnosed as MWS by *NLRP3* mutation (p.H312P) and typical clinical findings, 3 years after

the administration of canakinumab, she became pregnant. We thought clinical control of MWS was necessary for the continuation of pregnancy, canakinumab was continued during the pregnancy. Her symptoms were stable, and she gave birth to a 2,994-g girl by emergency cesarean delivery. Her baby was found to have the same *NLRP3* mutation and baby's follow-up is now continuing. This is the first report of the administration of canakinumab during pregnancy in a patient with CAPS. We also measured the concentration of canakinumab in umbilical cord blood and neonatal blood, and its results indicate the active placental transfer of the drug.

W19-5

Evaluation of a Phase III, randomized multicenter, double-blind, placebo controlled, global clinical trial of canakinumab in Japanese patients with colchicine resistant Familial Mediterranean Fever

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Conflict of interest: None

[Objectives] Phase III global clinical trial assessed the efficacy and safety of canakinumab (CAN), a human anti-interleukin-1β antibody, in patient (pt)s with Hereditary Periodic Fevers (colchicine resistant Familial Mediterranean Fever; crFMF, Hyper IgD Syndrome, and TNF receptor Associated Periodic Syndrome). We report the assessment of Japanese crFMF pts. [Methods] In this double-blind, placebo (PBO) controlled study, patients were assigned CAN150 mg (2mg/kg for pt <40 kg) or PBO, and non-randomized pts were administered CAN150mg/sc q4w. Primary objective is to demonstrate that CAN is superior to PBO with resolution of the index flare at Day15 and no flares over 16 weeks. [Results] One pt with MEFV (Familial Mediterranean Fever gene) mutation in exon10 (M694I) was PBO group and did not achieve primary endpoint, but serological and clinical complete response were observed at week16 by switching to CAN150mg on Day15. Non-randomized pts as open label treatment with non-exon10 (G304R and L110P-E148Q) showed efficacy with CAN150mg. The safety profile of overall data of this trial was similar to known data and that of Japanese pts did not differ greatly from overall data. [Conclusion] Japanese crFMF pts could improve their symptoms with CAN and there were no new safety concerns.

W19-6

Evaluation of a Phase III, randomized, multicenter, double-blind, placebo controlled, global clinical trial of canakinumab in Japanese patients with TNF receptor-associated periodic syndrome

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Conflict of interest: None

[Objectives] Phase III, multicenter, global clinical trial assessed the efficacy and safety of canakinumab (CAN), a human anti-interleukin-1β antibody, in patient (pt)s with Hereditary Periodic Fevers (colchicine resistant Familial Mediterranean Fever, Hyper IgD Syndrome, and TNF receptor Associated Periodic Syndrome; TRAPS). We report the assessment of Japanese TRAPS pts. [Methods] Patients were randomized to receive CAN150mg (2mg/kg for pts< 40 kg) or placebo (PBO), sc q4w. Primary objective is to demonstrate that CAN is superior to placebo with resolution of the index flare at Day 15 and no flares over 16 wks. [Results] Of 6 Japanese pts, 2 were administered CAN and 4 were PBO. One patient with CAN achieved primary endpoint with CAN150mg. The other with CAN did not achieve the primary endpoint, but showed serological and clinical complete response at Wk16 with uptitration to 300mgCAN on Day 8. 4 PBO showed serological and clinical complete responses at Wk 16 by switching to CAN150mg on Day 15. The overall safety profile was similar to known data and that of Japanese pts did not differ greatly from overall data. [Conclusion] These limited data demonstrated efficacy of CAN 150mg or 300mg q4w in JapaneseTRAPS pts and there were no new safety concerns.

W20-1

Comparison of radiographic remission in elderly and younger biologic-naïve rheumatoid arthritis patients with ACPA-positivity after treatment with abatacept

Masahiro Sekiguchi[1,2], Kosaku Murakami[2], Takao Fujii[2], Masayasu Kitano[1,2], Kiyoshi Matsui[1,2], Kenji Miki[2], Akira Yokota[2], Hideo Hashimoto[2], Takanori Kuroiwa[2], Keiji Maeda[2], Aihiro Yamamoto[2], Takashi Fujimoto[2], Toshihiko Hidaka[2], Naoki Shimmyo[2], Ichiro Yoshii[2], Koichiro Ohmura[2], Yutaka Kawahito[2], Norihiro Nishimoto[2], Tsuneyo Mimori[2], Hajime Sano[1,2]
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Conflict of interest: None

[Objective] To compare radiographic remission (REM) in bio-naïve patients with rheumatoid arthritis (RA) in 2 age groups (≥65 years vs <65 years) after treatment with abatacept (ABT). [Methods] We evaluated 81 RA patients positive for anti-citrullinated protein antibodies (ACPA) enrolled in the ABROAD study, who were treated with ABT for 48 weeks, and assessed using the van der Heijde modified Sharp score (TSS). We defined REM as a change in TSS to <0.5 after 1 year. The rate of REM in the 2 groups was examined and compared, and correlated with achievement of clinical remission (simple disease activity index [SDAI] ≤3.3) within 24 weeks after the start of ABT treatment (SDAI-REM) or not. [Results] The proportions of patients with REM were 65.1%(≥65 years) and 52.6%(<65 years). In elderly patients, there was no significant difference in the REM rate between those who achieved SDAI-REM and those who did not (78.6% vs 58.6%, P=0.17). However, for younger patients, the REM rate for those who did not achieve SDAI-REM was significantly lower than for those who did (90.0% vs 39.3%, P<0.01). [Conclusion] In bio-naïve RA patients with ACPA, early regulation of disease activity with ABT may be more important for younger patients compared with elderly patients, as indicated by REM.

W20-2

Abatacept showed the comparable effect on prevention of structural damage compared to anti-tumor necrosis factor inhibitors in the rheumatoid arthritis patients with high titer of anti-cyclic citrullinated peptide antibody

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Conflict of interest: None

【Object】The aim of this study was to assess the effect of abatacept (ABT) compared to tumor necrosis factor inhibitors (TNFi) for the rheumatoid arthritis (RA) patients with high titer of anti-cyclic citrullinated peptide antibody (aCCP) in the AIRTIGHT study.【Methods】In RA patients with high titer of aCCP (> 100 U/ml) treated with ABT (n=10) or TNFi (n=22), clinical, laboratory and ultrasonographic (US) assessment were performed. The GS (gray scale) and PD (power Doppler) signals were scored in 26 sites and radiographic damage was evaluated using van der Heijde modified total Sharp score (mTSS).【Results】There were no significant differences in age, disease duration, aCCP (ABT: 298.3, TNFi: 285.0 U/ml) and DAS at baseline between two groups. ABT and TNFi group showed the improvement of DAS at 4 and 2 months, respectively. Although there were no significant differences in the sums of GSUS and PDUS at 0, 6, 12 month between two groups, the sums of GSUS and PDUS at 12 month in ABT group tended to be higher than that of TNFi group. ΔmTSS/year showed no difference between two groups.【Conclusions】In RA patients with high titer of aCCP, the clinical effect of ABT

tended to be inferior to TNFi, but the suppression of structural damage of ABT was not inferior.

W20-3

In adalimumab treatment, Remission induction and treatment continuation at 152 weeks in 194 patients

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Conflict of interest: None

Objective Clinical usefulness and treatment continuation following 152 weeks of adalimumab (ADA) in rheumatoid arthritis (RA) patients were investigated. **Methods** Subjects were 194 analyzable patients introduced to ADA at the author's institution from May 2009 to Nov. 2013. Mean age was 54 years, mean duration of illness 6.8years. 157 received MTX ≥10 mg/week (≥10 group) and 30 MTX<10 mg/week (<10 group). **Results** Overall DAS28 (CRP) remission rate showed clinical remission in 43% of patients from 4 weeks, and achieved 75% from 152 weeks. Changes in DAS 28 (CRP) remission rates of 4, 12, 24, 52, 80, 104, 152 weeks for the <2 and ≥2 groups were similar to those seen in the N and S groups, but differed from those in the ≥10 and < 10 mg groups. Overall HAQ remission rate at 152 weeks was 81%; treatment continuation rate was 73.0%. Persistence rate at 152 weeks was 73.0%. **Conclusion** Remission was induced early with ADA in about 43% of patients, and achived 75% of patients at 152 weeks. ADA plus an adequate dose of MTX in early-stage RA and Bio Naïve patients is the best approach to maximally exploit the ADA potential.

W20-4

The study of the clinical outcomes after the treatment with either tocilizumab or abatacept in biologic-naive patients with rheumatoid arthritis in routine clinical practice

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Conflict of interest: None

【Object】There is increasing opportunity of selecting non-TNF-Targeted Biologic. There is a need to compare clinical outcomes of biologic-naive patients after the treatment with either tocilizumab (TCZ) or abatacept (ABT) with rheumatoid arthritis. 【Methods】This study evaluated the background, clinical efficacy, retention rates, and adverse events of TCZ and ABT. This study included patients treated with TCZ (n=68) or ABT (n=43). 【Results】The mean±SD age was 60.0±13.1 years in the TCZ group and 69.1±13.9 years in the ABT group. The mean disease duration was 9.8±8.2 years in the TCZ group and 7.9±10.4 years in the ABT group. The mean±SD DAS28-ESR score at baseline was 5.15±1.31 in the TCZ group, and 5.39±1.49 in the ABT group. The proportion of patients achieving C-DAI remission at 24 weeks was 19.6% in the TCZ group, and 17.1% in the ABT group. Retention rate at one year was 70.7% in the TCZ group, and 61.9% in the ABT group. Rate of discontinuations due to adverse event was 8.8% in the TCZ group, and 9.3% in the ABT group. 【Conclusions】The patients treated with TCZ were older, and higher proportion concomitantly used MTX. The clinical efficacies, safety and retention rate were generally similar.

W20-5

Efficacy of Tocilizumab 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 Tocilizumab (TCZ) for suppressing the radiographic progression of RA cervical lesions comparison with MTX for 2 years. [Methods] We used TCZ and MTX for treating each 38 and 71 Japanese patients with active RA for at least 2 years. For evaluation of cervical lesions, ADI, SAC, and the Ranawat value were measured by plain lateral radiographs at initiation and Year 1,2. [Results] In the patients receiving TCZ (n=38) and MTX (n = 71), the mean age was 57.3±12.4 vs 63.3±10.9 years (p=0.011); disease duration was 7.0±7.3 vs 8.8±9.7 years (p=0.929); the rate of patients receiving MTX was 76% vs 100%(p<0.001) and the mean dose was 9.0 vs 8.3 mg/w (p=0.335). The respective changes in cervical lesion parameters after 1 year were as follows: ADI: 0.21±0.53mm vs 0.25±0.44mm (p=0.327); SAC: -0.16±0.44mm vs -0.17±0.38mm (p=0.653) and Ranawat value: -0.13±0.34mm vs -0.11±0.32mm (p=0.773). The respective changes in cervical lesion parameters after 2 years were as follows: ADI: 0.32±0.70mm vs 0.52±0.67mm (p=0.045); SAC: -0.24±0.49mm vs -0.45±0.63mm (p=0.067) and Ranawat value: -0.24±0.49mm vs -0.35±0.56mm (p=0.270). [Conclusion] This study suggested that TCZ treatment can be used to suppress the progression of RA cervical lesions.

W20-6

Safety/tolerability, Pharmacokinetics and Efficacy of E6011, an Anti-Fractalkine Monoclonal Antibody, in a First-in-Patient Phase 1/2 Study in Japanese Patients with Rheumatoid Arthritis

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Conflict of interest: Yes

Background: Fractalkine (CX_3CL1/FKN) is a chemokine which regulates chemotaxis and adhesion of CX_3CR1-expressing inflammatory cells. We conducted a Phase 1/2, open-label, multiple ascending dose study of E6011; a humanized anti-FKN mAb, in Japanese RA patients for the first time in the world (NCT02196558). **Methods**: Active RA patients with inadequate response to MTX or TNF inhibitors received subcutaneous E6011 at week 0, 1, 2 and thereafter every 2 weeks up to week 10. The safety, pharmacokinetics and efficacy up to week 12 were evaluated. **Results**: Twelve, 15, and 10 subjects were enrolled in the 100, 200 and 400 mg cohorts, respectively. There were no severe AE or deaths, and no significant differences were observed in the incidence or severity of AE across the cohorts. Serum E6011 concentrations proportionally increased with escalated dose. ACR20, 50 and 70 response at week 12 (NRI) were 75.0%, 33.3%, 8.3% in 100 mg cohort, 66.7%, 20.0%, 13.3% in 200 mg cohort and 60.0%, 30.0%, 20.0% in 400 mg cohort. **Conclusion**: E6011 was safe and well tolerated, and demonstrated a promising efficacy in Japanese RA patients with MTX or TNFi-IR. The results obtained suggest that a novel approach to target FKN will be efficacious for RA.

W21-1

Efficacy of biologic DMARDs therapy evaluated by biomarkers and ultrasound indexes in patients with rheumatoid arthritis: Kyushu multicenter rheumatoid arthritis ultrasound prospective observational cohort study

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Conflict of interest: None

Objectives; We evaluated the efficacy of biologic DMARDs (bDMARDs) therapy by biomarkers and ultrasound (US) indexes in patients with rheumatoid arthritis (RA). Methods; One hundred fifty-three RA patients introduced by bDMARDs therapy (TNF inhibitor, 61 patients; TCZ, 45 patients; ABT, 44 patients) were enrolled from the Kyushu multicenter RA US prospective observational cohort study. We evaluated clinical disease activity and US synovitis score (GS and PD from 22 joints of bilateral hands) at baseline, 3 and 6 months, and serum levels of biomarkers (multi-suspension array, 38-plex) at baseline and 3 months. US remission was defined by the absence of PD score. Results; Clinical disease activity and US synovitis score significantly improved at 3 and 6 month from baseline ($p<0.0001$). Although most of biomarkers similarly decreased at 3 months by all three classes of bDMARDs, a part of biomarkers such as IL-6, GRO, and IP-10 changed differently by TCZ or others. A logistic regression analysis revealed that low level of IL-6 and short disease duration (< 2 years) at entry was predictive of US remission at 3 months or 6 months, respectively. Conclusion; Baseline biomarkers may predict the therapeutic response of bDMARDs evaluated by US indexes.

W21-2

Evaluation of bone-related biomarkers in rheumatoid arthritis patients treated with abatacept : Kyushu multicenter rheumatoid arthritis ultrasound prospective observational cohort study

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Conflict of interest: None

Objectives; We evaluated efficacy of abatacept by bone-related biomarkers and ultrasound (US) indexes in patients with rheumatoid arthritis (RA). Methods; 40 RA patients introduced abatacept therapy were enrolled from the Kyushu multicenter RA US prospective observational cohort study. We evaluated clinical disease activity, US synovitis score (22 joints of bilateral hands) and serum levels of bone-related biomarkers (TRACP-5b by EIA, sRANKL by ELISA, DKK-1, OC, OPG, OPN and SOST by multi-suspension array) at baseline, 3 and 6 months. Results; The median of disease duration was 72 months and that of DAS28-CRP was 4.56. Clinical disease activity and US synovitis score significantly improved at 3 and 6 month from baseline ($p<0.001$). TRACP-5b significantly increased ($p<0.01$), but sRANKL significantly decreased ($p<0.05$) at 3 and 6 month from baseline. Baseline OPN was significantly lower ($p<0.05$) and baseline DKK-1 tended to be lower ($p=0.06$) in patients achieving remission than in patients not achieving remission defined by power Doppler score. Conclusion; Each bone-related biomarkers differently changed after introduction of abatacept therapy. Therapeutic response of abatacept evaluated by US indexes may be predicted by baseline bone-related biomarkers.

W21-3

Osteopontin associates with subclinical synovitis evaluated by ultrasonography in rheumatoid arthritis

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Conflict of interest: Yes

【Objectives】Extracellular matrix proteins such as osteopontine (OPN) act on macrophages via a9 integrin receptor to mediate inflammation in rheumatoid arthritis (RA) synovitis. The aim of this study is to determine whether a9 integrin ligands (OPN etc) associate with subclinical synovitis evaluated by ultra-sonography in RA.【Methods】507 RA patients registered in KURAMA cohort were included. Total points (0-84) of Power Doppler (PD) signals (0-3) were evaluated in 28 joints including fingers and toes. Correlation between total score of PD and biomarkers such as OPN or Tn-C were investigated by Spearman's rank correlation coefficient.【Results】Total points of PD were in average 4.9 in all, and 3.0 in patients with DAS28 remission. Total points of PD well correlated with OPN and Tn-C concentrations (OPN: $r=0.24$, $p<0.0001$, Tn-C: $r=0.17$, $p=0.0005$). The correlation was more remarkable in patients who were on the treatment with biological DMARDs (OPN; $r=0.32$, $p<0.0001$, CRP; $r=0.27$, $p=0.0003$).【Conclusions】OPN could be a good serum marker for evaluating subclinical synovitis in patients with RA, especially under the treatment with biologics.

W21-4

Pathological changes in rheumatoid arthritis synovial tissues before and after the use of biological drug

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Conflict of interest: Yes

[Purpose] We examined the impact that Bio has on RA synovial tissues, using the pathological findings of a RA patient who underwent surgery and synovial tissues were collected before and after the use of Bio. [Methods] We targeted 26 joints of RA patients. We assessed pathological findings before and after the use of Bio by identifying the presence or absence of fibrinoid necrosis and using the Rooney score. We discussed the association with the synovial pathological findings, disease activity (CDAI) and blood biochemical findings. We used ETN15, IFX5, TCZ2, ADA2 and ABT2. [Results] Fibrinoid necrosis was identified in 4 joints (15.4%) after the use of Bio, which showed significant improvement. The Rooney score also improved significantly, from 30.6 to 12.6. The perivascular lymphocytic infiltrate, lymphoid follicles and lymphocyte infiltration decreased significantly. There was a correlation between the Rooney scores and MMP3 after the use of Bio. [Conclusions] The improvement of inflammatory in the synovial membrane was observed by the use of Bio. Furthermore, pathological findings in synovial tissues have been suggested to reflect the disease activity.

W21-5

Macrostructural and microstructural changes in the knee cartilage of patients with rheumatoid arthritis treated with biologic DMARDs (1 year follow up evaluation by T1ρ and T2 mapping)

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Conflict of interest: None

[Objectives] To study the effects of biologic DMARDs on articular cartilage in patients with rheumatoid arthritis (RA), we evaluated microstructural changes in the knee cartilage using qualitative MRI techniques.

[Methods] Sagittal 3D-WATS, T1ρ mapping and T2 mapping of the femorotibial joint in 16 RA patients were obtained before and 1 year after starting biologic DMARDs. Four regions of interest (ROIs) were placed on images of the cartilage in the medial and lateral femoral condyle (MFC, LFC) and the medial and lateral tibia plateau (MTP, LTP). Cartilage thickness, T1ρ and T2 were recorded. Their changes and correlations were evaluated. [Results] The % decrease of cartilage thickness were MFC2.8, LFC1.0, MTP1.6 and LTP1.2, although partly increases of cartilage thickness were identified. There was significant decrease in the MFC. The T1ρ and T2 tended to increase in all four condyles. Among them, T2 in the MFC significantly increased, and those both at baseline and 1 year follow up statistically correlated with the changes of cartilage thickness. [Conclusion] This study suggests that microstructure damage of the cartilage is based especially on the changes of collagen fibers and that the fibrocartilage-like repair tissue may be appeared on the articular cartilage.

W22-1

Implication of MPO-ANCA positivity during remission; subgroup analysis of nationwide prospective cohort study of ANCA-associated vasculitis and rapidly progressive glomerulonephritis (RemIT-JAV-RPGN)

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Conflict of interest: None

[Object] To evaluate transitions of MPO-ANCA related to characteristics and outcome using data set from RemIT-JAV-RPGN. [Methods] MPO-ANCA positive patients who achieved remission by 6 months were enrolled and divided into two categories by MPO-ANCA transition within 6 months; persistently positive or negative conversion, then patient characteristics and the relapse were compared. [Results] Two hundreds fifteen patients were included in this analysis; 11 with EGPA, 28 with GPA and 144 with MPA. The average age was 70.6 years and 123 (57%) were female. MPO-ANCA was persistently positive in 59 patients (27%) despite achieving remission. Japanese RPGN clinical grading (grade III & IV: 13.6% vs. 28.2%, p = 0.025) and mortality rate (0% vs. 6.4%, p = 0.046) were lower in persistently ANCA positive patients compared to those with ANCA negative conversion. Among patients with persistently positive ANCA, 9 patients (15%) experienced relapse. MPA patients (33% vs. 78%, *p* = 0.024) and renal involvement (56% vs. 94%, p = 0.001) was less frequent in the patients with relapse compared to those without relapse. [Conclusions] Careful monitoring may be necessary for relapse among patients with persistently positive for MPO-ANCA excepting MPA patients or the patients with renal involvement.

W22-2

Retrospective analysis of initial symptoms in microscopic polyangiitis

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Conflict of interest: None

【Background】Major organ dysfunction in microscopic polyangiitis (MPA) patients are rapidly progressive glomerulonephritis (RPGN), pulmonary hemorrhage and interstitial pneumonitis. Frequent clinical symptoms are purpura, subcutaneous hemorrhage, gastrointestinal hemorrhage, multiple mononeuropathy and so on. However at first medical contact, MPA presents various symptom with no context, which may lead to a delayed diagnosis. Patients admitted to our department from 2012 to 2016. 【Result】ANCA positive patients were 5 males and 8 females. The means of patients age is 75.5 years. Number of with definitive diagnosis MPA was 4. Initial symptom among ANCA associated vasculitis were 5 cases with cough and sputum, 8 cases with fever, and 4 cases with myalgia. Those with definitive diagnosis were as follows: cough and fever; cough and myalgia; fever; and fever and myalgia. 3 patients were treated with steroid pulse therapy as initial therapy. 6 patients were treated with immunosuppressive agents【Discussion】Patients may lead to prolonged dysfunction and death within months due to delayed treatment in MPA. Our cases show myalgia as initial symptom which polymyositis or polymyalgia rheumatica also presented. We will report our MPA cases with some literature review.

W22-3

Characteristics of MPO-ANCA positive GPA comparing to PR3-ANCA positive GPA and MPA

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Conflict of interest: None

(Objective) To confirm the difference among MPO-ANCA positive GPA (MPO-GPA), PR3-ANCA positive GPA (PR3-GPA) or MPA. (Methods) Retrospectively we recruited GPA and MPA patients through the two multi-center cohorts (Cohort A: 2001-2012, Cohort B: 2012-2016). We classified patients with EMEA classification and ANCA. (Results) MPO-GPA group had more female patients without smoking history than other two groups. MPO-GPA group had more ENT and pulmonary involvements, but less kidney involvements than MPA. Especially MPO-GPA had more bronchial involvements, and MPA had more pulmonary fibrosis. Although MPO-GPA group needed less aggressive treatments, their outcome was fair compared to MPA. PR3-GPA group had relapses most often. (Conclusion) The backgrounds, organ involvements and outcomes of MPO-GPA had the different characteristics from those of PR3-GPA or MPA. It is reasonable to differentiate MPO-GPA from other two groups.

W22-4

Inter-Organ Association Between Lung and Kidney in Patients with ANCA Associated Vasculitis

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Conflict of interest: None

[Object] In patients with ANCA-associated vasculitis (AAV), lung and kidney are the most critical involvements, which need more aggressive immunosuppressive therapies. The association between lung and

kidney remains unclear. [Method] We reviewed lung CT of 48 patients with AAV diagnosed by renal biopsy between 2006 and 2015. Lung lesions are classified as 5 categories;(1)airway lesion (bronchial wall thickening, bronchieactasis, bronchiolitis), (2)pleural lesion (pleural thickening, pleural effusion), (3)alveolar lesion (pure ground-glass opacity, mixed ground-glass opacity, consolidation), (4)focal lesion (nodular lesion, cavity), (5)interstitial pneumonitis, then statistically analyzed the association between lung lesions, renal pathological findings and clinical data. [Results] Glomerular crescent was seen in 96% of patients. 95.8% had any lung findings, (62.5%, 62.5%, 41.7%, 31.3%, 43.8%, respectively). Alveolar lesion, especially mixed GGO, was associated with heart failure. Nodular lesion was associated with glomerular fibrinoid necrosis. Interstitial pneumonitis was associated with hematuria. [Conclusions] The association between lung and kidney and renal pathological lesions was found, and this suggests interorgan communication between lung and kidney in patients with AAV.

W22-5

The prediction of survival by lung abnormalities on chest computed tomography (CT) in patients with microscopic polyangiitis before receiving immunosuppressive treatment

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Conflict of interest: None

Objectives: To clarify the associations between lung abnormalities on the chest CT and survival 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, and miscellaneous lesions. We also determined whether the global pattern of abnormalities in each case fits into a typical idiopathic interstitial pneumonia (IIP) pattern. We then analyzed associations between these lung lesions/patterns and survival. Results: Median follow-up period was 105.5 weeks (Interquartile range 26-220) and 32 patients (21.3%) died. In multivariate analyses, idiopathic pulmonary fibrosis (IPF) pattern of chest CT was independently associated with survival (OR 3.155, p=0.019). Cardiovascular involvement (OR 6.373, p=0.005), diffuse alveolar hemorrhage (OR 3.815, P=0.008), peripheral nerve involvement (OR 3.686, p=0.002), the levels of serum creatinine (OR 1.183, p<0.001), and age (OR 1.061, p=0.012) were also independently associated with survival. Conclusions: The only chest CT variable that was independently associated with survival was the IPF pattern.

W22-6

Prognostic factors for interstitial lung disease with microscopic polyangiitis

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Conflict of interest: None

[Objectives] To investigate the prognosis of pulmonary fibrosis with microscopic polyangiitis (MPA-ILD) and prognostic factors. [Methods] Of patients with MPA who were admitted to our hospital between 2001 and 2016, the subjects were MPO-ANCA-positive patients with ILD on HRCT. Using the clinical data and fibrosis score on HRCT, we examined prognostic factors. [Results] There were 52 patients with MPA-ILD, consisting of 26 males and 26 females, with a median age of 73 years. MPO-ANCA, KL-6, %FVC, and %DLco/VA values at the start of treatment were 139EU, 446U/mL, 82.9%, and 61.8%, respectively. Concerning HRCT images, 38 patients showed a UIP pattern. In 45 patients, it was combined with immunosuppressive drugs. In 8, apheresis was performed. In 47 patients, the MPO-ANCA level was maintained below the detection limit. With respect to the prognosis, 8 patients died. The 5-year survival rates after the treatment were 86.0%. Univariate analysis for lung disease-associated death included the HRCT score (p<0.001), WBC (p=0.003), and CPFE (p=0.001). However, on multivariate analysis of these factors, the HRCT score was significantly correlated (p=0.016). [Conclusion] HRCT fibrosis score at the start of treatment were considered to be prognostic factors for lung disease-associated death.

W23-1

Efficacy and safety of remission-induction/maintenance therapy in 70 cases of new-onset ANCA-associated vasculitis

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Conflict of interest: None

Objectives: To reveal current status of new-onset ANCA-associated vasculitis (AAV) treatment. **Methods:** All new-onset AAV cases who received induction therapy and visited to our rheumatology service from January 2007 until September 2016 were enrolled. Clinical information was collected from medical chart. **Results:** 70 new-onset AAV cases (MPA 36, GPA 20, EGPA 14) were evaluated. Mean age was 65 y/o and 60% were female. Clinical manifestations were various; fever 31, skin 15, nerve 27, upper airway 26, lung 36, and kidney 32. Mean initial dose of glucocorticoid was 0.87 mg/kg/day as PSL. Immunosuppressant (IS) was used for 39 cases (CY 36, MTX 1, RTX 2). Remission rate was 89%, and the cases with PR3-ANCA had significantly higher rate of induction failure. In maintenance therapy, IS was used for 42 cases (AZP 34, CY 5, MTX 2, RTX 1). 20 cases relapsed, and cases with ILD relapsed more frequently than the others. 21 cases had severe infection (bacterial pneumonia 18, PCP 5, phlegmon 3, etc). 13 cases died of 5 carcinoma, 4 infection, 3 vasculitis activity, and 1 suffocation by accident. **Conclusions:** Although induction therapy by glucocorticoid and immunosuppressant was effective in AAV, further optimization of treatment strategy for less adverse events including infection is needed.

W23-2

Safety profile of intravenous cyclophosphamide treatment in elderly patients with systemic vasculitis

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Conflict of interest: None

Background: Intravenous cyclophosphamide (IVCY) is considered to a world-standard remission-induction therapy for systemic vasculitis. However, the RemIt-JAV registry revealed the low usage rate of IVCY in Japan. **Aims**: To investigate the safety of IVCY in elderly patients with systemic vasculitis. **Method**: This retrospective study comprised 35 patients diagnosed as active systemic vasculitis from April 2009 to March 2016. These patients were treated with IVCY plus glucocorticoid (GC) therapy (IVCY group) or with GC therapy only (GC group). We analyzed the clinical data at the time after 24 weeks from the start of treatment. **Results**: Among underlying diseases, 21 microscopic polyangiitis, 6 granulomatosis with polyangiitis, 6 eosinophilic granulomatosis with polyangiitis, and 3 polyarteritis nodosa. Serious adverse events in ICVY group (n=21) and in GC group (n=14) were observed were 1 and 2, respectively. The reduction rate of GC at the time after 24 weeks from treatment is 74.8% and 62.5%, respectively (p=0.028). In the IVCY group, no significant difference was observed between patients over 70 age (n=9) and the others (n=12). **Conclusion**: IVCY is tolerable for elderly patients with systemic vasculitis, and makes it possible to reduce amount of GC.

W23-3

Effects of Cyclophosphamide Therapy in Japanese Patients with MPO-ANCA Positive Microscopic Polyangiitis

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Conflict of interest: None

[Objective] The aim of this study was to elucidate the efficacy of cyclophosphamide (CY) in MPO-ANCA-positive microscopic polyangiitis (MPO-ANCA-MPA). [Methods] One hundred-nine patients newly diagnosed with MPO-ANCA-MPA between 2000 and 2015 were enrolled in this retrospective study. The patients were divided into two groups based on whether they received combination therapy with a glucocorticoid (GC) plus CY (CY group, n=35) or GC alone (GC group, n=74) for remission induction. The primary outcome was all-cause mortality. [Result] The median follow-up period was 27 months. The mean age was higher in the GC group than that of in the CY group, but other factors were not different in the two groups. The remission rate was equivalent between the two groups. The survival rate was slightly higher in the CY group than in the GC group (0.89 vs. 0.80 at 1 year and 0.81 vs. 0.67 at 3 years, p=0.135). The hazard ratio of CY for the primary outcome adjusted for age, sex, Birmingham vasculitis activity score, and serum levels of creatinine, albumin and C-reactive protein was 0.612 (95% CI, 0.278-1.345; p=0.222). [Conclusion] This study suggested that the risk of death might decrease by 39% in the CY group compared with GC group in MPO-ANCA-MPA, though there was no statistical significance.

W23-4

Effectiveness of Intravenous immunoglobulin (IVIg) for Eosinophilic Granulomatosis with Polyangitis (EGPA) with *multiple* mononeuritis

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Conflict of interest: None

【Case1】70-year-old male admitted to ER complaining of myalgia of bilateral lower legs since one month ago. Physical examination revealed decreased muscle strength and abnormal sensations. Laboratory test showed eosinophilia 9204/μL, proteinuria and hematuria with erythrocyte cast and MPO-ANCA 128U/ml. He was diagnosed EGPA and treated with mPSL pulse, IVIg, cyclophosphamide.【Case2】79-year-old female was evaluated for acute fever and gait disturbance. On physical examination, decreased distal muscle strength was detected. Laboratory studies revealed severe eosinophilia 23244/μL and negative ANCA. After biopsy of sural nerve, she was treated with mPSL and additional IVIg for limb weakness.【Case3】55-year-old male was evaluated for acute abdominal pain. He was diagnosed as diverticulitis, but after treatment, intermittent pain, high fever and enosinophilia (22140/μL) were remained. On day10, he noticed decreased muscle strength in his right leg. He required open surgery because of intestinal perforation, then peritoneal tissue revealed necrotizing vasculitis with eosinophilia. Three courses of IVIg were initiated for persistent right drop foot.【Conclusion】EGPA is highly associated with multiple mononeuritis. We're considering the future efficacy of IVIg.

W23-5

The efficacy and safety of tocilizumab monotherapy for Takayasu arteriris: a prospective, single-center, open study

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Conflict of interest: None

[Objectives] To evaluate the efficacy and safety of tocilizumab (TCZ) monotherapy for Takayasu arteriris (TAK). [Methods] Six TAK patients (all female) who had been newly diagnosed at our hospital from January 2013 to December 2015 were enrolled in a prospective open study. TCZ (8mg/kg) was given every 2 weeks for the first 2 months and every 4 weeks for the next 10 months (total 15 times) without corticosteroids (CSs). Patients were followed up for another 1 year after without any treatment. The efficacy was assessed by clinical symptoms (fever, etc), CRP/ESR and CT findings (arterial wall thickening) at week 12,52 and 104. Complete remission was defined as normalization of CRP/ESR and disappearance of clinical symptoms, CT findings. [Result] The mean age was 43, the mean disease duration was 34.2 months, mean CRP level was 7.9mg/dL and mean ESR was 92mm/hr. Arterial wall thickening on CT was seen in all. Four patients completed the study successfully and 3 of them were in complete remission at week 52. After 1-year course of TCZ monotherapy, we started CSs for iritis and CRP elevation. There were no serious adverse events. [Conclusion] Although TCZ monotherapy may be useful as a remission induction therapy for TAK, maintenance therapy seems to be necessary after cessation of TCZ.

W23-6

The efficacy of tocilizumab (TCZ) therapy in steroid-resistant and methotrexate (MTX)-resistant rheumatic polymyalgia (PMR)

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Conflict of interest: None

Objectives: We report the efficacy and safety of TCZ in steroid / MTX resistant PMR. **Methods:** 35 patients, diagnosed with PMR according to the 2012 EULAR/ACR provisional classification criteria for PMR, were treated according to the 2015 EULAR / ACR recommendations. Twelve cases were steroid / MTX resistant PMR patients. We treated 9 cases of severe PMR with TCZ and assessed the effect of TCZ. **Results:** Of the 35, 24 patients were recurred, after 8.2 ± 5.4 months, PSL 6.2 ± 3.9 mg / day. MTX was added in 22 patients (8.8 ± 3.4 mg / week, 11.9 ± 12.9 months) and PSL was increased in 2 patients. Ten out of 22 cases using MTX were effective and PSL could be withdrawn. Only 6 patients cured with PSL alone. TCZ was added to 9 out of 12 patients with steroid / MTX resistance. Duration of TCZ therapy was 7.6 ± 4.9 months. Dose of PSL significantly decreased from 7.9 ± 3.0 to 1.4 ± 1.4 mg / day with TCZ treatment, and dose of MTX (8.0 ± 4.7 to 3.8 ± 4.6 mg / week) and CRP (1.1 ± 1.0 to 0.02 ± 0 mg / dL) also declined. In 3 cases PSL could be withdrawn and in 3 cases MTX could be withdrawn. One patient cured. **Conclusions:** 2015 EULAR/ACR recommendations were effective for most PMR patients (65%), but severe cases (35%) will require further treatment options including TCZ.

W24-1

Assessment of DAPSA in disease activity states of peripheral joint involvements in psoriatic arthritis with biologics

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Conflict of interest: Yes

Objectives: Disease Activity for Psoriatic Arthritis (DAPSA) is useful for the assessment of peripheral joint involvement in several clinical trials for PsA. In last year's this meeting, we reported that DAPSA was also useful for PsA in daily clinincal practice. We assess whether DAPSA is valid as a clinical, functional and structural parameter in patients with received biologics through one year. Methods: Using 109 clinical data

from 35 patients with received biologics for at least 3 months, we compared DAPSA with DAS, PASDAS, MDA and ACR&EULAR response as clinical parameters, HAQ as a functional damage, and TSS as a structural damage. Results: DAPSA strongly associated with DAS-CRP (66) (r=0.86), DAPSA remission almost agreed with MDA.W observed agreement with DAPSA50 at ACR50 (κ0.79), DAPSA75 at ACR70 (κ0.77). On the other hand, DAPSA response did not agree with EULAR response. DAPSA scores were significantly associated with HAQ and TSS (p=0.03, p=0.02). Conclusions: Although DAPSA improvement rate did not agree with ACR&EULAR response, DASPA was suggested to be a useful instrument for evaluating peripheral joint involvements in PsA patients with biologics in daily clinincal practice.

W24-2

The relationship between dactylitis and radiological changes of hands and feet in patients with psoriatic arthritis

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Conflict of interest: None

Object: To examine the relationship between dactylitis and radiological changes of hands and feet in patients with psoriatic arthritis (PsA). Methods: 30 patients with PsA from the outpatient clinic were retrospectively collected and were the subjects of the study. In small joints of hands and feet, bone erosion and joint space narrowing were quantified according to the PsA-Sharp-van der Heijde modified scoring method, and proliferative changes around the joints were evaluated using proliferation score by Wassenberg et al (Z Rheumatol 2001). The effect of dactylitis on those radiographic changes was investigated. Results: The mean age/ disease duration of psoriasis/ disease duration of arthritis at baseline were 50/ 13/ 4 years, respectively. The mean interval of radiographic examination was 4.2 years. Dactylitis was observed in 40% of patients. The changes of erosion, joint space narrowing and proliferation scores per year were not different between patients with dactylitis and those without dactylitis. The progression rate of bone destruction in DIP/ PIP/ MCP joints with dactylitis was significantly faster than that in DIP/ PIP/ MCP joints without dactylitis. Conclusion: The study suggests the association between dactylitis and rapid progression of joint damage.

W24-3

The assessment of ultrasonographic findings of arthritis and dactylitis in juvenile psoriatic arthritis

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Conflict of interest: None

Objective: Psoriatic arthritis in people under 16 years is called juvenile psoriatic arthritis (JPsA). In Japan, such cases are rarely reported, and the pathogenesis is still unclear. This study aimed to investigate the ultrasonographic characteristics of arthritis and dactylitis in patients with JPsA. **Patients and Methods:** The ultrasonographic features of both knee joints, five entheses, and dactylitis in patients diagnosed with JPsA based on the Vancouver criteria were analyzed. **Results:** We analyzed 24 knee joints and 120 entheses of 12 JPsA patients. Synovitis was found in 50%, and enthesitis in all of them. The Power Doppler Signal (PDS) was frequently abnormal (58/120, 48.3%). Joint abnormalities were detected in 14/18 joints (77.8%) from 5 patients who were examined for dactylitis. The most frequent abnormalities were pseudotenosynovitis and collateral ligament abnormalities with joint synovitis (5/18, 27.8%). No bony erosion or osteophytes were detected. **Conclusion:** In the entheses in JPsA patients, PDS abnormalities are more frequent and structural abnormalities are infrequent compared to adult PsA. Structural abnormalities are also infrequent in JPsA dactylitis. Whether this difference reflects pathogenic differences between JPsA and adult PsA requires further elucidation.

W24-4

The clinical features of RF/ACPA positive patients with psoriatic arthritis

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Conflict of interest: None

Object: Seronegativity is not always true in patients with psoriatic arthritis (PsA) and clinical features of seropositive PsA patients are not well understood. In this study we analyze clinical features of seropositive (RF or ACPA) PsA patients in comparison with seronegative PsA patients. **Methods:** One hundred patients with psoriasis referred from dermatologists for assessment for arthritis between July 2015 and August 2016 were enrolled. PsA was diagnosed by CASPAR criteria. **Results**: Between 52 PsA patients and 48 PsO patients without any musculoskeletal manifestations there were significant differences in onset age of psoriasis ($p<0.01$), clinical parameters (CPDAI: $p<0.01$; PASE: $p<0.01$), ACPA positivity ($p=0.04$), and CRP ($p=0.03$). Among 44 patients whose ACPA data was obtained in 52 PsA patients, duration from skin onset to joint onset was shorter in ACPA positive 7 patients (49.5 months) than in negative 37 (99 months), although it was not statistically significant ($p=0.30$). The same tendency was observed in RF positivity and duration of skin onset and joint onset. **Conclusions:** Among PsA patients in this series, ACPA positivity was 15.9% and RF positivity was 12.8%. Seropositive patients with PsA had likely shorter duration between skin onset and joint onset.

W24-5

The assessment about importance of sacroiliitis in psoriatic arthritis

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Conflict of interest: Yes

【Objective】The axial involvement in Psoriatic arthritis (PsA) is classified in Spondyloarthritis, so the presence or absence of sacroiliitis is also important. Last year, at this meeting, we reported that there were many findings of axial involvement in PsA regardless of symptoms. Now we assessed about differences between sacroiliitis and clinical and imaging findings in PsA.【Methods】Enrolled one hundred patients with PsA were classified into with or without sacroiliitis by X-ray. We compared with sacroiliitis and BASDAI, ASDAS, BASFI and BASMI, and also the imaging of the lumbar.【Results】About 40% were sacroiliitis according to New York criteria. There was no relation between sacroiliitis and BASDAI, ASDAS and BASFI. But PsA with sacroiliitis was related with BASMI (Schober's test (p=0.031), lumber side flexion (p=0.012)). As for imaging, PsA with sacroilitis were higher mSASSS (P=0.0001), but there was no difference about positive findings of MRI of the lumbar.【Conclusions】PsA with sacroiliitis was a significant limitation in range of motion and the change of imaging of the lumbar. Though there were spinal involvements without sacroiliitis. In axial involvement of PsA, the range of motion and the imaging need to be assessed over time regardless of sacroiliitis.

W24-6

The radiographic progression of axial involvement in patients with psoriatic arthritis

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Conflict of interest: None

【Object】To quantitate the radiographic progression rate of axial involvement in patients with psoriatic arthritis (PsA) by mSASSS and PASRI. 【Methods】23 patients with PsA and 6 patients with ankylosing spondylitis (AS) were subjects of the study. mSASSS and PASRI were used to evaluate spinal involvement. The progression rates were compared. 【Result】The demographic data such as males/age/disease duration of psoriasis/disease duration of arthritis at baseline in patients with PsA were 78%/53.4±10.6 years/15.9±13 years/7.4±5.9 years. The interval of radiographic examination was 5.0±1.7 years. In AS patients, %males/age/disease duration at baseline were 100%/39.4±12.7 years/5.8±6.4 years. The interval of radiographic examination was 4.8±1.6 years. The mean mSASSS at baseline in patients with PsA was11.1±14.6, and that in patients with AS was 17.1±22.2. The changes of mSASSS per year were not different between patients with PsA and patients with AS (p=0.26). In PsA patients, the changes of mSASSS and PASRI per year were higher in men than women, and the patients with sacroiliitis had higher changes of mSASSS and PASRI than patients without sacroiliitis. 【Discussion】The study suggests that progression rate of axial change is not significantly different

W25-1

Efficacy of mycophenolate mofetil with the moderate doses of corticosteroids for remission induction in patients with active lupus nephritis

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Conflict of interest: None

Objective: Mycophenolate mofetil (MMF) has been approved for lupus nephritis (LN). However, the efficacy and optimal dosing regimen in Japanese patients remains unclear. We investigated the efficacy of MMF with the moderate doses of corticosteroids (Mo-CS) in active LN patients. Methods: This study comprised 21 LN patients treated with MMF plus Mo-CS. We defined complete renal remission (CR) as proteinuria <0.5g/gCr and normal or near normal GFR. Mycophenolic acid (MPA) concentration was assessed and MMF doses were titrated to achieve a target MPA-$AUC_{0\text{-}12}$ 30-45 mg·h/L. Results: Twelve of 21 cases had been newly diagnosed and resting 9 were relapsed or refractory cases. The initial doses of prednisolone (mean±SD) were 0.59±0.13 mg/kg and the adjusted doses of MMF were 1.88±0.56 g/day. CR rates of all patients (treatment-naïve patients) at 1, 3, 6 months after initiation of therapy were 19% (23%), 43% (66%) and 50% (82%) respectively. Nephrotic proteinuria, high SLEDAI, pathological findings including class V and relapse were predictive factors of non-remission at 6 months. Two patients with extremely high MPA exposure had severe infection. Conclusion: The remission induction regimen using fine-controlled dosing of MMF plus Mo-CS would be a promising therapy for LN.

W25-2

High plasma concentration of Mycophenolate acid in early phase of induction therapy predicts good renal outcome in lupus nephritis class III or IV

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Conflict of interest: None

【Object】To investigate the relationship between the plasma concentration of MPA in induction therapy and renal response. 【Methods】We prospectively enrolled patients with biopsy proven lupus nephritis class III or IV who hospitalized form Apr to Oct 2016. As induction therapy, PSL was started at dose of 1mg/kg/day and tapered to 10mg/day by 12 weeks. Fixed dose of MMF at 2,000mg/day was started and continuously introduced for 12 weeks. We measured 2 points of MPA plasma concentration at early (week 2) and middle (week 12) phase of induction therapy. We evaluated the association between these concentration and complete renal response (CR) rate at week 12. 【Results】Six patients were enrolled. $AUC_{0\text{-}12}$ between the early and the middle phase was not correlated (R^2=0.17, p=0.7), but that of the early phase tended to be lower (47.4±25.6 vs 58.9±19.1 mg·h/L). All the patients with high $AUC_{0\text{-}12}$ (over 40mg·h/L) at the early phase achieved CR at week 12. But we could not find any association between $AUC_{0\text{-}12}$ at middle phase and CR rate at week 12. 【Conclusions】High $AUC_{0\text{-}12}$ of MPA at the early phase of induction therapy might predict good renal response.

W25-3

Evaluation of mycophenolate mofetil in patients with lupus nephritis

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Conflict of interest: None

[Object] To evaluate the efficacy and safety of mycophenolate mofetil (MMF) in patients with lupus nephritis (LN). [Methods] We retrospectively analyzed 34 LN patients treated with MMF following 24 weeks in our hospital. SLE disease activity index (SLEDAI), anti-dsDNA antibody value, complements, and urine protein were examined at baseline and after starting to MMF. Usefulness difference of nephritis type and long using safety of MMF treatment were also observed. [Results] Mean age was 40-year-old, female 32 patients, male 6 patients. Serositis was seen in 18%. Sixteen patients were treated to MMF as multitarget therapy. The mean values of complement, anti-ds-DNA antibody, SDAI were significantly improved three months after, and also erythema and arthralgia improved. After 6 months, proteinuria significantly decreased to 0.47 g/day from 1.45 g/day. Serositis history patients were relatively poor response. In subtype, proteinuria levels decreased significantly in type V. On the other hand, Proteinuria of mixed type (III+V and IV+V) was not better than the other. Corticosteroid reduced rate was 41%. Serious adverse events were not seen. [Conclusions] Our study shows that MMF therapy is useful for erythema, arthralgia, and proteinuria with LN, especially with type V.

W25-4

Pharmacokinetics of mycophenolic acid in lupus nephritis

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Conflict of interest: None

[Object] The optimize dosage of mycophenolate mofetile (MMF) for lupus nephritis (LN) is unclear. The AUC0-12 of mycophenolic acid (MPA) correlates with rejection and side effects in renal transplantation recipients, and AUC0-4 was clinically represented. We analyzed available limiting sampling strategy correlated with AUC0-12. [Methods] Nine LN patients treated with MMF were included. Nine point blood samples were collected just before dosing (C0) and at C0.5, C1, C2, C3, C4, C6, C8, C12 after oral administration. MPA plasma concentration were measured using enzymatic method (Cobas MPA, Roche), and AUC was calculated using trapezoid method. We examined whether a limited sampling strategy to available or not in LN. [Results] AUC0-12 (median 48μg.h/mL) was significantly correlated with AUC0-4. The C max (5.5-32μg.h/mL) was seen in C0.5, C1 or C2. MPA-C1 showed correlation with AUC0-12 (R^2=0.5023, P=0.02). The regression formula for AUC0-12 (= AUC0-12=30.8+1.48C1) were obtained. In LN patients, the formula of AUC0-

12 using renal transplantation recipients at our hospital could not be replaced. [Conclusions] AUC0-12 was correlation with C1 single point sampling, resulting in a regression formula of AUC0-12=30.8+1.48C1.

W25-5

Mizolibine versus mycophenolate mofetil for combination therapy with calcinuerin inhibitors in patients with lupus nephritis

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Conflict of interest: None

[Object] The aim of this study was to compare the efficacy and safety between combination therapy of calcinuerin inhibitors (CNI) and mizolibine (MZB) and that of CNI and mycophenolate mofetil (MMF) in patients with lupus nephritis (LN). [Methods] The subjects of this study were 34 LN patients who received the combination therapy from January 2008 to October 2016. The efficacy outcomes included the rate of complete or partial renal response (CR or PR) at 3 and 6 months, and the changes of eGFR, proteinuria, serum C3, serum anti-dsDNA levels and corticosteroid doses. [Results] 23 and 11 LN patients received MZB and MMF in combination with CNI, respectively. The baseline characteristics of the patients did not differ between the MZB and MMF groups. At month 3, the rate of CR was 21.7% in the MZB and 45.5% in the MMF group (p=0.23). The serological markers remarkably improved and corticosteroid doses were reduced similarly in the both groups. Although adverse events were almost the same between the groups, diarrhea and Herpes Zoster were more often seen in the MMF group. [Conclusions] The both combination therapy showed high efficacy in LN patents. MMF might be superior in efficacy to MZB.

W25-6

The first-year results of mizoribine-tacrolimus-based multitarget treatment for consecutive patients with active lupus nephritis

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Conflict of interest: None

Objectives: To elucidate efficacy, safety, and clinical impact of mizoribine-tacrolimus-based multitarget treatment for active lupus nephritis. **Methods**: Between 2009 and 2015, a total of 32 consecutive patients were underwent kidney biopsy and were diagnosed active LN (Class III, IV, V, III+V, and IV+V). They all were treated with multitarget treatment and analyzed retrospectively. **Results:** All patients could continue original treatment without dropout nor flare-ups till month 12. At month 6 and 12, proteinuria remission (≤0.2 g/day), CR (Liu Z, et al. 2015), SLEDAI remission, and prednisolone dose were 66% and 91%, 47% and 63%, 34% and 47%, and 12.2 and 8.8 mg/day, respectively. The treatment responses were similar among histologic groups. Serum levels of mizoribine/tacrolimus was correlated with efficacy parameters, especially with increase of serum C3 (R^2 = 0.55, 0.38). Serious infections were not observed. Four cases turned positive in cytomegalovirus antigenemia method, but improved spontaneously without treatment. **Conclusions:** Our results suggest that multitarget therapy using mizoribine as opposed to mycophenolate mofetil may provide high safety in addition to high efficacy at month 6 and 12. The therapy may enable faster dose reduction of concomitant corticosteroids.

W26-1

Neuropathic-like pain in patients with rheumatoid arthritis

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Conflict of interest: None

【Purpose】To examine the frequency and clinical characteristics of neuropathic-like pain in rheumatoid arthritis (RA) patients.【Methods】The disease activities of 145 outpatients with RA were evaluated from December 2015 to July 2016 using DAS28, CDAI, SDAI, and mHAQ. Neuropathic-like pain was evaluated using the painDETECT questionnaire (PDQ). Depression and anxiety were evaluated using the hospital anxiety and depression scale (HADS). QOL was evaluated using short-formed 36 (SF-36). We compared the clinical parameters between the patients with (PDQ≧13) and without neuropathic-like pain (PDQ<13).【Results】Thirty (21%) of 145 patients with RA had neuropathic-like pain in PDQ. In patients with neuropathic-like pain, the PGA, EGA, PainVAS, TJC, CDAI, SDAI, mHAQ scores, mental component summary scores (MCS), and role-social component summary scores (RCS) in SF-36 were significantly higher than in patients without neuropathic-like pain. In multivariable analysis, significant differences were seen in the SJC (OR 0.690), TJC (OR 1.625), physical component summary scores (PCS) (OR 0.958), MCS scores (OR 0.937), and RCS scores (OR 0.958) in SF-36.【Conclusion】These findings suggest that neuropathic-like pain in patients with RA is associated with low SJC and high TJC, and an exacerbated QOL.

W26-2

Analysis of cognitive impairment in elderly patients with rheumatoid arthritis

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Conflict of interest: None

Background/Purpose:To evaluate the cognitive impairment in elderly patients with RA, we assessed the cognitive assessment examination. Methods: 129 patients with elderly RA (over 65 years old), analysis of frequency, clinical course, comorbidities, treatment, HAQ-DI, and laboratory data in RA patients with cognitive impairment. 65 RA patients without cognitive impairment were examined by MMSE and Moca-J. Results: RA 129 patients mean age 74.3±6.8, disease duration 9.8±3.8 years, diagnosis of cognitive impairment 26.4%. 62 RA patients without cognitive impairment MMSE 26.3±2.5. In 5 patients mild cognitive impairment, Moreover MCI was diagnosed by Moca-J examination in 32 elderly patients with RA. Elderly RA MCI was correlated with bone change X ray examination TSS, MMP-3 and HAQ-DI by multivariate logistic regression analysis. These data may suggest that risk of cognitive impairment in elderly RA patients was correlated with ADL disorders and RA disease activity. Conclusion: The assessment of cognitive function in elderly RA is a important step in treatment of disability by arthritis. To evaluate of the effect of RA treatment on prevention of cognitive impairment, a prospective analysis is needed for the useful in elderly RA therapy.

W26-3

Factors to disturb accomplishment of treat to target strategy (T2T) in rheumatoid arthritis (RA)

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Conflict of interest: None

【OBJECT】We often experience a situation that achievement of clinical remission and functional remission is difficult in RA patients with articular destruction caused by their long disease duration. Therefore, we

thought that we could contribute to efficiency of RA treatment by clarifying factors to disturb treatment accomplishment. 【METHOD】We examined data for 388 RA patients who passed more than 3 months from the day when treatment was changed and had consultation by July from January, 2016. We performed the listening comprehension investigations such as onset time, the the 1st treatment starting date. And we calculated time required for until various events such as 1st consultation from their onset. Furthermore, we collected data until the last observation, such as disease activity and using drugs, and examined by logistic analysis for factors to influence the achievement of the treatment target. 【RESULT】In treated with MTX and PSL off, and about the duration until 1st consultation, we found statistical significant high achievement rate of treatment target. 【CONCLUSION】We indicated that practice of Treat to Target strategy from early RA, treatment with MTX, and PSL reduction were important for an achievement of clinical deep remission.

W26-4

Analysis of patient reported outcome in feet of rheumatoid arthritis: KURAMA cohort study

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Conflict of interest: Yes

Object; In rheumatoid arthritis (RA) patients with clinical remission, subclinical synovitis often exists using ultrasound (US) in MTP joint. The purpose of this study is to clarify the relationship between patient-reported outcome (PRO) and US detected subclinical synovitis in midfoot and hindfoot. Methods; 446 RA patients were included. US were performed. The target joint were ankle, Chopard, Naviculo-cuneiform, Lisfranc, and 2-5MTP. PRO of foot and ankle were performed using SAFE-Q. Results; In 208 patients with DAS28 remission, US detected subclinical synovitis was more frequent in midfoot and hindfoot than in forefoot. To compare PD-positive with PD-negative in midfoot and hindfoot, there were statistically difference in pain VAS, morning stiffness, Stage, and Class. Pain score, physical function score, and shoe related score in SAFE-Q were statistically lower in PD-positive than in PD-negative of midfoot and hindfoot, but were not statistically differences of forefoot. Conclusions; In RA patients with remission, US detected subclinical synovitis was more frequent in midfood and hindfoot than in forefoot. In patient detected subclinical synovitis of midfoot and hindfoot, there were statistically differences in pain VAS and PRO.

W26-5

Consideration between the depressive state and the patient backgrounds in rheumatoid arthritis (RA)

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Conflict of interest: None

[Object] 181 female and 38 male RA patients were surveyed during May~June in 2016. QIDS-J questionnaire was used for self-assessment and evaluated. [Result] 46.2% mild to severe depressive symptoms existed. No difference of severity of the depressive state in the genders. Elderly patients were more depressive in both oral medicated group (OM) and biologics treated group (BIO), female BIO was milder depressive than female OM. There were strong relations between the disease period and the decrease of the non-depressive state in OM and also between the disease period and the increase of the non-depressive state in BIO. No relation was recognized between the variations of biologic agents and the depressive state. Disease period was tend to be related to the depressive severity. No apparent relation was seen between RA severity and the depressive severity. [Discussion] Severity of the depressive state is considered to be related to the patient age and disease period, but the good control of the pain and the stability of RA symptom are more important than the disease period in BIO. [Conclusion] Patient age and the disease period were related to the severity of the depressive state. Non-depressive patients tend to increase in BIO and to decrease in OM in the long disease period patients.

W26-6

Ultrasound evaluation after joint surgery in patients with rheumatoid arthritis

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Conflict of interest: None

[Purpose] We evaluated arthritis after joint surgery in patients with RA by using ultrasound, which has been used for systemic evaluation of the disease. [Patients & Methods] Four patients with RA who underwent surgery in our hospital from January to July in 2016 were examined before and at the times of 1 and 3 months after surgery. All patients were women, average age was 59 and average disease duration was 10 years. The performed surgery was TKA, THA, right wrist arthroplasty and bilateral knee arthroscopic synovectomy. Sonographer performed ultrasound for 26 and 16 joints of the upper and the lower limbs, respectively. Power Doppler grade 1 and Gray Scale grade 2 or more were defined as arthritis. The number of arthritis and DAS 28-CRP (4) were investigated. [Results] In all cases, arthritis improved after surgery. An average number of arthritis decreased from 8.3 to 6.5 and 3.0, before and at the times of 1 and 3 months after surgery, respectively. An average DAS 28-CRP (4) decreased from 3.75 to 3.30 and 2.76, before and at the times of 1 and 3 months after surgery, respectively. [Conclusion] Evaluation by ultrasound is considered as an useful method after surgery because it is possible to detect on synovitis directly and is objective evaluation.

W27-1

Erythrocyte MTX-polyglutamates levels of RA patients in remission are related to polymorphisms in genes associated with MTX-efficacy

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Conflict of interest: None

[Object] Dosage of MTX, required to suppress disease activity, varies among patients and is unpredictable. Here, we measured MTX-polyglutamates (MTX-PG) levels in erythrocytes using LC-MS/MS, and investigate their relation to MTX dosage and also to 9 polymorphisms reported for associations with MTX-efficacy by us. [Methods] Concentrations of MTX-PGn in erythrocytes were detected by LC-MS/MS (collaborated with Dr. Shinohara, Kobe University). MTX-PGn levels were measured for 125 RA patients in remission with stable dosage of MTX, and also the 9 SNPs including 5 SNPs in MTX-PG related genes were identified by RT-PCR. [Results] Total concentrations of MTX-PGn were 82.1±31.7 nmol/L (mean±SD), and positively correlated with the dosage of MTX (Rs= 0.410, $p < 0.001$), but there were several cases with lower MTX-PG concentration. Among the 9 SNPs, 2 SNPs, 1 SNP, and another SNP were associated with total PGs, PG_3, and PG_1/PG_2, respectively. Three SNPs were associated with the dosage of MTX required to maintain the effective concentration. [Conclusions] We detected the erythrocyte MTX-PG concentration in 125 RA patients in remission with MTX, and speculated association of MTX-PG concentration with polymorphisms in not only MTX-PG related genes but also efficacy-related genes.

W27-2

Serum 14-3-3η levels Predicts responsiveness to tocilizumab in patients with RA

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Conflict of interest: Yes

[Background] Whether serum levels of 14-3-3η, direct and potent inducer for IL-6, are predictive marker for the responsiveness to tocilizumab (TCZ) in RA was estimated. **[Methods]** Serum 14-3-3η levels were measured in a cohort of 106 Japanese patients. 14-3-3η positivity was defined as ≥0.19 ng/ml, 0.40, and 0,80 ng/ml respectively. Patients were sub-grouped based on a change in HAQ of ≥0.22, 0.31, and 0.49. **[Results]** 71% of enrolled patients with RA were 14-3-3η positive at baseline. At year 1 after TCZ therapy, 70, 58 and 52 of the 106 patients achieved changes in HAQ of ≥0.22, 0.31, and 0.49, respectively. Serum 14-3-3η levels were significantly lower in patients achieving HAQ MCID of 0.31 & 0.49. In patients achieving a DHAQ ≥ 0.49, the best cut-off of 14-3-3η levels was ≤0.18 ng/ml by ROC analysis. Univariate analysis revealed lower levels, at all 3 14-3-3η cut-points, were significantly associated with better HAQ outcomes. Multi-variable modeling controlling for BL HAQ revealed that lower 14-3-3η levels, age & disease duration were independent predictors of achieving the HAQ MCID outcomes. **[Conclusions]** Lower serum 14-3-3η levels prior to the initiation of TCZ therapy are associated with better patient reported outcomes in RA patients treated with TCZ.

W27-3

The Value of Longitudinal Measurement Serum IL-6 in Rheumatoid Arthritis Patients under Biologics Treatment

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Conflict of interest: None

We have reported the usefulness of IL-6 quick measure system in RA in JCR 2014. Therefore, we aimed to examine the value of longitudinal measurement of serum IL-6 in RA patients under biological treatment. 30 RA patients (Tocilizumab[TCZ]:13, Etanercept[ETN]:17) were measured serum IL-6, we examined the correlation between serum IL-6 and clinical parameter of RA. Next, we examined the correlation between delta serum IL-6 and delta clinical parameter in TCZ cases. Finally, we examined the factor that serum IL-6 became low value. There were a correlation between serum IL-6 and clinical parameter in ETN (DAS28-ESR:r=0.457, CDAI:r=0.35), but no correlation in TCZ (DAS28-ESR:r=0.268, CDAI:r=0.213). There were a correlation between delta serum IL-6 and delta clinical parameter in TCZ (⊿DAS28-CRP:r=0.445, ⊿CDAI: r=0.418). The factors that serum IL-6 low value were DAS28-ESR, DAS28-CRP and drug dose. Longitudinal measurement of serum IL-6 can lead to dose individualization of BIO.

W27-4

Influence of flare after loading of certolizumab pegol on treatment outcome for rheumatoid arthritis

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Conflict of interest: None

[Objectives] The present study was undertaken to investigate the influence of flare after loading of certolizumab pegol (CZP) on treatment outcome in RA patients. [Methods] This study included 96 RA patients treated with CZP in Tsurumai Biologics Communication Registry. Patient characteristics, transition of DAS28-ESR and low disease activity rate after 52 weeks were compared between flare group (with higher DAS28-ESR for the eighth week than the fourth week: n=37) and non-flare group (with lower DAS28-ESR: n=59). In flare group, we performed multivariate analysis for contributory factors to low disease activity after 52 weeks. [Results] Patient characteristics showed no significant difference between both groups. DAS28-ESR was significantly lower in non-flare group from the eighth week on. (the eighth week: 3.7 vs 3.0, p=0.02; the 52th week: 3.6 vs 2.9, p=0.01) Low disease activity rate after 52 weeks tended to be higher in non-flare group. In flare group, biologic naïve was extracted for contributory factor to low disease activity after 52 weeks. (OR 35.8, 95%CI=3.1-416.3) [Conclusions] Disease activity is not improved in patients with flare after loading of CZP. However, in flare group, CZP has more efficacy in biological naïve patients than switch patients.

W27-5

The significance of measuring drug concentration in blood during treatment with Infliximab

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Conflict of interest: None

Purpose: To elucidate the significance of measuring IFX concentration during treatment of rheumatoid arthritis (RA) patients with Infliximab (IFX). **Materials and Methods:** The subjects were 51 RA patients (11 male, 40 female) treated with IFX. Their ages ranged from 26 to 81 (mean age: 59.5). Cryopreserved serum was used to measure IFX concentration using the ELISA method. The IFX concentration was measured in ineffective cases at the time when the medication was switched to another drug and in the effectively treated cases in December 2013. **Results:** Treatment was effective in 36 cases and ineffective in 15 cases. Of the effectively treated cases, the concentration was higher than 1 μg/ml in 19 cases (mean: 4.58). In 17 of the effectively treated cases the concentration was lower than 1 μg/ml. Also, the concentration was higher than 1 μg/ml in 4 out of the 15 cases in which the treatment was ineffective. In the 11 cases of ineffective treatment the concentration was lower than 1 μg/ml. **Conclusions:** During IFX treatment there are many effective cases in which the IFX concentration is lower than 1 μg/ml, and therefore measurement of the IFX concentration is not considered necessary for clinical assessment.

W27-6

Predictors of response to methotrexate in early rheumatoid arthritis: results from MRC RA cohort

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Conflict of interest: None

Objective: To identify predictors of response to methotrexate (MTX) in early rheumatoid arthritis (RA). Patients and Methods: Among MRC Rheumatoid Arthritis cohort, baseline and 6 month data were used from patients with disease symptom duration <1 year who started MTX. Multivariable logistic regression analyses were used to identify significant predictors of not achieving SDAI remission at 6 months. Results: At 6 months, 35 of 54 (65%) patients did not achieve SDAI remission. Independent predictors of not achieving SDAI remission was higher patient global VAS (adjusted OR 1.42, 95% CI 1.06 to 1.84). Conclusion: Higher patient global VAS predict a worse response to MTX in patients with new-onset RA.

W28-1

Osteophyte size in knees of patients with rheumatoid arthritis increased by anti-TNF inhibitor

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Conflict of interest: None

Cases of secondary osteoarthritis (OA) in knee joints of rheumatoid arthritis (RA) patients following a total knee arthroplasty (TKA) are increasing. We analyzed 33 knees in 29 RA patients (25 females, 4 males; mean age 62.4 years; mean disease duration 18.5 years) who underwent TKA from January 2013 to August 2016, including preoperative AP view radiographs of the knee joint. Using the ImageJ software package, osteophyte size in the medial femur (MT), medial tibia (MT), lateral femur (LF), and lateral tibia (LT) regions was determined. The mean femorotibial angle (FTA) was 179˚, while Larsen grade was 2 in 1, 3 in 12, 4 in 18, and 5 in 2. Osteophyte size in the MF, MT, LF, and LT regions was 86.2, 50.6, 49.1, and 24.6 mm^2, respectively. Medial compartment size (MF+MT) was significantly correlated with FTA ($r=0.658$, $p<0.001$), while lateral compartment size (LF+LT) was correlated with disease duration ($r=0.406$, $p=0.019$). Total osteophyte size (MF+MT+LF+LT) in patients who received anti-TNF treatment (n=11) was significantly greater ($p=0.0136$). Our results suggest that secondary osteoarthritis can progress in RA and use of an anti-TNF inhibitor likely increases osteophyte size.

W28-2

The change of the CRP value before and after TKA and persistence of chronic inflammation

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Conflict of interest: None

[Objective] The ratio, diagnosis and the treatment of abnormal CRP value before and after TKA were surveyed. [Patients and methods] 503 knees of 452 cases were able to follow up over 6 months after TKA. They included 80 male and 372 female, 430 OA, 52 RA and 21 ON. Average age was 75.2 years old and follow-up period was 3.2 years. CRP value was examined before TKA, and at 1 week, 4weeks after TKA. A blood was taken periodically when an abnormal value appeared, and the cause was investigated when the abnormal value continued. The treatment and the clinical course were surveyed by the medical records. [Results] 41 cases (9.1%) showed high CRP value before TKA, including 32 RA, 4 postoperative states for opposite knees and 5 unknown origins. As for 66 cases (14.6%) that showed high CRP value at 4 weeks after TKA, 22 cases of those became negative without any treatment at 2 or 3 months after TKA. Remaining 44 cases included 32 underlying RA, 5 infection at other lesions, 3 newly contracted RA, 1 malignant lymphoma and 3 undifferentiated state. There were no cases that diagnosis of SSI established. [Conclusion] Follow-up of high CRP value is important as not only a monitor of the SSI but also a marker of chronic inflammation due to TKA.

W28-3

The positive correlation between serum MMP-3 and Rooney score in RA and OA with hydrarthrosis

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Conflict of interest: None

Serum level of MMP-3 is useful for monitoring synovitis in Rheumatoid arthritis (RA). In histopathological examination, synovitis in osteoarthritis (OA) with hydrarthrosis was similar to those in RA. In previous study, there was no correlation between Rooney score and serum MMP-3 in RA, but the validation has not been. Therefore, we aimed to examine the validation. 40 patients (RA:18, OA:22) were evaluated Rooney score, we examined the correlation between Rooney score and serum MMP-3. Multiple regression analysis was also examined (objective variable: serum MMP-3, explanatory variable: each item of the Rooney score). Further the OA examined devided into with hydrarthrosis group and without hydrarthrosis group. There was positive correlation between Rooney score and serum MMP-3 in RA ($r=0.61$, $p<0.01$). Fibrosis and Perivascular infiltrates of lymphocytes were significant factor in multiple regression analysis. There was positive correlation between Rooney score and serum MMP-3 in OA with hydrarthrosis group ($r=0.66$, $p<0.05$). Against previous reports, Rooney score and serum MMP-3 was correlated. OA with hydrarthrosis is similar to RA.

W28-4

Clinical efficacy of patient specific template for short stem in THA

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Conflict of interest: None

Bone preservation of the proximal femur is an important issue in primary total hip arthroplasty (THA) for future revision surgery. Short stems can be a potential resolution for this problem. However, it is difficult to acquire appropriate intramedullary contact of short stem and to insert short stem precisely according to the preoperative planning. There are wide variations in shape and concept of short stem . Some clinical results of short stem were reported in the literature. Survivorships are relatively high for two to six years after operation. However, early revision rate of short stem is various stem by stem in midterm results. It is significant to get appropriate intramedullary contact in order to achieve good primary fixation of short stem. However, there are few reports on three dimensional (3D) digital analysis and patient specific template (PST) for short stem. The purpose of the present study is to investigate efficacy of PST on clinical score, complications and bone reactions in short stem for THA.

W28-5

Reconstruction of the hip joint for the patient with rheumatoid arthritis using cemented total hip arthroplasty

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Conflict of interest: None

(Objective) In our institute, we have performed THA for all patients including the patients with rheumatoid arthritis (RA) using cemented implants. In current study, we aim to demonstrate the advantage of cemented THA for the patients with RA. **(Patients and methods)** From January 2006 to December 2014, we had performed 98 cemented THA for 82 patients with RA in our institute. There are 12 males (14 joints) and 70 females (84 joints). The mean age was 64.1 years old. All surgeries were performed via direct lateral approach using all polyethylene socket and polished tapered stem with antibiotic-loaded acryl cement (ALAC). We evaluate survivorship of implants, clinical results, and the occurrence of adverse events. **(Results)** There was only one revision for postoperative multiple dislocation. The mean of JOA hip score was improved 39.3 points preoperatively to 83.4 points and 86.2 points postoperatively 2 and 5 years respectively. Postoperative dislocation had occurred 5 joints including the case mentioned above. **(Conclusion)** It has been considered that even in the patient with RA by using ALAC and appropriate cementing technique the predicted problems; aseptic loosening and deep infection; were able to overcome.

W28-6

Factors affecting recovery of muscle strength after THA

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Conflict of interest: None

Background. There has been a controversy over how hip center affects the muscle strength after total hip arthroplasty (THA). **Methods**. We evaluated 65 patients who underwent unilateral primary THA with a normal contralateral hip. Muscle strength of hip abductor, hip flexor, and knee extensor was evaluated using handheld dynamometer. The ratio of strength of the affected side to that of the contralateral side was calculated as strength ratio. The horizontal and vertical center of rotation (H-COR

and V-COR) was defined as the distance from the hip center to the tip of the teardrop. The vertical shift (V-shift) was defined as a difference in V-COR between the affected hip and the contralateral normal hip. **Results**. There was no significant correlation between H-COR and abductor muscle strength. No significant correlation was observed between V-COR and postoperative recovery of muscle strength ratio. When V-Shift was divided into 4 subgroups (< 5 mm, 5 to 10 mm, 10 to 15mm, > 15 mm), no significant differences in hip abductor muscle strength were observed between groups. **Conclusion**. Superior placement of a hip center, at least less than 15mm above the true hip center, did not affect the postoperative recovery of muscle strength.

W29-1

A case of severe adult onset Still's disease with interstitial pneumonitis which responded well to IVCY after tocilizumab therapy failed

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Conflict of interest: None

Case: a 73-year-old woman was diagnosed as having adult onset Still's disease (AOSD) complicated by hemophagocytic syndrome 6 months before admission. Because she did not improve by methylprednisolone pulse therapy (mPSL) followed by prednisolone (PSL) p.o., cyclosporine A (CyA) and plasma exchange (PE), tocilizumab (TCZ) of 8mg/kg of every 2 weeks was introduced. Then her condition was improved and PSL and CyA doses were tapered and the interval of TCZ was reduced to 4 weeks. Two months later, however, she was admitted to our hospital because of relapse of AOSD. In spite of increase of the frequency of TCZ infusion (every 2 weeks), PSL and CyA doses and PE, CyA being replaced by tacrolimus (TAC) later, her condition did not completely improved, and serum ferritin level stayed over 400 ng/ml after PSL dose was reduced to 40mg /day. Furthermore, interstitial pneumonitis was complicated and we decided to cease TAC and TCZ, and IVCY started. Later, her symptoms and interstitial pneumonitis gradually improved and ferritin level normalized. Reports have been rare on the strategy for severe AOSD cases resistant to TCZ. We present with a case in which IVCY managed to succeed in overcoming the disease activity of AOSD resistant to a combination therapy.

W29-2

The first characteristic symptoms of adult onset Still disease

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Conflict of interest: None

Objective: The first symptoms of adult onset Still disease (AOSD) are confusing with those of common cold, which could lead to the delay of the diagnosis. The aim of this study was to clarify the characteristic symptoms of AOSD at the onset. **Methods:** We retrospectively collected AOSD patients visiting our hospital after March 2012 with enough information of onsets in their charts. **Results:** A total of 26 patients were enrolled. The mean age at diagnosis is 44.3±19.7 and female 73%. The duration from the first symptoms to diagnosis was 34.7 days, from the first symptoms to the first visit to medical facility was 9.8 days, and from the first visit to the first blood test was 5.3 days. Fever was found in all patients, pharyngalgia and arthralgia in 88.5%, skin lesion in 84.6%, white blood cell (WBC) count increase in all patients, lymphadenopathy, liver enzyme elevation and ferritin elevation in 80.8%. Skin lesions preceded the diagnosis by 29.0 days, fever and pharyngalgia by 26.0 days, arthralgia by 22.3 days. WBC increase by 16.8 days, lymphadenopathy by 12.9 days, liver enzyme elevation by 10.3 days, ferritin elevation by 9.5days. **Conclusions:** Our analysis revealed skin lesion was an important initial manifestation as well as common cold-like symptoms in new-onset AOSD patients.

W29-3

Two Cases of Multicentric Catsleman Disease with Cystic Lung Lesions

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Conflict of interest: None

Case 1: A 48-year-old man visited our hospital for abnormal lung shadows at a medical checkup. But, he stopped attending to a hospital. Two years later, he urgently admitted to our hospital because of dyspnea and bloody sputum. Laboratory tests revealed anemia, elevated CRP, abnormal urinalysis, and polyclonal hyper γ-globulinemia (Glb). Serum IL-6 was 33.2 pg/mL. CT scan showed multiple cystic lung lesions and systemic lymphadenopathy. Pathological findings of his axilla lymph node showed hyperplasia of germinal center and a marked infiltration of plasma cells in the interfollicular area. Case 2: A 39-year-old male visited our hospital for renal disorder at a medical checkup. Laboratory tests revealed anemia, elevated CRP, abnormal urinalysis, and polyclonal hyper γ-Glb. Serum creatinine and serum IL-6 were elevated to 3.55 mg/dL and 33.2 pg/mL, respectively. CT scan showed multiple lung cysts and systemic lymphadenopathy. Pathological findings of his axilla lymph node showed hyperplasia of germinal center and a prominent infiltration of plasma cells in the interfollicular area. He received tocilizumab twice a month His serum creatinine decreased to 1.62 mg/dL 16 months later. Conclusion: Castleman disease should be reminded when a patient presents with multiple lung cysts.

W29-4

TAFRO syndrome successfully treated with tocilizumab: 2 case reports

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Conflict of interest: None

Case1: A 66-year-old man was referred to our clinic with anasarca, fever, thrombocytopenia, renal insufficiency and lymphadenopathy. He had the same symptoms 3 years ago. He had been treated with steroids until 1 years ago. TAFRO syndrome was suspected, and pulse steroid therapy was initiated followed by tocilizumab (TCZ). Although TCZ was administered only once due to the persistent neutropenia, his symptoms were improved. After 6 months, disease activity flared up during steroid tapering, however, it could be controlled with pulse steroid therapy and 3 courses of TCZ. Now, he has been in remission with steroid therapy alone. Case2: A 42-year-old woman presented to our clinic with fever, thrombocytopenia, renal insufficiency, pleural effusion, ascites, and lymphadenopathy. TAFRO syndrome was strongly suspected. Pulse steroid therapy and TCZ were immediately started, and she got better gradually. The pathology of her lymph node biopsy was compatible with Castleman's disease. The diagnosis of TAFRO syndrome was made. She has been in remission with steroids and TCZ. TCZ is continued because her serum IL-6 level remains mildly elevated. These cases suggest the efficacy of TCZ for TAFRO syndrome. Further studies are needed to assess the adequate dose and the discontinuation of TCZ.

W29-5

A case treated with secukinumab for psoriasis associated with IgA nephropathy

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Conflict of interest: None

A 60-year-old male was diagnosed as psoriasis four years ago. He was started adalimumab treatment two years after the diagnosis. However, the treatment came to failure after one year treatment. Proteinuria and urinary occult blood were observed at that time. After a treatment of psoriasis with secukinumab (a human anti-IL-17A monoclonal antibody), an activity of psoriasis was remitted and the intensity of proteinuria and hematuria were also improved. Although psoriasis kept remission after the treatment, severe proteinuria (14 g/g·Cr) with pitting edema was exacerbated again one year later. He was admitted to our hospital and a renal biopsy was performed. Mesangial proliferative glomerulonephritis with cellular crescents were observed under light microscopy. Moreover, immunofluorescence and electron microscopy indicated that the presence of IgA and β1c in the mesangial and paramesangial area. According to these findings, we diagnosed the case as IgA nephropathy. The treatment with secukinumab was continued after admission, and the edema and proteinuria improved (1~2 g/g·Cr). We reported here a case treated with secukinumab for psoriasis associated with IgA nephropathy.

W29-6

The association between initial glucocorticoids doses and a therapeutic response for patients with polymyalgia rheumatica

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Conflict of interest: None

[Purpose] Polymyalgia rheumatica (PMR) is characterized by a rapid response to glucocorticoids. The recommended initial glucocorticoids doses in Europe and the United States are 12.5–25 mg prednisone (PSL) equivalent daily, whereas the appropriate initial dose for Japanese is not clear. This study aims to examine the association between initial PSL doses and therapeutic responses. [Methods] Thirty-one PMR patients diagnosed from 2012 at our hospital by Bird criteria or 2012 EULAR/ACR criteria were analyzed retrospectively. The mean age was 75.6± 1.5 years (15 male and 16 female). A good therapeutic response was defined as the disappearance of clinical symptoms of PMR and enabling PSL tapering within the first 4 week. [Results] The mean initial dose per kg in good responders was 0.27 ± 0.02 mg and 0.21 ± 0.03 mg for poor responders, respectively. The percentage of poor responders was significantly increased in the group of < 0.20 mg/kg compared with that treated with ≧ 0.20 mg/kg (3/23 (14%) vs 5/9 (56%); $P = 0.016$). Other patient demographics were similar between the two groups. [Conclusions] Initial PSL doses per kg in poor responders were significantly lower than in good responders. These results suggest that a dose of ≧ 0.20 mg/kg is required as initial therapy for PMR.

W30-1

Use of serum ferritin and heme oxygenase 1 for the classification of adult-onset Still's disease: 3rd report of multicenter study

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Conflict of interest: Yes

[Object] To evaluate the use of measuring serum ferritin and heme oxygenase (HO)-1 levels for the diagnosis of adult-onset Still's disease (AOSD). [Methods] A total of 107 AOSD cases whose diagnosis was judged by 3 experts' opinion, and 41 disease controls were enrolled. Serum ferritin and HO-1 levels were measured in all of the collected samples by means of ELISA. An association among clinical symptoms, serum ferritin, and HO-1 was explored. [Results] Serum ferritin and HO1 levels were significantly higher in active and relapsed AOSD cases. In remission patients, whose serum ferritin were normal, 20.6% exhibited high HO-1 levels. Remission-induction therapy normalized serum ferritin levels in most of the cases, but more than half of them had high HO-1 levels. ROC analysis revealed cutoff values of serum ferritin >833 ng/ml (sensitivity 77.5%, specificity 81.1%) and HO-1>96.4 ng/ml (sensitivity 92.5%, specificity 81.1%), for the diagnosis of AOSD. Multivariate analysis showed typical rash, persistent high-grade fever, sore throat, and either ferritin/ HO-1 high, were factors independently associated with AOSD. [Conclusions] We confirmed that serum ferritin and HO-1 serve as a biomarkers useful to classify AOSD. (UMIN000012912).

W30-2

A case of TAFRO syndrome who had various symptoms and had difficulty in diagnosis

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Conflict of interest: None

[Case] A 49 years old woman. In March 201X, she complained of general malaise and temperature. Malignant lymphoma or Castleman's disease was suspected by lymphadenopathy and high IL-6 (13.9pg/ml), but biopsy did not lead to diagnosis, only Sjogren's syndrome was confirmed. Afterwards, pleural effusion, ascites, heart failure, urine protein had appeared. POEMS syndrome was suspected by hyperserumVEGF (969pg/ml), hypothyroidism, hemangioma. TAFRO syndrome was suspected by Thrombocytopenia, Anasarca, Fever and Organomegaly, but Reticulin fibrosis wasn't found. In August, increasing ascites and hepatic venous pressure suggested the possibility of Budd-Chiari syndrome, but stenosis wasn't clear. In September, reticulin fibrosis was confirmed, therefore she was diagnosed TAFRO syndrome. After PSL60mg and CyA150mg was started, the pleural effusion and ascites decreased markedly, IL-6 and VEGF decreased. [Clinical Significance] In this case, since various symptoms had exhibited, the differential diagnosis was diversified, and it took some time to establish definite diagnosis. It is often reported that to distinguish TAFRO syndrome and POEMS syndrome, Castleman disease is difficult, and that various symptoms recognized in this case may be related to TAFRO syndrome.

W30-3

Clinical features of old onset adult onset Still's disease

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Conflict of interest: None

[Objectives] Adult onset Still's disease (AOSD) is a systemic inflammatory disorder that is characterized by skin rash and arthritis with high fever. Though most of them are young onset cases, we often experience old onset cases. The present study aimed to clarify the clinical features of old onset AOSD. [Methods] 4 old onset AOSD cases (all women) that

admitted to our hospital from 2015 to 2016 were analyzed retrospectively. We investigated clinical characteristics and treatments. [Results] The median age of disease onset was 78±1.2 years old. All cases had high fever and polyarthritis on proximal joints. All cases had brown and keratotic eruptions on trunk and proximal limbs. Any case showed typical evanescent eruption of light pink papules. All cases were attempted to skin biopsy. Histopathological findings revealed superficial dermal lymphocytic infiltration in common. Colon cancer was discovered by general examination in one case. High dose corticosteroids were used for initial therapy in all cases. [Conclusions] We confirmed that old onset AOSD cases tend to have brown and keratotic eruptions on trunk and proximal limbs. Similarity of histological finding of these lesions was established. These results indicate that old onset AOSD is separable from traditional AOSD.

W30-4

A women with Macrophage-activation syndrome in adult-onset Still's disease occurred after tocilizmab therapy, but remitted spontaneously

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Conflict of interest: None

A 62 year-old woman was admitted to previous doctor on September 20XX, because of fever, arthralgia, and skin rash. Serum ferritin revealed 9193ng/ml. She was diagnosed adult-onset Still's disease (AOSD). Steroid pulse therapy, and high-dose PSL and cyclosporine (CyA) started, but fever and elevated serum ferritin didn't improved. As intractable AOSD, tocilizmab (TCZ) started. But 5 days after started TCZ, ferritin elevated to 21899ng/ml and thrombocytopenia appeared. She was suspected to be developed Macrophage-activation syndrome (MAS). And she changed to our hospital on November 20XX, for appling plasmapheresis. But serum ferritin decreased and platelets increased when she came to our hospital. We continued PSL and CyA, and didn't applied plasmapheresis after all. Bone marrow biopsy conducted at previous doctor revealed hemophagocytic cells. After that, disease activity of AOSD decreased. She discharged on January 20XX+1. We continue PSL tapering, and she could be maintananced low dose of oral PSL and CyA. Although there are many effective reports of TCZ for intractable AOSD which is treated with steroid and immunosuppressants, we should be careful that few reports of MAS induced by TCZ also exist. This is a first case that MAS induced by TCZ was remitted spontaneously.

W30-5

A case report: PET-CT can be useful to the assess activity of upper airway lesions of relapsing polychondritis

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Conflict of interest: None

A 64-year-old woman was diagnosed with relapsing polychondritis (RP) 1 year ago. She was successfully treated with prednisolone (PSL) 30 mg/day. She felt her right eye congested and pain 3 months before, and cough and sputum 2 months before. She was prescribed antibiotics, but the symptoms were not improved. Therefore she was admitted to our hospital. On admission, congestion of right eye was continued, and she had tenderness around left ear canal. Laboratory findings showed increased CRP. A chest CT revealed hypertrophy of tracheal cartilage. PET-CT revealed FDG uptake in the larynx and trachea of the thyroid level. We diagnosed her as relapse of RP based on tracheal chondritis, scleritis and otitis externa. She was treated with PSL 50 mg/day and intravenous cyclophosphamide, after that her symptoms immediately improved. Tracheal hypertrophy and FDG uptake disappeared by PET-CT after 34 days from admission. Half case of RP have the airway lesions, and these cases thought to be severe because tracheal stenosis can be cause of death by airway obstruction. In this case, chest CT can't detect larynx and upper trachea lesion, but PET-CT clearly revealed these active lesions. PET-CT is useful modality to detect for the lesions especially in larynx and upper airway.

W30-6

Characteristics of 17 patients with paraneoplastic rheumatic disease

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Conflict of interest: None

Objective: This study was conducted to evaluate the correlation of malignant neoplasm and paraneoplastic rheumatic disease. Methods: A total 29 consecutive patients of rheumatic disease with malignant neoplasm between 2011 and 2016 in Nagasaki Medical Center. Clinical manifestations and therapeutic courses were retrospectively reviewed. Results: In all, 9 males and 8 females with a mean age of 70.8±6.7 years. 6 patients had a hematological malignancy, and 11 a solid cancer (colon 5, stomach 3, bile duct 1, prostate 1, brest 1, neuroendocrine 1). 6 patients developed polymyalgia rheumatica, 4 rheumatoid arthlitis, 2 RS3PE syndrome, 3 dermatomyositis, 1 microscopic polyangiitis and 1 relapsing polychondritis. 9 of 17 malignancies were diagnosed at the same time of rheumatic diseases. 10 patients were received chemotherapy and 7 were operation. As the treatment of rheumatic disease, 15 patients were received corticosteroid. 2 patients died of malignancy, and 2 did infection.

W31-1

Biologic Disease-Modifying Anti-Rheumatic Drug Use and the Risk of Non-Vertebral Osteoporotic Fractures in Japanese Patients with Rheumatoid Arthritis: Results from the IORRA Cohort Study

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Conflict of interest: None

[Object] Our objective was to determine the association between biologic DMARD use and the risk of non-vertebral osteoporotic fractures in Japanese patients with RA. **[Methods]** A nested case-control study was conducted using the IORRA cohort. RA subjects were followed from cohort entry until the earliest non-vertebral osteoporotic fracture at elbow, forearm, hip, humerus, pelvis, shoulder, and wrist. Controls were matched to cases (4:1 ratio) by age, sex, and date of cohort entry. Biologic DMARD exposure was defined as being on treatment for ≥ 180 days pre-fracture (index). Conditional logistic regression was used to assess the association between biologic DMARD use and the risk of non-vertebral osteoporotic fractures. **[Results]** Over the study period, 565 cases were identified (2,822 controls). The most common fracture sites were hip (25%). In total, 230 subjects were exposed to biologic DMARDs. We were unable to demonstrate an association between biologic DMARD use and fracture risk (hazard ratio 1.1; 95% CI, 0.8-1.7). Baseline JHAQ disability index, daily prednisone dose, and bisphosphonate use were significantly associated with fracture risk. **[Conclusion]** We were unable to demonstrate a reduction in the risk of non-vertebral osteoporotic fractures in Japanese patients with RA.

W31-2

Change in bone mineral density in patients with rheumatoid arthritis after a 10-year follow-up

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Conflict of interest: None

[Object] To investigate the long-term change in bone mineral density (BMD) in patients with rheumatoid arthritis (RA). [Methods] We analyzed 43 patients with RA who measured BMD at baseline and after more than 10 years. BMD of the lumbar spine and femoral neck measured as percent young adult mean (YAM). The mean age was 59.6 years old and the mean disease duration of RA was 11.6 years. Female was 91%. We compared differences between the osteopenia group (BMD < 80% of YAM) and the normal group (BMD ³ 80% of YAM) at baseline. [Results] Lumbar spine YAM was 85.0% at baseline and increased in 91.9% after 10 years, while femoral neck YAM was 80.0% at baseline and decreased in 77.3% after 10 years. Femoral neck YAM in the osteopenia group at baseline slightly increased from 71.3% at baseline to 73.3% after 10 years, and in the normal group significantly decreased from 93.2% at baseline to 82.4% after 10 years. The intervention rate of osteoporosis treatment in the osteopenia group was higher than that in the normal group. [Conclusions] Even the normal group of BMD should be aggressively started osteoporosis treatment in RA patients who was decreased BMD.

W31-3

Effect of bisphosphonate on osteoporosis in patients with rheumatoid arthritis – minodronate vs risedronate

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Conflict of interest: None

[Objectives] We evaluated effect of minodronate on osteoporosis for patients with rheumatoid arthritis (RA) in comparison with risedronate. [Method] RA patients who were diagnosed as osteoporosis were enrolled in this study. Patients were treated with monthly administration of minodronate (n=36) or risedronate (n=34). Bone mineral density (BMD) of lumbar spine and femoral neck were measured by dual-energy x-ray absorptiometry. Bone turnover markers including serum TRACP-5b, NTX and BAP were elevated. [Results] BMD was significantly increased from baseline level in both treatment groups. However, there was no significant difference between two treatment groups. Bone turnover markers were significantly decreased from baseline level in both treatment groups. Change in bone turnover markers was significantly greater in minodronate group than in risedronate group. [Conclusion] This study suggested that minodronate is as effective as risedronate for treatment of osteoporosis in RA patients.

W31-4

Factors influencing lumbar and femoral bone densities in patient with rheumatoid arthritis

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Conflict of interest: None

[Objectives] Rheumatoid arthritis (RA) is a diseases to cause a decrease in bone mineral density (BMD). Various factors of inflammation, age, menopaus, glucocorticoid (GC) are related at the onset. We examined various factors influencing lumber and femoral BMD of RA patients. [Methods] Sixty-eight RA patients (average age 68.4 y/o, male/female=16/52) were subjected to the measurement of lumbar and femoral bone mineral density (BMD) by DXA and examined influencing factors including age, gender, RA activity and medications. [Results] 67.5% and 64.7% of patients were treated with MTX and GC, respectively. The means of lumbar and femoral BMD were 87% and 84% from YAM, respectively. Patients were divided into two groups: group A femoral>lumbar BMD, group B femoral <lumbar BMD. Lumbar and femoral BMD in each group was 80% and 95% in group A and 96% and 78% in group B. Patients of group B had longer duration of disease and higher RA activity compared to group B. Gender, age, and BMI were similar in both groups. Marker of bone resorption, TRACP5b of group B was higher than that of group A. [Conclusion] Decreased femoral BMD in RA patients is associated with high disease activity, long duration of RA and elevated TRACP5b level.

W31-5

Effect of TNF inhibition on systemic and local bone loss

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Conflict of interest: None

【Object】The aim of this study is evaluate this issue from published studies assessing the effect of treatment with TNF inhibitors on systemic and local bone loss using FIRST registry which is our university cohort of over 2, 500 RA patients treated with biologics.【Methods】We investigated that effect of TNF inhibitors on disease activities, bone metabolism (urine NTx, bone ALP) and local osteoporosis (hand BMD) besides systemic osteoporosis (lumbar, femoral BMD) in RA patients.【Results】RA patients with TNF inhibitors (IFX 54, ADA 69) with MTX (exclude patients on Bisphosphonates (BPs), 5% of the patients on corticosteroids) showed younger age, less damage of ADL but higher disease activities despite of higher dose of MTX compared with those of MTX alone. TNF+MTX markedly reduced disease activity and u-NTx compared with those in MTX alone. TNF inhibitors suppressed Hand (UD) BMD and increased BAP significantly in patients who achieved clinical remission. Concomitant use of BPs inhibited both systemic and local osteoporosis.【Conclusion】TNF inhibitors suppressed activation of osteoclasts well in comparison with MTX alone. Use of TNF inhibitors in the treatment of RA was associated with improvement of hand BMD, but had no significant effect on lumbar spine and hip BMD.

W31-6

Effect of treatment of biologic agents for 10 years on bone mineral density in rheumatoid arthritis patients

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Conflict of interest: None

[Objectives] The purpose of this study is to examine the effects of treatment of biologic agents for 10 years on bone mineral density (BMD) in RA patients. [Methods] Twenty six patients (23 women, three men) with active RA who have been treated with biologic agents for more than 10 years were analyzed. The mean age of the patients was 55.8 years old, and the mean duration of disease was 11.9 years on average. Clinical evaluation and laboratory data showed high disease activity of RA, including SDAI of 33.4, mHAQ of 1.11, ACPA of 106 U/ml, rheumatoid factor of 203 mg/dl. Mean value of amount of steroid and methotrexate is 5.0 mg/day and 4.1 mg/week, respectively. Assessment includes dual x-ray absorptiometry scans of the lumbar spine and femoral neck, and yearly change of BMD for 10 years was calculated. [Results] In these RA patients, treatment of biologic agents for 10 years significantly reduced clinical parameters. Mean values of BMD have been maintained for 10 years in both lumber spine and femoral neck. Especially in patients treated with bisphosphonate in addition to biologics, BMD was significantly increased. [Conclusion] BMD of RA patient is maintained by the biologics administration for 10 years and further increases by combination therapy of bisphosphonate.

W32-1

Comparison of clinical and laboratory features of patients with and without allergic conditions in IgG4-related disease: a single-center experience in Japan

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Conflict of interest: None

Objective: To compare the clinical and laboratory features of IgG4-RD patients with and without allergic conditions. *Methods:* We retrospectively examined the clinical and laboratory features of 45 patients with IgG4-RD, with reference to the presence of allergic conditions. *Results:* Of the 45 patients, 18 (40%) had allergic conditions. Males accounted for 7 (38.9%) of the 18 in the allergic group and 19 (70.4%) of the 27 in the non-allergic group (p=0.036). The mean age at diagnosis was 61.9 yr in the allergic group and 71.6 yr in the non-allergic group (p=0.003). Kidney disease was evident frequently in the non-allergic group, and there was no significant difference in the frequency of involvement of other organs. The ratio of the total number of affected organs in the upper body (head, neck and thoracic area) to that in the whole body was 79% in the allergic group and 56% in the non-allergic group. There was no significant inter-group difference in the absolute number of peripheral blood eosinophils, or the levels of serum IgG4 and IgE. *Conclusions:* Eosinophilia, and high serum levels of IgE and IgG4 are common features in IgG4-RD patients regardless of allergy, although there may be some clinical differences according to the concomitant allergic conditions that are present.

W32-2

Successful treatment with rituximab in two cases of IgG4-related ophthalmic disease

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Conflict of interest: None

Most of Patients with IgG4-related ophthalmic disease (IgG4-RD) are recovered by prednisolone (PSL) administration though a few cases will relapse during gradual reduction of PSL. rituximab (RTX) has been reported to be effective in these PSL resistant cases, thus we report here two cases of PSL-resistant IgG4 related eye disease who are successfully treated with RTX. (Case 1) A 44-year-old man, caused onset with orbit swelling and retro-bulbar tumor, was diagnosed as IgG4-RD by orbital biopsy. Symptoms once recovered by PSL pulse therapy but relapsed when relieving PSL to 10mg. After introduced RTX, he achieved partial clinical resolution at 1 month. Serum IgG4 decreased from 750 to 279mg/dl, and tumor and inflammation image on MRI disappeared at 6 month. (Case2)A 61-year-old woman caused onset with orbit swelling, and once recovered by PSL (30mg/day). She underwent dacryoadenectomy when PSL was reduce to 10mg/day. Thereafter, RTX was introduced since limitation of eye movement and diplopia occurred by extraocular myositis when PSL was reduce to 5mg/day. After RTX administration, she achieved clinical resolution at 1 month. Serum IgG4 decreased from 350 to 134mg/dl, and extraocular myositis on MRI improved at 6 month.

W32-3

Process and purpose of 2016 ACR/EULAR Classification Criteria for Primary Sjogren's Syndrome

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Conflict of interest: None

Introduction AECG classification was used as a gold standard for Sjogren's syndrome (SS) diagnosis. SICCA-ACR classification has been published in 2012. In order to solve double standard in SS diagnosis, international SS diagnostic criteria working group was organized. Material and method 1. Extensive data analysis was conducted based on 3514 cases of SICCA, 837 cases of Oklahoma study and 1011 cases of Paris-Sud cohort. 2. Criteria items were selected by MCDA. 3. 1196 cases were diagnosed as SS confirmed cases on 3 steps of examination (vignette study). 4. Diagnostic items were scored according to the importance. 5. The validity of the new diagnostic criteria was examined by ROC analysis. Result Under the new criteria, a case with a score of > 4 is diagnosed as SS, when the weights from the 5 criteria items below are summed. 1. Anti-SSA/Ro positive (score 3) 2. focus score of ≧1 (score 3), 3. ocular staining score 5 or more in at least one eye (score 1) 4. Schirmer's test ≤ 5 mm / 5 min (score 1) 5. saliva flow rate 0.1 ml / min or less is 1 point each (score 1) Conclusions The new ACR / EULAR classification criteria has good sensitivity and specificity, 96% and 95%, respectively. From now on, SS diagnosis in Japan should be conducted according to the new ACR / EULAR classification.

W32-4

Verification of cutoff value of the chewing gum test in criteria for Sjogren's syndrome (SS)

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Conflict of interest: None

We reported that the immunosuppressive therapy is valid in the early stage of the SS, but effectiveness attenuates in the example of progress and it becomes irreversible. The early treatment is preferable to aim at the remission and healing. In a current Japanese criteria, when the The salivary flow rates stimulated by chewing gum is 10ml /10min. or more, the SS is often denied. The result of the chewing gum test was reported that there was no difference by the modality of the chewing gum. Afterwards, when acetous strong chewing gum is used diagnosis utility rises when the setting of the cutoff value is adjusted from 10ml /10min. to 14ml/min. It becomes possible to diagnose an earlier SS in case of this setting. We verified the cutoff value when the chewing gum of the mint taste used well in the this hospital and another facilities. In 278 cases that receive the labial minor salivary gland biopsy being doubted the SS, the accuracy to the diagnosis of the chewing gum test using the chewing gum of the mint taste was calculated. When the accuracy to the Japanese criteria of each 1ml is calculated from 10ml. 54.6% in case of 10ml, 56.7% in case of 13ml. It is necessary to unite chewing gum in the criteria for the SS and set the cutoff value again. /10min

W32-5

Clinical and immunological features of anti-centromere antibody positive Sjögren's syndrome

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Conflict of interest: None

Object: Anti-centromere antibody (ACA)-positive Sjögren's syndrome (SjS) is considered as a distinct clinical subgroup in SjS. The purpose was to clarify clinical and immunological features of ACA-positive SjS. Methods: Patients with positive ACA were enrolled. Clinical information were collected and statistically analyzed. Results: 198 patients were enrolled. 142 patients were classified into any autoimmune disease. 59 and 19 patients were diagnosed with systemic sclerosis (SSc) without SjS and SSc/SjS cases. 33 patients were diagnosed with primary SjS. Raynaud's phenomenon and sclerodactyly were less frequent in SjS patients. Dryness symptoms were more frequent in SjS patients. Anti-SS-A antibodies were positive in 39% of SjS patients, which were higher than SSc patients. Peripheral leukocyte count in SjS patients was lower than in SSc patients. Leukocyte count and C4 in anti-SS-A antibody positive SjS patients were lower than the negative patients. Conclusions: ACA-posi-

tive cases were dominantly classified into SSc and/or SjS, presenting different clinical characteristics. Additional anti-SSA may determine leucocyte and neutrophil count in ACA-positive patients.

W32-6

A case of paraneoplastic IgG4-related disease associated with gastric cancer

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Conflict of interest: None

A 67-year-old man noticed bilateral swelling of his lacrimal glands and dry eye in 20XX-2. He then developed the bilateral swelling of submandibular glands since October 20XX, and he was referred to our hospital. The serum IgG4 level was elevated (835mg/dl), and a PET-CT showed diffuse FDG uptakes in salivary glands and pancreas. The histological examination of minor salivary gland and pancreas showed lymphoplasmacytic infiltration with IgG4+/IgG+ plasma cells 85% and 80%, respectively. He was diagnosed with IgG4-related Mikulicz's disease and definite autoimmune pancreatitis. Through the general screening examination, a gastric tumor was found and diagnosed as early gastric cancer histologically and a distal gastrectomy was carried out. After the gastric surgery, the bilateral swelling of his lacrimal and submandibular glands as well as enlargement of the pancreas improved gradually. The histological examination of resected specimen of the gastric cancer revealed IgG4-positive plasma cell infiltration (the IgG4/IgG ratio of the cancer lesion was 26.6%). This is an important case regarded as genuine paraneoplastic IgG4-RD. Our cases of IgG4-RD patients with malignancies including the present case indicate a close relationship between IgG4-RD and malignancy development.

W33-1

Evaluation of clinical prognostic factors of interstitial pneumonia in anti-melanoma differentiation-associated gene 5 (MDA5) antibody (Ab) positive dermatomyositis patients

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Conflict of interest: None

[Objectives] We retrospectively investigated the clinical prognostic factors of interstitial pneumonia (IP) in anti-MDA5 Ab-positive dermatomyositis (DM) patients. [Methods] Subjects were 18 patients (13 were clinically amyopathic DM, 16 were acute/subacute IP, 9 were died of IP). [Results] In the death group, the initial serum albumin levels was significantly lower than in the survivor group (2.9 vs. 3.6 mg/dl, $P = 0.033$) and the serum ferritin levels and the ground-glass opacity (GGO) scores of the right middle lobes were significantly higher (1010 vs. 426 pg/ml, $P = 0.013$, and 3 vs 0.7, $P = 0.005$). The initial P[A-a]O_2 were also higher in the death group than in the survivor group (50.4 vs. 29.9 mmHg). The survival rate after 24 weeks were lower in patients with an initial serum albumin level of ≤ 3 mg/mL (25%), a serum ferritin level of ≥ 450 ng/mL (25%), a P[A-a]O_2 of ≥ 30 mmHg (30.8%), a right middle lobe GGO score of ≥ 2 (GGO ≥ 5% of the lobe) (11.1%). [Conclusions] Initial serum albumin, ferritin level, P[A-a]O_2, and right middle lobe GGO score predict the prognosis in anti-MDA5 Ab-positive DM-IP patinets.

W33-2

The long term outcome of acute/subacute progressive interstitial pneumonia with dermatomyositis / polymyositis

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Conflict of interest: None

Objective: To evaluate long term outcome of acute/subacute progressive interstitial pneumonia with dermatomyositis/polymyositis (DM/PM-A/SIP). Methods: We assessed long term outcome of 59 DM-A/SIP patients started to treat in Osaka medical College or Yodogawa Christian Hospital between March 2003 and September 2015. Results: The mean of age, gender ratio (female) were 61.3±12.1 years old, 69.5%, respectively. Of the 59 cases, 40 cases were diagnosed as clinically amyopathic dermatomyositis,17 cases were DM, 2 cases were polymyositis. Anti-MDA5 antibody positive were 13 cases and anti-ARS antibody positive were 20. Fifty eight cases were initiated with PSL and calcineurin inhibitor (cyclosporine 49 cases, tacrolimus 9 cases). Intravenous cyclophosphamide pulse therapy (IVCY), intravenous gammaglobulin were used in 35 cases, 11 cases, respectively. Twenty one cases were dead. The causes of death were divided into interstitial lung disease (12 cases), infection (5 cases), cancer (3cases), and SLE (1 case). The mean follow-up period was 1045 days and cumulative survival at 5 years was 60.5%. Conclusion: The prognosis of DM/PM-A/SIP treated with calcineurin inhibitor or IVCY has been improved. But management of infection after immunosuppressive treatment is an important subject.

W33-3

ADAM-17 is expressed in the inflammatory myopathy, and is involved with interstitial lung disease

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Conflict of interest: None

【Object】A disintegrin and metalloprotease (ADAM) -17 is a one of the proteases, and is involved in autoimmune disease. Here, we have shown the expression of ADAM-17 in inflammatory myopathy.【Method】ADAM-17 in inflammatory myopathy serum (polymyositis (n=26), dermatomyositis (n=34), and clinically amyopathic dermatomyositis (n=10)) was measured using ELISA. The association with clinical manifestations and clinical data were examined. ADAM-17 expression was determined in muscle tissues from DM using immunohistological staining. ADAM-17 expression in lung fibroblasts was also determined using immunohistological staining and ELISA.【Result】ADAM-17 in inflammatory myopathy was significantly higher than in healthy control. ADAM-17 was decreased after treatment with corticosteroid and/or immunosuppressant. ADAM-17 in interstitial lung diseases (ILD) was significantly higher than in non-ILD. We found the expression of ADAM-17 in muscle biopsy tissue. ADAM-17 in IL-6 and IL-6 receptor stimulated lung fibroblast conditioned medium was elevated compared with in non-stimulated lung fibroblast conditioned medium.【Conclusion】ADAM-17 is expression in inflammatory myopathies especially ILD, suggesting that ADAM-17 may play the role in lung fibrosis.

W33-4

Myalgia in patients with dermatomyositis and polymyositis is attributable to fasciitis rather than myositis

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Conflict of interest: None

Objectives. To determine the association between fasciitis and the clinical parameters in patients with dermatomyositis (DM) and polymyositis (PM). **Methods.** We retrospectively reviewed the medical records of

patients with newly diagnosed DM and PM and in whom fascia and muscle specimens were histopathologically examined. The relationship between fasciitis and the clinical parameters was statistically analyzed. These parameters included age, sex, myalgia, muscle enzyme levels, anti-Jo-1 antibody, interstitial lung disease, and malignancy. **Results.** Twenty of the 32 patients who underwent the histopathological examination of a fascia specimen, had fasciitis, including: 18 of 24 DM patients and 2 of 8 PM patients. The frequency of fasciitis was significantly higher among the DM patients than among the PM patients. The frequency of myalgia in patients with fasciitis was significantly higher than that in patients without fasciitis. However, myalgia was not associated with myositis. There were no significant differences in the other clinical parameters in the patients with and without fasciitis. **Conclusions**. The frequency of fasciitis was significantly higher among patients with DM than those with PM. Fasciitis, rather than myositis, was associated with myalgia.

W33-5

Angiogenesis and high expression of VEGF, identified from the early phase of dermatomyositis-associated fasciitis

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Conflict of interest: Yes

Objective: To investigate whether angiogenesis and VEGF expression are demonstrated in the fascia from the early phase in dermatomyositis (DM) and which factor is involved in VEGF expression. **Methods:** We evaluated 22 DM patients and 11 polymyositis (PM) patients. Immunohistochemical stains for CD31, VEGF, and TNF-α were performed. Total vascular inflammation score (TVIS), angiogenesis score (AS), and numbers of VEGF and TNF-α positive cells were analyzed in the fascia and muscle. **Results:** The AS and the number of VEGF positive cells were significantly greater in the fascia of DM patients compared with PM patients, while no difference in the muscle between the DM and PM patients. The number of VEGF positive cells correlated with the AS in the fascia of DM patients. In the early phase of DM, the AS and the number of VEGF positive cells were significantly higher in the fascia compared with the muscle, however, no difference in the late phase between the muscle and fascia. In DM patients, the TVIS correlated with the AS in the fascia. The number of TNF-α positive cells correlated with the TVIS and the number of VEGF positive cells in the fascia of DM patients. **Conclusion:** The VEGF expression level in the fascia of DM was higher from the early phase and correlated with angiogenesis.

W33-6

Intracellular signaling and kinetic analysis of peripheral blood T cells in dermatomyositis and polymyositis

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Conflict of interest: None

Objective. To investigate intracellular signaling and kinesis of peripheral blood T cells (PBTC) in dermatomyositis (DM) and polymyositis (PM). **Methods.** Fifty-seven patients with DM, 29 with PM, and 23 healthy controls were enrolled. Phenotypes and proliferation of PBTC after stimulating T cell receptor (TCR) were analyzed by flow cytometry. Transcriptional activators (STATs) and some inhibitory factors in T cells were also detected by qRT-PCR. **Results.** The expressions of STATs, FoxP3, and phosphorylated ZAP70 (pZAP70) in CD4+ cells were significantly decreased in DM. Those of STAT3 and pZAP70 in CD8+ cells were significantly increased in PM. Increase of SOCS3 and decrease of IL6ST in CD4+ cells were significantly shown in both DM and PM. DM patients with interstitial pneumonia and cutaneous ulcer indicated significant decrease of STATs and IL6ST in CD4+ cells, which recovered after clinical remission. **Conclusion.** Intracellular signaling via TCR stimulation in CD4+ cells was suppressed in DM, whereas that in CD8+ cells was activated in PM. Suppressive activity of CD4+ cells may be implicated in prognostic factors in DM. Meanwhile, activation of CD8+ cells in PM is suggestive of forming characteristic histology based on CD8+ cells invasion into muscle tissue from peripheral blood.

W34-1

Analysis of the effect of early introduction of adalimmab (ADA) and bio-free condition (BF) in patients with rheumatoid arthritis (RA)

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Conflict of interest: Yes

Purpose: To analyze the effect of early introduction of ADA (within 3 M from the introduction of MTX) and BF in RA patients. Methods: Among 152 patients (M25, F127) who received ADA, 28 (M1, F27) started ADA as an early introduction. Two patients switched to tocilizumab due to inefficacy and achieved clinical remission (CR). One patient developed interstitial pneumonia and stopped both MTX and ADA. We analyzed 20 patients (age 51±9 years, disease duration 14.2±27.4 months) who were followed up more than 52 W. Results: DAS28-CRP decreased from 4.38±0.91 to 1.72±0.50 ($p<0.001$). Seventeen patients achieved CR (85%), and 8 patients (40%) achieved BF. One patient relapsed and re-started ADA, but achieved CR again and wanted BF with the adjustment of csDMARDs. MTX (mg/W) was significantly increased from 7.3±2.1 to 9.5±3.6 ($p< 0.00679$), The numbers of csDMARD other than MTX were 0.90±0.64 to 1.35±0.81 ($p=0.065$). One patient discontinued bucillamine due to proteinuria. PSL (mg/day) was 2.1±3.1 to 1.5±1.8 ($p=0.33$). Three patients with CR did not want BF. Four patients with sustained CR wanted BF and discontinuation of ADA was already scheduled. Conclusion: Early introduction of ADA was effective and it might be a good choice in terms of medical cost due to BF.

W34-2

Factors that associate with the maintenance of biologics free remission in daily clinical practice − ANSWER cohort study −

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Conflict of interest: Yes

【Objectives】Biologics can be discontinued after achieving remission in some rheumatoid arthritis (RA) patients keeping the remission with cDMARDs. In this study, we tried to determine the factors that associate with the maintenance of biologics free remission (BFR) in daily clinical practice.【Methods】Disease activity was monitored in 101 RA patient whose biologics were discontinued after achieving DAS28 remission. We generated survival curve until they failed to maintain DAS28 remission or restarted biologics. Factors associated with the maintenance of BFR were studied by Log rank test and cox proportional hazard model.【Results】BFR was maintained in 23% of all the patients after 1 year of bio-

logics discontinuation. Maintenance of remission for more than 6 months before biologics discontinuation (p<0.0001), use of anti-TNF antibodies (p=0.0003), disuse of glucocorticoids at the time of discontinuation (p=0.012), Boolean remission at the time of discontinuation (p=0.013), etc. were found to be associated with BFR by Log rank test, and the former three items remained independent factors after multivariate analysis. 【Conclusion】BFR can be achieved after the maintenance of long term remission with anti-TNF antibodies with no use of glucocorticoids.

W34-3

Bio free remission in early rheumatoid arthritis THE RAINBOW STUDY (second report)

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Conflict of interest: None

Objective Early RA patients who discontinued biologics (bio) for rheumatoid arthritis after achieving clinical remission were enrolled, and the rate of bio-free remission was assessed 1 year after discontinuation of bio. Methods Early RA patients were treated with either Infliximab (IFX; n=32)or Tocilizumab (TCZ; n=54), and if patients were fulfilled our criteria of remission (DAS28ESR<2.6, and the dose of prednisolone≦5mg/day) for over at least 6 months, they discontinued bio. If they were still fulfilled the remission criteria one year after discontinuation of bio, we define them as bio-free remission. Result Fifty one RA patients could be assessed 1 year after baseline. Nineteen patients could discontinue bio fulfilling remission criteria for 6 months within 2 year. Then 13 of 19 patients achieved bio-free remission after 1 year discontinuation. Conclusion This is our second report of THE RAINBOW STUDY, study of bio free remission in early rheumatoid arthritis in two years. Our result suggested that early intervention of bio might raise the possibility for bio free remission.

W34-4

Tapering biological therapy in patients with rheumatoid arthritis in the real world

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Conflict of interest: None

Objectives: It is shown, mostly in clinical trials, that many rheumatoid arthritis (RA) patients who achieved clinical remission are able to taper biological disease-modifying antirheumatic drugs (DMARDs) therapy. However little is known about its prevalence in the real world. This study investigates the frequency of biologics dose reduction and patients characteristics associated with tapering in our hospital. Methods: We retrospectively reviewed clinical charts of 120 consecutive patients (age63.4±14.4 y.o., female 85.8%, disease duration 12.2±7.8 years), who were treated with biologics more than 6 months. Clinical characteristics, X-ray, and concomitant DMARD use were examined. Results: 68 (56.7%) patients were treated with standard dose and 47 patients (39.2%) treated with reduced dose of biologics. Five patients (4.2%) experienced disease flare after tapering biologics after 8.4±5.7months. There were no differences in onset of age, disease duration, and X-ray between two groups. Patients with dose reduction compared with standard dose had received significantly less biologics (p=0.0002), and longer treatment duration (p=0.0287). Conclusion: Tapering of biologics might be achieved especially in RA patients treated for a considerable time with first biologics.

W34-5

Identification of factors associated with maintenance of clinical remission after discontinuation of certolizumab pegol: Post-hoc analyses of C-OPERA study

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Conflict of interest: Yes

Objective: To identify factors associated with maintenance of clinical remission (REM) after discontinuation of certolizumab pegol (CZP) treatment. Methods: MTX-naïve early RA patients (pts) were randomized to CZP+MTX (n=159) or placebo +MTX (n=157). After completing 52-week (wk) double-blind period, MTX therapy without CZP continued up to Wk104 (PT period). Pts who were initially randomized to CZP+MTX and entered PT period (CZP+MTX→MTX; n=108) were included in post-hoc logistic regression analyses which investigated factors associated with Wk104 REM. Results: DAS28 (ESR) (DAS28), SDAI, and Boolean REM rates were 77.8%, 79.6%, and 61.1%, respectively, at Wk52, and 54.6%, 55.6%, and 46.3%, respectively, at Wk104 (LOCF). Wk52 DAS28 was associated with Wk104 DAS28, SDAI, and Boolean REM (OR: 0.30, 0.24, 0.36); Wk52 RF was associated with Wk104 SDAI and Boolean REM (OR: 0.67 and 0.69). Pts with combination of low DAS28 and low RF at Wk52 showed high Wk104 remission rate. Radiographic non-progression rate achieved during CZP+MTX treatment was maintained after stopping CZP (linear extrapolation). Conclusion: Both low disease activity and low RF at CZP discontinuation were associated with maintenance of clinical REM. Radiographic non-progression was observed even after CZP discontinuation.

W34-6

Discontinuation of Biologics in Forty Patients with Rheumatoid Arthritis: A Single-Center Three-Year Prospective Observational Study – Analysis of Coincidence Rate of Affected Joints at Relapse –

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Conflict of interest: None

[Objectives] With the biologics, many patients with rheumatoid arthritis (RA) can achieve remission. Although some patients maintain bio-free remission, more than half of the patients will relapse in the long-term observation. There is no report of analysis of the coincidence rate of affected joints at relapse. [Methods] We registered 40 RA patients who maintained of clinical remission (DAS28-CRP < 2.3) for more than a

year. If the patients had more than low disease activity, the patients dropped out of this study. Patients who remained in remission were observed for up to 3 years. The coincidence ratio of the affected joints at relapse was analyzed by comparing the 28 joints. [Results] Fourteen (35%) patients remained remission for three years and 26 (65%) relapsed during the observation period. The median (minimum - maximum value) of tender joints before the start of the biologics and at the relapse after bio-free remission was 5 (1-15) and 3.5 (1-11). The swollen joints were 5 (1-10) and 2 (1-8). The coincidence ratio of the swollen and tender joints at relapse was 100 (0 to 100) (%). The mean ± standard deviation was 70.4 ± 37.5 (%). [Conclusion] In this analysis, the affected joints showed a high coincidence ratio at the relapse after bio-free remission.

W35-1

Significant association between renal function and area of amyloid deposition evident in kidney biopsy specimens in both AA and AL amyloidosis

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Conflict of interest: None

[Object] To clarify the correlation between the area occupied by amyloid in renal tissue, renal pathological findings, and clinical parameters in AA and AL amyloidosis. **[Methods]** One-hundred and sixteen patients with AA and AL amyloidosis were participated in this study. For statistical analyses, the percentage area of amyloid deposition was transformed to a common logarithmic value. In addition, renal pathological findings were evaluated in the study. **[Results]** Results of sex-, age-, and Log_{10}%amyloid-adjusted analyses showed that systolic BP was higher in the AA group. RBC count and Ht were lower in the AA group. In relation to renal function, Cr, Ccr, and eGFR indicated significant impairment in the AA group, whereas UP indicated significant impairment in the AL group. In the renal pathological findings, amyloid in the AL group was significantly deposited in the glomerular capillary wall, whereas in the AA group, amyloid was deposited in the arteriole walls and small artery significantly. **[Conclusions]** There are significant differences between AA and AL amyloidosis with regard to the association between the amyloid-positive area in renal tissue and renal function, especially Ccr, eGFR and UP. These differences could be attributed to the pattern of amyloid deposition.

W35-2

Incidence of chronic kidney disease and disease activity in patients with RA

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Conflict of interest: None

OBJECTIVES: Chronic inflammation is one of risk factor of the incidence of Chronic kidney disease (CKD). We assessed the association between incidence of chronic kidney disease and disease activity in patients with RA. MATERIALS AND METHODS: Patients were divided into two groups: group 1, including patients that their average disease activity score 28-erythrocyte sedimentation (DAS28-ESR) was <3.2 and group 2, the patients that their average DAS28-ESR was >3.2. The outcome was incidence of CKD, defined as an estimated glomerular filtration rate (eGFR) <60ml/min/1.73m2 and/or quantity of uric protein >1.5g/gCr. Using a propensity score–matched patients, we evaluated incidence of CKD using Kaplan-Meier curves, and calculated hazard ration using Cox proportional hazards models. RESULT: 128 RA patients (group 1: n=64, group 2: n-64) were extracted. The incidence of CKD in group 1 was higher than that in group 2. High average DAS28-ESR was an independent predictor of the incidence of CKD (hazard ratio, 2.117; 95% confidence interval 1.143-4.751, p=0.049). CONCLUSION: High disease activity was a significant risk factor for incidence of CKD.

W35-3

Cluster analysis of pulmonary lesions in rheumatoid arthritis; clinical features of the clusters and their response to biological DMARDs

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Conflict of interest: None

Object: To determine patterns of the existence of pulmonary lesions in rheumatoid arthritis (RA) by cluster analysis, and to clarify the clinical features of each cluster, particularly the effects of biological DMARDs (bDMARDs) on pulmonary abnormalities. **Methods:** Subjects were 208 RA cases who started bDMARDs from Feb. 2004 to Sep. 2015 in our department and received HRCT scan before and after bDMARD therapy. Pulmonary lesions were classified into 20 categories and examined their existence and distribution. Cluster analysis was conducted by the existence of the lesions and clinical features of each cluster was analyzed. **Results**: Imaging findings before bDMARDs therapy were reticular pattern; 19.2%, curved linear opacity; 6.7%, bronchiolitis; 40.4% and bronchioectasis; 41.3%. They were classified into 6 clusters. 1; bronchiolitis and bronchiectasis (15.9%), 2; bronchiectasis (9.6%), 3; reticular pattern and bronchioectasis (12.5%), 4; no pulmonary lesions (41.3%), 5; bronchiolitis (13.9%) and 6; curved linear opacity (6.7%). Pulmonary lesions were excerbaterd in all clusters at 33-36% in frequencies during bDMARDs. **Conclusion:** Interstitial lung lesions are frequently associated with bronchiectasia. bDMARDs treatment failed to improve pulmonary lesions in many cases.

W35-4

Clinical characteristics and predictors of the development and recurrence of organizing pneumonia associated with rheumatoid arthritis

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Conflict of interest: None

Objective: To reveal the clinical features of organizing pneumonia (OP) in rheumatoid arthritis (RA), the relationship between OP development and RA exacerbation, and the predictors of OP relapses. **Methods:** We retrospectively analyzed 33 RA-OP patients admitted to our hospital over 2006–2016. **Results:** RA preceded OP in 82% of cases, and OP preceded or co-occurred with RA in 9% each. OP first occurred at 62.9 ± 11.6 years of age, 12.2 ± 13.6 years after RA onset. Although bilateral shadows are typical of OP, 42% showed unilateral shadows. Twenty-seven relapses were observed in 10 cases (30%) during prednisolone tapering; the recurrence-free period was 21.9 ± 27.4 months. RA was exacerbated in 18% of cases at OP onset and was controlled well in 52%. Comparisons of 10 recurrent cases and 14 cases that were recurrence-free for more than 6 months showed that the recurrent cases included significantly more OP-preceding cases (30% vs. 0%; p = 0.03) and smokers (80% vs. 36%; p = 0.03). The age at first OP occurrence was lower (59.5 vs. 67.1 years; p = 0.053) and bilateral shadows were more frequently observed (89% vs. 50%; p = 0.056) in the recurrent cases. **Conclusions:** OP mostly develops independent of RA exacerbation, and OP-preceding cases or smokers are at high risk for OP relapses.

W35-5

51 cases of lymphoproliferative disorder in patients with RA treated with MTX

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Conflict of interest: None

[Object] To characterize MTX-LPD and to consider optimal treatment after occurrence of LPD in pts with RA. **[Methods]** We retrospectively evaluated 51 RA pts with LPD from 2006 to 2015. MTX-LPD pts were divided into two groups regarding to the status of LPD after MTX cessation; regressive LPD (R group) and persistent LPD (P group), and the clinical characteristics, clinicopathological features, and outcomes were compared. **[Results]** Although there was no significant difference in disease duration, stage, and disease activity of RA and the positive rate of EBERs (half of both groups), age of LPD onset (59 vs 68), CRP (2 vs 5), and the weekly MTX dose (10.9 vs 8.4) significantly differed between the groups. Among R-group, 3 pts developed DLBCL later. P-group showed poor prognosis and high short term mortality. An older age and anemia were poor prognostic factors. Of 51 pts, 41% achieved sustained low disease activity (LDA) with other DMARDs except MTX. Of note, Tocilizumab contributed to sustained LDA in nine pts (90%) and showed high retention rate. **[Conclusion]** From our findings, it seems unreasonable to be lump persistent-group into the same category as MTX-LPD. EBV infection and IL-6-signaling are likely to play a role in the development of LPD in pts with RA.

W35-6

Risk of herpes zoster in patients with rheumatoid arthritis in biologics era

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Conflict of interest: None

[Object] To elucidate the incidence and risk factor for herpes zoster (HZ) in rheumatoid arthritis (RA) patients in the IORRA cohort. [Methods] The incidence of HZ was extracted based on patient's self-report in the surveys from 2010 to 2015 and confirmed by the medical records. The standardized incidence rate (SIR) with 95%CI was calculated and risk factors for HZ were analyzed using Cox regression analysis. [Results] A total of 7,815 patients (female 84.7%) with median [IQR] age 61.0 [49.7-68.9] years and disease duration 10 [4-18] years were analyzed. Prednisolone was used in 36.8% with 4 [2-5] mg/day, methotrexate (MTX) in 70.4% with 8 [6-10] mg/week and biologics in 14.7%. Among 25,863 patient-years observation, 340 HZ events were confirmed in 309 patients. The SIR per 1,000 patient-years was 8.5 (95%CI 6.9-10.5) in total, 6.0 (95%CI 3.7-9.2) in male, 11.0 (95%CI 8.7-13.7) in female. The hazard ratio (HR) for HZ was age (HR 1.14, 95%CI 1.03-1.26, $p<0.05$), J-HAQ 0.5-1.5 (reference 0) (HR 1.51, 95%CI 1.09-2.10, $p<0.05$), MTX use (HR 1.58, 95%CI 1.06-2.36, $p<0.05$), biologics use (HR 1.88, 95%CI 1.44-2.47, $p<0.01$). [Conclusion] The drugs for risk of HZ were MTX and biologics in this study in the era when potent antirheumatic drugs especially biologics are frequently used.

W36-1

Nursing Intervention through foot care VAS (Visual Analogue Scale) ~ Sweet Cohort~

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Conflict of interest: None

As EULAR 2016 recommendation encourage foot care, we have been engaged in foot care and studying association of foot issues with patient characteristics. While there has been reports on foot care VAS as patient reported outcome, there is a few study assessing association with patient background. Objectives: Here we report association of nursing intervention with foot care assessing with patient background and clinical characteristics. Methods: Sixty two patients treated for foot care through Jan 2016 to September are target for this analysis. We assessed association of Foot care VAS (overall, persistence, satisfactory; lower the score is, it is better) with various patient background (age, disease duration, class, stage, DAS, PtPVAS, and PtGHVAS) Results: Average foot care VAS is below 10 points and generally in good position. There is no correlation with age, disease duration, class, stage. Analysis on HAQ, DAS-28CRP, DAS28ESR, PtPVAS, and PtGHVAS showed that foot care VAS is significantly worse as disease activity and PtVAS are higher as well as among group comparison. Discussion: As patients with high disease activity showed worse foot care VAS, it is indicated that persistent nursing intervention through foot care is meaningful for patients at stable disease.

W36-2

Analysis on patients characteristics and foot care score in RA patients ~ Sweet Cohort~

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Conflict of interest: None

While biologics has changed RA landscape, any foot issues are not measureable that is persistent unmet medical need. Objectives: Purpose of this study is to translate foot issues into measurable foot score which are then analyzed for association with patient characteristics and clinical characteristics. Methods: Sixty two patients treated for foot care through Jan 2016 to September are target for this analysis. Foot care check list includes symptom, transformation, callus, and infection and those factors are analyzed for association with patient characteristics. Results: Overall foot care score is significantly higher in "progression class" and likely to be higher as stage is progression. There are significant correlation with age and disease duration and, strong correlation with HAQ is observed. There are also following correlation; symptom with DAS28-CRP and HAQ, transformation with disease duration, callus with disease duration, DAS28ESR, PtPVAS and PtGHVAS, and infection with age and HAQ. Discussion: Factors associated with foot care score are age, disease duration, and HAQ. Through our foot care score, association of foot issues in RA patients with patient characteristics was revealed. It is indicated that foot care intervention may improve further patient satisfaction.

W36-3

Chronological changes of background of the patients who needed surgery associated with rheumatoid arthritis: Analysis using the NinJa cohort

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Conflict of interest: None

[Object] Disease activity of the patients with rheumatoid arthritis (RA) seems to have become suppressed in a low level owing to biologics or strategy based on T2T. Although disease activities of patients registered in NinJa (National Database of Rheumatic Diseases by iR-net in Japan) are becoming lower year by year, chronological changes of preoperative disease activities of the patients who had surgeries are not clear. The object of this study was to explore recent changes of preoperative status of the patients with RA who had surgeries. [Methods] We extracted patients who had surgeries from NinJa, and chronologically compared DAS28-ESR, DAS28-CRP, pain VAS and mHAQ in each surgery. [Results] There was a trend of DAS28, pain VAS and mHAQ becoming lower in NinJa cohort. But in the group of patients who had surgeries, tendency of lowering was not observed after 2010. Regarding mHAQ in the group of all patients who had surgeries, there remained a tendency of lowering. Although DAS28 and pain VAS in patients who had total knee arthroplasty (TKA) were decreasing even after 2010, those in the group of patients who had total hip arthroplasty (THA) had no tendency of lowering after 2010. [Conclusions] TKA is performed in patients whose disease activity and mHAQ are lower than before.

W36-4

Association of alcohol consumption with disease activity in Japanese patients with RA using IORRA cohort

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Conflict of interest: None

[Object] To investigate the association alcohol consumption and change in disease activity in patients with rheumatoid arthritis (RA) longitudinally using the IORRA cohort. [Methods] Subjects were RA patients who consecutively participated in the IORRA study between 2014 to 2015. Patients were divided into 5 groups by alcohol drinking status at baseline; never-drinking (Group N, GN), and Group I (G1) (amount of drinking ≦ 14g/day), Group II (G2) (14-28g/day), Group III (G3) (28-50g/day) and Group IV (G4) (>50g/day). Multiple regression analyses were used to assess the relationship between status of alcohol consumption and change in DAS28 for 1 year. [Results] A total of 4,695 patients were analyzed. The number of the patients (%female, mean age and mean DAS28 at baseline) were GN: 2,735 (92.8%, 64.0, 2.7), G1:646 (89.9%, 58.7, 2.4), G2:497 (82.5%, 56.7, 2.3), G3:444 (71.6%, 56.4, 2.3), and G4:373 (58.2%, 57.5, 2.2), respectively. Baseline DAS28 in G2, G3 and G4 were significantly lower than that in the GN. There were no association between status of alcohol consumption and change in DAS28 for 1 year. [Conclusion] Alcohol drinking status was not associated with the change in following disease activity in 1 year.

W36-5

Supplemental Treatment of Rheumatoid Arthritis with Natural Milk Antibodies against Pathogenic bacteria: Linkage of Intestinal Flora Changes and the Therapeutic Effect of Milk Antibodies (UMIN CTR 000009492)

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Conflict of interest: None

Objective: Determining the linkage between intestinal bacteria changes and the therapeutic effect of milk antibodies in RA. **Methods**: Eightyseven patients with RA, whose DASESR value was 3.2 or greater, were divided into 3 groups, and treated with 600 mg of natural milk antibodies (Ab 600), 300 mg plus 10 g of skim milk (Ab 300) and 20 g of skim milk (Skim) every day for 12 weeks. Disease marker values were determined every 4 weeks, and fecal bacterial changes were determined by PCR analysis before and after 12 weeks treatment. **Results:** The populations of *B. fragilis, C. perfringens,* and *C. difficile* were significantly lower in the RA group compared to normal controls, whereas *S. aureus* was higher, indicating intestinal dysbiosis in RA. DAS28 -ESR was significantly reduced from 4.6 to 4.1 ($P<0.05$) during the first 4 weeks, and this effect remained until the 12th week in Ab 300 group, but not in other groups. DAS-ESR reduction in the Ab 300 group was associated with an increasing in the Lactobacillus population, but was associated with a decrease of Lactobacillus in the Ab 600 group. **Conclusion:** Milk antibody treatment influences intestinal bacterial flora, and consequently modifies disease activity. The roles of different types of bacteria toxins are currently under investigation.

W36-6

Rheumatoid Arthritis (RA) Patients Survey Regarding Generic (GE) and Bio-similar Drugs (BIO-S) – cohort study by Japanese clinician biologics research group-

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Conflict of interest: None

(Purpose) In Japan the market share for generic drugs is 50%. Why patients themselves turn down the opportunity to switch to GE is not clear. The use of BIO-S was approved, but the degree of patient knowledge regarding them is unknown. We carried out a patient survey about GE and BIO-S. (Methods) 4151 RA patients from 20 facilities participated. Patients were then asked their impressions of GE, their attitudes towards changing to a GE, questions regarding adverse effects with GE, their knowledge regarding BIO-S, and if they had any interest in or experience with using BIO-S. (Results)RA patients were 78% female (the majority in their 60s) and disease duration is over 10 years. Good impressions of GE were 41%, but bad impression is only 9.4%. RA patients who change to GE are 34%, but 24% patients don't change. 13% had heard of BIO-S, about half stated no interest in them, even after reading information. As for changing to a BIO-S, 63% said they would rely on physician opinion. 10% answered that they would switch for the cost benefits. (Conclusion)There is not enough education regarding BIO-S. The authors recommend that new avenues of patient education be explored, in order to help patients feel competent in making decisions about their medications.

W37-1

Predictive value of Matrix metalloproteinase (MMP)-3 for changes of modified total sharp score (mTSS) for one year in male patients with rheumatoid arthritis (RA)

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Conflict of interest: None

Purpose:MMP-3 is known as one of markers of joint destruction. In this study, we examined the association of MMP-3 level with findings of ultrasonography (US) and radiography. Methods:A total of 259 (213 females)patients with RA were enrolled. Baseline (BL) data and the date after one year from BL were collected and examined the association of MMP-3 level at BL with other BL data, including age, disease duration, bDMARDs use, prednisone (PSL) use, disease activity, mTSS, RF, CRP, power doppler score (PD) in US using Spearman's rank correlation coefficient. And also MMP-3 data at BL and changes (⊿) of other factors at one year from BL. Statistical analysis was performed separately by sex. Result:There were no correlation between MMP-3 level at BL and other

BL data in both genders. Correlation between MMP-3 level at BL and ⊿mTSS or ⊿JSN were statistically significant only in men. ⊿MMP-3 and ⊿mTSS or ⊿PD were correlated significantly in both. By multiple regression analysis MMP-3 level at BL was correlated independently with⊿mTSS in men (p=0.025). Conclusion: MMP-3 level at BL has a predictive value for deterioration of mTSS in one year only in men with RA. Because ⊿MMP-3 was also correlated positively with⊿PD and⊿JSN, high MMP-3 level is thought to be related to synovitis and chondrolysis.

W37-2

Chronological changes of achieving HAQ remission in patients with early stage of rheumatoid arthritis using the IORRA cohort

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Conflict of interest: None

[Object] To investigate chronological changes of achieving HAQ remission in patients with early rheumatoid arthritis (RA). [Methods] Among RA patients who enrolled in the IORRA cohort for the first time in Term 1: 2000-2002, Term 2: 2005-2007, and Term 3: 2010-2012 within 2 years from the onset, patients in Term 1 and Term 2 were selected by matching sex, age and J-HAQ to patients in Term 3, respectively. Among them, patients with J-HAQ>0.5 were assessed for the time until achieving HAQ remission (J-HAQ≦0.5) and its percentages at 3 years. Multivariate analysis was performed to assess factors related to achieve HAQ remission. [Results] In all terms, 408 patients were extracted. The mean time until achieving HAQ remission was significantly shorter chronologically (Term 1: 2.2 years, Term 2: 1.8 years, Term 3: 1.7 years; p<0.005). HAQ remission rates significantly increased in both Term 2 (55.2%) and Term 3 (57.4%) compared to Term 1 (37.5%; p<0.005). Younger age (OR 1.02; 95%CI 1.00-1.04) and enrollment in Term 2 (OR 2.0; 95%CI 1.2-3.5) and Term 3 (OR 2.3; 95%CI 1.3-4.1) compared to enrollment in Term 1 were related factors for achieving HAQ remission at 3 years. [Conclusions] Along with the improvement of RA therapy, patients can achieve remission more frequently and in shorter time.

W37-3

Prospective analysis of Role/Social QOL component by SF-36 in patients with rheumatoid arthritis

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Conflict of interest: None

We analyzed the role and social QOL component in patients with RA using patient reported outcome SF-36. Method In 223 RA, SF-36 v2™ assessed at 24 weeks and 52 weeks after therapy. We analyzed the relationship between clinical findings. SF-36 assessed 3 summary component summary score (physical component: PCS, mental component:MCS, role/social component:RCS) calculated according to summary standard score 50±10 in 2007 Japanese. Result: 223 RA patients, mean age is 62±16, 81%female, mean disease duration 6.5±15years. DAS28-ESR5.12±2.10, HAQ-DI1.02±0.85, SF-36 PCS34.3±13.6, MCS49.8±8.5, RCS34.3±14.6, 56 weeks after treatment (MTX 68.2%, bDMARD30%, PSL32%), reached 78% remission or low disease activity. 56 weeks SF-36 PCS39.9±10.0, MCS49.6±13.9, RCS43.3±14.6. PCS and RCS significantly improved by treatment. RCS in SF-36 is significantly correlated with CRP change, HAQ-DI and ACPA positivity. Conclusion: Improvement of RCS is a important factor in treatment of patients with RA. Measurement of RCS in SF-36 is a useful tool in confirm of QOL in patients with RA.

W37-4

Evaluation in physical dysfunction in early rheumatoid arthritis patients treated with biologics for one year

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Conflict of interest: Yes

Objective: To evaluate whether the treatment goal of remission is effective in suppression of physical dysfunction in early RA patients. **Methods:** Subjects were all 70 early RA patients within the onset two years, continuously treated with biologics for 12 months. We evaluated HAQ-DI at 6 and 12 months after initiation of therapy. **Results:** Multivariate logistic regression analysis revealed that duration of disease and SDAI at 6 months were significantly associated with achievement of functional remission at 12 months. The best cut-off value of SDAI at 6 months for predicting functional remission at 12 months was 15.7 by ROC analysis. In the remission (REM) group and the low disease activity (LDA) group, rates of remission were 90% and 83% at 6 months, 97% and 86% at 12 months, HAQ-DI were 0.11±0.30 and 0.30±0.58 at 6 months, 0.03±0.10 and 0.24±0.28 at 12 months, respectively. In 12 cases which LDA at 6 months achieved to REM at 12 months, HAQ-DI was significantly decreased 0.42±0.79 from 0.045±0.14. **Conclusions:** In early RA patients after initiation of therapy, LDA at 6 months is a prerequisite for functional remission at 12 months. HAQ-DI at 12 months in patients with LDA at 6 months could be improved if disease activity is achieved to REM at 12 months.

W37-5

HAQ score at the start of biologic agents therapy is associated with radiographic progression of large joint damage in patients with rheumatoid arthritis

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Conflict of interest: None

【Objectives】We have shown that in RA patients treated with biologic agents (BAs) radiographic progression of large joint damage (RPD) is expected to be increased when Larsen grade is III or higher (Mod Rheumatol 2016). However, relationship between patients' background characteristics and RPD has not been elucidated.【Methods】Eighty-eight patients receiving BAs for 1-3 years were included in this study. The mean age at the start of BAs was 62.9 year-old, and the mean disease duration was 11.7 years. A total of 400 joints including shoulder, elbow, hip, knee, and ankle were evaluated whether there was RPD by comparing radiographs before and after the treatment.【Results】RPD was found in 16 patients (18.2%) and 21 joints (5.3%). A multivariate logistic regression analysis revealed that HAQ was an independent risk factor for RPD (odds ratio: 2.965, 95% CI: 1.234-7.226). An AUC of the ROC curve was 0.732 and the cut-off value was 1.4375 (sensitivity: 0.769, specificity: 0.729).【Conclusion】HAQ at the start of BAs was associated with RPD to large joints during a therapeutic period of 1-3 years. RPD is expected to increase when functional disability exceeds an HAQ of 1.5.

W37-6

Anti-nuclear antibodies may predict development of anti-drug (TNF inhibitors) antibodies

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Conflict of interest: None

[Objectives] Anti-drug antibodies (ADAbs) are often developed in rheumatoid Arthritis (RA) patients treated with TNF inhibitors (TNFi) and lead to insufficient response. ABs such as anti-nuclear Abs (ANA) and anti-dsDNA Abs sometimes appear during the therapy and occasionally show drug-induced lupus. We compare the presence of ANA with appearance of ADAbs in RA patients during TNFi therapy. [Methods]

ANA (IIF with HEp-2010 cells) were examined for 66 RA patients treated with biologics (28 infliximab, 12 adalimumab, 6 golimumab 5 tocilizumab and 15 abatacept) before and after the treatment. Sera were sent to Sanquin, The Netherlands and anti-infliximab and anti-adalimumab Abs were detected by EIA. [Results] Elevation of ANA titers was found in 8 of 28 in infliximab and 2 of 12 in adalimumab patients, but not in other biologics patients. ADAbs developed in 10 of 25 in infliximab patients and 3 of 9 in adalimumab patients. Prevalence of ADAbs was significant high in ANA-positive patients before the treatment and also in patients with an increase in ANA titers during the therapy (p=0.006 and p=0.013, respectively). [Conclusion] Existence of ANA before and increase in the titer of ANA after TNFi therapy may predict the development of ADAbs.

W38-1

Clinical characteristics and prognosis in patients with connective tissue diseases-associated pulmonary hypertension; comparison between patients with systemic sclerosis and non-systemic sclerosis

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Conflict of interest: None

[Aim] Pulmonary hypertension (PH) associated with systemic sclerosis (SSc) (SSc-PH) affects the survival. Meanwhile, favorable response to immunosuppressants (IS) is observed in some non-SSc-PH. We compared clinical characteristics between SSc and non-SSc patients (SLE / MCTD). [Methods] Ninety-four patients who had right heart catheterization (RHC) from 2006 through 2015 were analyzed. Deterioration was defined by introduction of home oxygen therapy (HOT) or death, and complete remission (CR) by WHO-FC I and mean pulmonary arterial pressure <25mmHg by RHC (or TRPG <35mmHg by cardiac US). [Results] Mean follow-up period (SD) after RHC was 34 (26) months. Twenty-seven patients were SSc-PH and 9 were non-SSc-PH. Thirty-three % of the SSc-PH patients were group 3 by Nice classification (0% in non-SSc-PH, P = 0.0760). IS were introduced in 33% and 100% SSc-PH and non-SSc-PH patients, respectively. No SSc-PH patients achieved CR, while 58% of the non-SSc-PH did it (P <0.0001). Introduction of HOT or death was more common in SSc-PH than non-SSc-PH (54% vs. 12% at 2-year, respectively, P = 0.0090). Four of 9 in SSc-PH died from interstitial lung disease (ILD). [Conclusions] SSc-PH patients had poor prognosis and did not achieve CR. Establishment of therapeutic strategies for SSc-ILD is needed.

W38-2

Screening of pulmonary arterial hypertension (PAH) in patients with SSc using DETECT algorithm – Validation of the usefulness of the algorithm in our cohort

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Conflict of interest: None

Background: To detect PAH in patients with SSc at earlier phase, DETECT algorithm is reported as a good tool with high sensitivity to identify candidates who need right heart catheter test (RHC). However, the usefulness has not been validated in Japanese cohorts. Methods: A hundred forty patients with SSc who were suspected to have PAH during from 2005 to 2016 were involved. Clinical information was retrospectively collected from records. The algorithm was consisted of 2 steps, “Step 1” for detection of the candidates for UCG, and “Step 2” for RHC. Based on the result of RHC, the sensitivity and the specificity of the algorithm were examined. Results: Of 140 cases, 92% was female and 19% was diffuse SSc. 47 were dropped at Step 1, 43 at Step 2, then 50 were eventually extracted as candidates for RHC. Compared with the results of RHC, sensitivity was 100%, specificity 41%, positive predictive value 25%, and negative predictive value 100%. However, a case, who initially dropped at Step 1, found to have PAH 2 years later. Conclusion: DETECT algorithm was reassured as a good tool at the timing of evaluation, however, we have to keep in mind that the drop from this algorithm does not guarantee the patient to be free from future development of PAH.

W38-3

Evaluations of exertion dyspnea in patients with collagen disease by CPX (cardiopulmonary exercise testing)

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Conflict of interest: None

Background: Patients with collagen disease often complain of exertion dyspnea, due to interstitial pneumonia (IP), pulmonary hypertension (PH), and so on. Early diagnosis of PH is difficult, because cardiac ultrasonography or right heart catheterization at rest is not always sufficient, but can lead to better prognosis with growing choices of treatment. We tried to detect it by CPX. Methods: From June 13th in 2015 to October 28th in 2016, We performed CPX and evaluate their clinical state in 28 patients, 17-80 years 2 males / 26 females, 5 mixed connective tissue disease (MCTD), 15 systemic sclerosis (SSc), 3 SLE, 2 Sjögren syndrome, 3 dermatomyositis. Results: Twenty cases presented decreased peak oxygen consumption (peak VO_2). Elevated VE (minute ventilation)/ VCO_2(CO_2 production) ratio, which represent increased ventilation-perfusion mismatch, increased in 23 cases. 7 cases, with decreased peak VO_2 but normal VE/VCO_2, were advised daily exercise. 13 cases with decreased peak VO_2 and elevated VE/VCO_2 were estimated to have PH and/or IP. In 2 cases, CPX was also useful for early detections of therapeutic gains in PH or IP. Conclusions: We performed CPX in every patient safely. Although more research is required, CPX may provide valuable information notably in early PH.

W38-4

Detecting the changes of indices for right heart circulation and of gene activation profiles in patients with Raynaud phenomenon including very early systemic sclerosis

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Conflict of interest: None

[Object] To detect the specific changes at the stage of subclinical PVD of SSc in patients with RP. **[Methods]** 48 cases without PAH symptoms with RP were investigated. To detect the early PVD, mean pulmonary artery pressure-cardiac output (mPpa-Q) response was estimated by exercise DE, which reflects the elasticity of pulmonary artery. Then, the expressed genes in peripheral blood were explored with using next-generation sequencing. The differences between SSc-related autoantibody negative (R=19) and positive group (S:scleroderma+(S1=20), consisting of with (S1=20) and without (S0=6) scleroderma were investigated. **[Results]** The level of serum BNP was significantly higher in S group than R group. The estimated mPpa-Q by exercise DE was also significantly elevated in S group (R<S0<S1). The hierarchical clustering of gene expressions showed major 2 clusters. If we focused on 117 genes reported to be implicated in the development of PAH, 11 of genes were differentially expressed between Group R and S0. **[Conclusions]** The elasticity of pulmonary arteries was shown to be increased in S group. The changes toward PVD had already started at the very early stage of SSc as Some of reported genes involved in PAH were differentially expressed in S0 group as compared with R group.

W38-5

Characteristic of pulmonary hypertension (PAH) in patients with anti-U1RNP antibody-positive connective tissue diseases (CTDs) is determined by the underlying disease rather than autoantibody profile

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Conflict of interest: None

Background: In Japanese cohort, mixed connective tissue disease (MCTD) is the most frequent underlying disease of CTD-PAH. However, U1RNP-positive (U1 (+)) CTDs other than MCTD also exist, and also can be complicated with PAH. The aim of this study is to clarify whether antibody profile or underlying disease can determine the characteristics of PAH in this group. Methods: Thirty patients with U1 (+) CTD-PAH patients (17 MCTD (all patients had feature of systemic sclerosis (SSc) and systemic lupus erythematosus (SLE)), 9 SLE, 2 SSc, 2 Sjogren's syndrome) and 7 U1 (-) SLE patients were involved. Clinical information was retrospectively collected and baseline characteristics, changes of the parameters of right heart catheter test and survival were compared among patients with MCTD, U1 (+) SLE and U1 (-) SLE. Results: Age at the PAH diagnosis is younger and frequency of ILD is less in both U1 (+) and (-) SLE than MCTD. Decrease of mPAP and DLCO was tended to be greater in both U1 (+) and (-) SLE than MCTD. Survival rate showed no difference, however, deceased patients in U1 (+) and U1 (-) SLE were seen within 13 months, but those in MCTD was distributed through the course. Conclusion: Clinical characteristics of PAH complicated with U1 (+) CTDs were determined by underlying diseases.

W38-6

Clinical characteristics of critical limb ischemia in systemic sclerosis

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Conflict of interest: None

[Objective] To analyze clinical characteristics of critical limb ischemia (CLI) in systemic sclerosis (SSc). [Methods] Among 333 SSc cases who visited our clinic between 2007 and 2015, we retrospectively analyzed clinical characteristics of 14 consecutive cases who developed gangrene. In addition, we conducted multivariate analysis to identify risk factors associated with CLI in 218 cases in whom serum lipid profiles were available. [Results] Among 14 CLI cases, all were women, 12 were limited cutaneous SSc, and 12 were anticentromere antibody (ACA) positive. Age at CLI onset was 68±13 years old and disease duration was 17±9 years. CLI developed in upper and lower limbs in 4 and 10 cases. Angiography showed arterial occlusion of forearm, lower leg, or thigh in 13 cases. Although 4 lower leg CLI cases underwent percutaneous transluminal angioplasty, amputation was inevitable. Ten cases underwent amputation, and 7 of 10 did more than once. In addition, multivariate analysis identified ACA positivity and lower HDL-C level as independent risk factors associated with CLI ($P = 0.003$ and 0.02). [Conclusions] CLI in SSc frequently required amputation and had a poor prognosis. In contrast to CLI with atherosclerosis, CLI in SSc might be a vasculopathy which has a specific pathogenesis.

W39-1

Prospective study on MTX cessation in RA patients who have remained remission with combination of MTX plus tocilizumab

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Conflict of interest: None

Method;24 RA patients who have been in remission with combination of MTX plus TCZ for more than 6 months were randomly assigned to the MTX cessation group and MTX continuation group. We compared the efficacy and safety of these 2 treatment groups at week 72. Results;12 patients were assigned to the MTX cessation group and the other 12 cases were to the MTX continuation group. DAS28-ESR and HAQ-DI score respectively and the difference was not significant. At week 72, and were no significant elevation of both DAS28-ESR and HAQ-DI score after cessation of MTX and the difference of both parameters at week 72 between the 2 groups was also not significant. 5 cases in the MTX cessation group and 6 cases in the MTX continuation group were in remission at week 72. The change of van der Heijde modified Sharp score during 72 weeks (DTSS)were 1.6 and 2.0 respectively and the difference was not significant. Adverse events were seen in 8 patients in the MTX continuation group and only one in the MTX cessation group. Conclusions; As a whole both DAS28-ESR and HAQ-DI scores were maintained in remission after cessastion of MTX, although some patients relapsed. Cessastion of MTX may be possible in some patients with sustained remission with TCZ plus MTX and may be safer than MTX continuation.

W39-2

Safety and Efficacy Results of Adalimumab and High-dose Methotrexate Combo Therapy in Japanese Patients with Rheumatoid Arthritis under the Clinical Practice (HAWK study)

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Conflict of interest: Yes

Purpose: To assess safety and efficacy of adalimumab (ADA) and high-dose (≧12mg/w) methotrexate (MTX) combo in Japanese RA patients under the clinical practice. Method: Multicenter observational study in 119 hospitals. Patients diagnosed of RA within 2 years, had received MTX at least 3 months, DAS28-CRP >3.2 and no previous biologics were included. The primary endpoint was the observed rate of DAS28-CRP <2.6 at week 52. The secondary endpoints were CDAI, SDAI, HAQ, EQ-5D and mTSS. All adverse events were collected. Result: 346 patients were enrolled from Sep2012 to Dec2014 (safety set 275; efficacy set 264). Baseline characteristics of the safety set: females 72.7%, mean age 54 years, mean RA duration 12.3 months, Mean MTX dose 13.4mg/w. Mean DAS-CRP of the efficacy set was 4.52. The rate of DAS28-CRP <2.6 at 24 and 52 weeks were 67.3%(148/220) and 78.9%(86/109), respectively. The adverse drug reaction rate was 20.7%(57/275), comparable with the all cases investigation (23.9%, 1847/7739). Twelve patients were discontinued due to ADRs. Detailed analysis is ongoing. Conclusion: This study did not indicate additional safety signals in early RA patients treated with an ADA high-dose MTX combination but proved significant efficacy of such a regimen in the real-world.

W39-3

A Retrospective Comparison of Radiographic Outcome and its Prognostic Factors between Maintained Remissions with Patient-reported Outcome Index and Physician-oriented Disease Activity Indices

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Conflict of interest: None

Objectives: We compared radiographic progression or its prognostic factors among patients with the maintenance of Routine Assessment of Patient Index Data 3 (RAPID3) remission for 1 year (RAPID3-MR), with the maintenance of clinical disease activity index remission for 1 year (CDAI-MR) or with the maintenance of 28 joint count disease activity score remission for 1 year (DAS28-MR). **Methods**: Of 1220 patients

with available clinical data, 92 with RAPID3-MR, 45 with CDAI-MR, and 75 with DAS28-MR were retrospectively investigated. The modified total Sharp score (mTSS) for radiographic joint damage was investigated for 1 year. **Results:** In baseline data, the RAPID3-MR group appeared to be more active and seemed to show more deterioration in radiographic joint damage compared to other groups, especially to the CDAI-MR group. However, there was no significant difference of the mean annual ΔmTSS among RAPID3-MR patients (0.12±0.55), CDAI-MR patients (0.06±0.85) and DAS28-MR patients (0.11±0.89). The baseline mTSS (P=0.038) and monotherapy with non-biological disease-modifying antirheumatic drugs (P=0.033) were good prognostic factors in RAPID3-MR patients. **Conclusions:** One-year RAPID3 remission maintenance may predict good radiographic outcomes.

W39-4

Significance of Monitoring Serum Interleukin-6 Levels in Patients with Rheumatoid Arthritis during Tocilizumab Treatment

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Conflict of interest: None

[Objectives] This study aimed to clarify the significance of monitoring serum interleukin-6 levels in patients with rheumatoid arthritis (RA) during tocilizumab (TCZ) treatment. [Methods] We conducted a prospective and observational study. Fifty-four RA patients who started TCZ therapy were enrolled. Serum IL-6 levels were obtained every 4 weeks, and, in addition, at the time when any adverse events occurred. The relationships between serum IL-6 levels and RA disease activity or occurrence of adverse events were analyzed. [Results] RA disease activity at 52 weeks was significantly lower and the remission rate at 52 weeks was significantly higher in the patients with serum IL-6 < 30 pg/ml at 12 weeks and 24 weeks than those with serum IL-6 ≥ 30 pg/ml. Multiple regression analysis and age- and sex-adjusted logistic regression analysis showed serum IL-6 at 12 weeks and 24 weeks to be predictive factors for RA activity and remission at 52 weeks. Concerning adverse events, rapid changes in serum IL-6 in comparison with C-reactive protein (CRP) were observed in a patient with adverse events. [Conclusion] Monitoring serum interleukin-6 levels in patients with RA during TCZ treatment may be useful to predict the efficacy of TCZ and evaluate the occurrence of adverse events.

W39-5

Relation of HLA-DRB1 genotype to the efficacies of Abatacept and Tocilizumab in patients with rheumatoid arthritis

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Conflict of interest: Yes

[Object] To investigate whether clinical efficacy of abatacept (ABT) and tocilizumab (TCZ) differs depending on whether or not HLA-DRB1 Shared Epitope (SE) is present in patients with rheumatoid arthritis. [Methods] HLA-DRB1 genotype of patients treated with ABT (n=68) and TCZ (n=48) was identified. HLA-DRB1 0101, 0401, 0404, 0405, 1001 genotype was defined as SE. Retention rate and clinical efficacy were assessed by Cox proportional hazard model and multiple regression analysis. [Results] The patients with SE positive were 43 in ABT (63%) and 28 in TCZ (68%). The retention rate of ABT at 52 week was 94.6%/51.0% in the SE positive /negative group (significantly higher in SE positive group, p <0.0001, log rank), and of TCZ was 77.8%/77.3%(not significant). Average CDAI at 24 week was 3.6/10.7 in SE positive/negative group with ABT (p <0.0001, ANOVA), and 6.3/5.8 with TCZ (p = 0.87). The risk of withdrawal of drugs in SE negative group was 8.2 (p <0.0001) in ABT by Cox regression analysis but was not significant in TCZ (p = 0.41). In addition, the predictor of CDAI at 24 week by multiple regression analysis was SE (p = 0.0002) in ABT but RF high titer (RF> 150, p = 0.04) in TCZ. [Conclusions] ABT is effective in SE positive group, but TCZ is not relevant for SE.

W39-6

Strategy for obtainment of pharmaceutical approval of rituximab to rheumatoid arthritis (RA) in Japan

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Conflict of interest: None

Although the rituximab (RTX) is one of the usual biological DMARDs in the world, Japanese civil authority (Ministry of Health, Labour and Welfare; MHLW) does not approve RTX for the treatment of RA. Tokyo Medical and Dental University Hospital was authorized as equivalent hospital to the core leading hospital of clinical research in Japan in the National Strategic Special Zone and has got the benefit able to accelerate assessment procedures for advanced medical treatment. Because the target of advanced medical treatment is off-label in Japan, but is approved in other countries, RTX to RA just meets these conditions. MHLW rejected the approval application and decided not to receive the application by the former rule any more. However, the rule changed and the position of RTX in RA management was corrected in the modified guidelines by ACR and EULAR as preferred to patients under special conditions. Based on discussion with MHLW, we and JCR re-demanded pharmaceutical approval of RTX to RA again in 2015. Preliminary discussion in the working group is underway in November, 2016. To solve the pharmaceutical discrepancy between Japan and other countries, strategies for effective approval acquisition are necessary by keeping interests and discussion with regulatory authorities.

W40-1

Increasing Prevalence of Otitis Media with ANCA Associated Vasculitis

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Conflict of interest: None

[Object] We clarify clinical features of otitis media with ANCA associated vasculitis (OMAAV). [Methods] One hundred and eighty two patients (85 males and 97 females) with ANCA associated vasculitis (AAV) were admitted to Niigata University Hospital from 1989 through 2016. Thirty two patients (15 males and 17 females) with otitis media were recruited. [Results] Nineteen patients were diagnosed as having definite granulomatosis with polyangiitis (GPA). Five were probable GPA. Lung or kidney lesions were not detected in other eight patients (Ears (E) only group). The initial symptoms in 26 patients (81%) were ears' one, such as impaired hearing, congested feeling, otalgia, or tinnitus. MPO-ANCA titer in GPA group and in E only group were 110 ± 102 U/ml and 43.2 ± 24.8 U/ml, respectively (p<0.05). From 1989 through 2009, 10 OMAAV (0.48 /year) out of 84 AAV (4.0 /year) were observed, whereas 22 OMAAV (3.1 /year) out of 94 AAV (13.4 /year) were observed from 2010 through 2016 (p<0.05). Cyclophosphamide was used in 67% of GPA group and 25% of E only group (p<0.05). Azathioprine was chosen in 46% of GPA group and 88% of E only group (p<0.05). Relapse was observed in 54% of GPA group and 13% of E only group (p<0.05). [Con-

clusion] The prevalence of OMAAV was increasing.

W40-2

The MRI findings of lower leg muscles in 6 cases of myopathy associated with vasculitis syndrome

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Conflict of interest: None

[Object] We extracted the features of muscle MRI findings of myopathy as observed in cases with vasculitis syndrome. [Methods] We retrospectively investigated the muscle contrast MRI findings obtained for 6 cases showing muscle symptoms in the limbs among cases newly diagnosed with vasculitis syndrome in our hospital during the 2-year period. [Results] The subjects comprised 4 women with polyarteritis nodosa, 2 cases with microscopic polyangaitis. The comparison site of the image was the lower both legs where muscle symptoms existed and MRI was performed in all cases. A diffuse high signal was observed in muscles in the bilateral symmetry in all of the STIR images, and the high signal was observed to be more conspicuous in the interfascicular septa. In addition, a high signal was prominent in the fascia and subcutaneous area. However, in the Gd-enhanced image, the high signal was observed to be confined to the blood vessel area. In all cases, a muscle biopsy was performed using a contrast MRI as a guide, and fibrinoid necrotic vasculitis was proven from all specimens. [Conclusion] MRI was thus found to be useful for the imaging of myopathy associated with vasculitis syndrome, and especially under enhanced conditions, it may be possible to clarify the affected blood vessels.

W40-3

Clinical features of microscopic polyangiitis with musculoskeletal findings

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Conflict of interest: None

[Objective] We described five patients with microscopic polyangiitis (MPA) diagnosed only by musculoskeletal findings without signs of other organ involvement. [Methods] We reviewed medical records of MPA patients diagnosed by musculoskeletal magnetic resonance imaging (MRI) or muscle biopsy at the University of Yamanashi hospital from April 2015 to September 2016. [Results] Five patients (4 male, 1 female) with mean age of 80.4 years old (60-88) at diagnosis were analyzed. Two patients had apparent myalgia, but other patients showed only muscle tenderness in lower limbs. All patients were positive for MPO-ANCA and mean titer was 51.1 U/mL (12.7-108). Muscle biopsy revealed definite vasculitis only in 2 patients although all patients showed MRI findings of muscle inflammation. No patient showed other organ involvement. Dose of glucocorticoid (GC) at initial treatment was prednisolone 0.3-0.8 mg/kg except for two patients who did not require GC treatment. Two patients received oral azathioprine treatment due to recurrence. [Conclusions] It is difficult to diagnose MPA when patients show only nonspecific symptoms such as fever or general fatigue without signs of pulmonary or renal involvement. Musculoskeletal symptoms and MRI can provide useful information for the diagnosis of MPA.

W40-4

Three cases of microscopic polyangiitis presenting with myalgia as the initial manifestation

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Conflict of interest: None

Case 1: An 83-year-old man was admitted for fatigue and myalgia of the lower legs. MPO-ANCA and CRP were elevated, while CK levels were normal. MRI showed increased signal in the crural muscles on the STIR sequences. Proteinuria and hematuria were detected on urinalysis. A kidney biopsy revealed peritubular capillaritis, compatible with microscopic polyangiitis (MPA). Case 2: An 82-year-old woman, who had been followed up of interstitial pneumonia in a different hospital was admitted for edema and myalgia of the lower limbs. MPO-ANCA and CRP were increased. Despite normal CK levels, MRI revealed increased signal in the crural muscles on the STIR sequences. A muscle biopsy showed capillary vessel vasculitis with fibrinoid degeneration, compatible with MPA. Case 3: A 51-year-old woman was admitted for fever and myalgia of the lower legs. MPO-ANCA and CRP were elevated without CK increase. MRI showed increased signal in the crural muscles on the STIR sequences. A muscle biopsy was performed. Discussion: Renal and lung involvements are most common in MPA, but myalgia can be an initial manifestation. There are some cases of myalgia without CK increase in MPA, which suggest that myalgia is caused by ischemia secondary to vasculitis. MRI may be useful for diagnosis of MPA.

W40-5

Clinical features of 28 cases of limb restricted vasculitis and fasciitis

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Conflict of interest: None

[Objectives] We sometimes experience the cases with fever and muscle pain of lower limbs without any other specific features. There are sporadic case reports of eosinophilic fasciitis and limb restricted vasculitis. However, few reports compare and discuss such cases. [Methods] We retrospectively analysed the clinical features of 28 patients who were admitted to our hospital because of fever and muscle pain of lower limbs from 2004 to 2016. [Results] Among the 28 patients, 18 were vasculitis syndrome (10 were limb restricted vasculitis, 8 were microscopic polyangiitis), 8 were fasciitis (3 were eosinophilic fasciitis, 4 were diffuse fasciitis without eosinophilia and one were tuberculous fasciitis), one was relapsing polychondritis and one was Behçet's disease. Muscle biopsy was performed in 26 patients. Abnormal findings of MRI in non-infectious fasciitis and vasculitis syndrome were bilateral and diffuse. Tuberculous fasciitis showed specifically abnormal intensity in unilateral thigh and fluid collection. All patients were treated with glucocorticoids. Immunosuppressants (e.g. azathioprine) were added in 15 and anti-tuberculous drugs in one. [Conclusion] MRI and muscle biopsy were useful for diagnosis of disease with fever and muscle pain of lower limbs.

W40-6

Clinical Features of Three Patients with Dual ANCA-Positive Vasculitis

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Conflict of interest: None

To demonstrate clinical characters of dual antineutrophil cytoplasmic antibody (ANCA) positive against both myeloperoxidase (MPO) and proteinase 3 (PR3), we evaluated clinical features of 3 patients with dual ANCA positive ANCA associated vasculitis (VVA). Of the 30 VVA pa-

tients in our hospital from January 1, 2013 until October 31, 2016, we found 3 dual ANCA positive patients. There're 1 males and 2 females, and the average age was 75.0 years. The ranges of serum MPO-ANCA and PR3-ANCA levels were 8.4 to 1460 U/ml, 35.5 to 350 over U/ml, respectively. All cases fulfilled Microscopic Polyangiitis and Polyangitis Granulomatosis disease diagnostic criteria in 1998 by the Ministry of Health and Welfare. All cases had lung involvements (2:interstitial pneumonia, 1:alveolar bleeding), and crescent-forming nephritis. Other organ lesions included multiple mononeuropathy and sinusitis in one case. The average BVAS was 20.6 points. Dual ANCA positive VVA are rare, and tend to be high in antibody titer and high in severity.

W41-1

Hepatic disorder in rheumatoid arthritis treated with methotrexate

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Conflict of interest: None

【Aim】To analyze the cause of hepatic disorder in the RA treated with MTX.【Method】Folic acid (FA) is usually administered to hepatic disorder seen in RA treated with MTX, however, the hepatic disorder sometimes continue. The platelet counts and the value of choline esterase in combination with US were examined. Ferritin and liver fibrosis marker such as hyaluronic acid and type 4 collagen levels were also examined. Liver biopsy was performed finally.【Results】Eleven patients of 12 had chronic liver diseases; 1 had precirrhotic phase of chronic hepatitis and 10 had NASH. Four of 10 had no risk factors for NASH. Nine patients were followed-up more than one year after quit MTX. They showed decrease of the level of ferritin and/or liver fibrosis marker. Number of platelets and choline esterase levels were recovered in some. We compared the histology before and after withdrawal of MTX in three. Demonstrable improvement of hepatitis and fibrosis were seen. The observation indicated that MTX could have caused hepatic disorder.【Conclusion】FA is effective to improve hepatic disorder, but in some case, FA is not effective. Eleven of 12 patients showed chronic liver diseases, such as NASH, suggesting that MTX should be used with caution.【Conflict of interest:none】

W41-2

Analysis of risk factors of liver fibrosis by Real-time Tissue Elastography in Methotrexate-Treated patients with Rheumatoid Arthritis

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Conflict of interest: None

[INTRODUCTION] Liver Fibrosis Index (LFI) measured using Real-time Tissue Elastography (RTE) is an indicator of noninvasive liver fibrosis and is used in chronic hepatitis. We measured LFI of patients treated with MTX and evaluated liver fibrosis. [METHODS] In MTX administered cumulative 200 mg or more of female RA patients 239 (M group: 55 ± 11 years old, BMI 21 ± 3) and 229 female patients without MTX (C group: 58 ± 12 years old, BMI 22 ± 4), LFI was measured. [RESULTS] In both M group and C group LFI showed a positive correlation with BMI and significant ly increased with fatty liver. M group showed a positive correlation with age and showed a negative correlation with eGFR. In patients with low disease activity and less than low disease activity at the time of LFI measurement, the LFI in the group of which maximum dose is 8 mg / day or less and not adding other DMRDs is significantly lower than in the maximum The dose was significantly lower than in the group to which other DMARDs were added without decreasing the dose at 12 mg / week or more. [CONCLUSIONS] Risk factors of liver fibrosis by MTX were obesity, fatty liver, elderly, decreased renal function. Furthermore, attention should be paid to the therapeutic reactivity after administration of MTX.

W41-3

A retrospective study of methotrexate associated lymphoproliferative disorder (MTX-LPD) 15 cases experienced at our hospital

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Conflict of interest: None

Objective: To evaluate the characteristics of MTXLPD with RA at our hospital. **Methods:** We examined the clinical features of 15 cases of MTX-LPD retrospectively. **Results:** MTX was administered to about 750 RA patients during the 26 years from 1990 to 2016, LPD occurred in 15 cases (2%), 3 males and 12 females. The mean age at onset of LPD was 74.7 years, the mean disease duration of RA was 18.3 years, the maximum MTX dose was 11.5mg/w the MTX dose just before LPD onset was 10.4mg/w, MTX cumulative dose was 6723.6 mg. In 4 cases infliximab were also used. There was no case with Sjogren's syndrome. Diffuse large-cell B-cell lymphoma 6 cases, Hodgkin's disease 3 cases, and extranodal lesions were observed in cases (49.7%). EBER was positive in 6 cases (75%) out of 8 cases examined. In one case, surgery was performed, and in 4 cases chemotherapy was performed. 8 cases regressed with MTX discontinuation. Only one case of death was complicated with lymphoma-related hemophagocytosis. **Conclusion:** Although there are many cases disappeared only by stopping MTX, there is a case in which the patient died in a rapid course with LAHS, the prognosis varied. We also participate in a multicenter prospective study led by the JCR, and we want to reconsider how we use MTX referring to the results.

W41-4

The aged and maximum methotrexate dose seem to be risk factors for development of MTX- associated lymphoproliferative disorders

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Conflict of interest: None

Background: Since February 2011, an approved MTX dose for RA treatment has been raised in Japan. Recently we have an impression that incidence of MTX-associated lymphoproliferative disorders (MTX-LPD) are increasing. Objectives: To investigate incidence and risk factors of MTX-LPD. Methods: All of adult patients receiving MTX for treatment of autoimmune diseases (n=281) in our hospital from May 2012, to September 2016 are surveyed. In each case, the possible risk factors for development of MTX-LPD including minimum MTX dose, maximum MTX dose, administration period, and cumulative dose were investigated in detail. Results: The incidence of MTX-LPD in our hospital was accounted for 3.2%(9 patients) in all patients. By the statistical analysis, the aged (p=0.001) and maximum MTX dose (p=0.048) may be the most important risk facters. Conclusions: In our cohort, the incidence of MTX-LPD was quite frequent as compared to previous Japanese report (0.5%; before 2011) or reports from worldwide (0.05-0.3%). It is notable that the aged and maximum MTX dose seem to be risk factor for development of MTX-LPD. Although our cohort is rather small, we believe that higher dose MTX for aged patients is one of the risk factors of MTX-LPD.

W41-5

The Boolean remission rate and the annual hospitalization number for serious adverse events for high dose MTX monotherapy in Japanese patients with RA using NinJa 2015 cohort

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pital, NHO, Kanagawa, Japan

Conflict of interest: None

(Material and Methods) In 15101 Japanese RA patients registered with NinJa2015, 4514patients medicated MTX monotherapy without biological DMARDs and combination synthetic DMARDs were divided 6 groups by MTX dose once a weekly.; 4mg/week n=556 average age 68.8years old, mean duration of illness 14.1years, 6mg/week n=1083, 65.7yo, 13.2y, 8mg/week n=1226, 64.1yo,11.4y,10mg/week n=771, 62.2yo,10.5y, 12mg/week n=584, 59.3yo, 9.9y, over14mg/week n=284, 56.9yo, 8.8y, respectively. We defined hospitalization for various infectious disease, interstitial pulmonary disease, pancytopenia, malignant lymphoma as serious adverse event and research annual hospitalization in each groups. (Results) The Boolean3 remission rate in each groups were 4mg groups 34.9%,6mg 33.7%, 8mg 32.4%, 10mg 32.3%, 12mg 28.7%, over14mg 28.6mg, respectively. Incidence of serious adverse event of the all NinJa 2015 cohort was 557patients (3.8%), and the OR with MTX each groups were 0.47, 0.41, 0.77, 0.55, 0.36, 0.83 respectively. (Conclusion) In this current study, the annual hospitalization number for serious adverse events was not high, especially over 8mg/week of MTX dose. MTX monotherapy within 12mg/week in Japan is safe, but the efficacy was not getting better by dose depending.

W41-6

Is it possible to achieve remission in RA patients by add Iguratimod to MTX?

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Conflict of interest: None

Objective: To evaluate efficacy and safty of combination of Iguratimod (IGU) and MTX to RA patients. Methods: From December 2012, 49 cases treated with IGU were evaluated by recording DAS28 (4/ESR) and SDAI and CDAI at week 27, 54 and two years. The average amount of IGU was 41mg. Results: DAS28 was 4.3 and decreased to 2.4 at two years, CRP was also reduced from 1.9 to 0.7. The proportions of patients who obtained clinical remission were 65.6% at two years according to DAS28-ESR score. SDAI was 19.6 and decreased to 5.1 at final follow up. CDAI was also improved 17.7 to 4.6. Conclusion: The therapy of combination of IGU and MTX was effective for short-term results.

W42-1

Treatment for early rheumatoid arthritis patients by low-dose predonisolone for no longer than a year enables earlier improvement of their disease activity and never worsen the rate of new complications

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Conflict of interest: None

【Objectives】To investigate the effectiveness of treatment of early rheumatoid arthritis by low-dose predonisolone for no longer than a year for their disease activity and the rate of new complications.【Materials and Methods】Seventy four RA patients with a disease duration less than 2 years were included. We classified patients in 2 groups, one group treated without GC (N group) and the other with 5mg or less of GC for no longer than a year (GC group). We evaluated the change of DAS-28CRP scores and the rate of new complications and compared them between the two groups.【Results】There were no significant differences of DAS28CRP at baseline. Both groups had significant improvement of the scores at final evaluation although there was a significant difference of the improvement rate in DAS28CRP of the GC group in comparison with the N group at 1 month after treatment. In GC group, mean dose of GC was 2.14 mg/day. New complications were occurred 5 cases (2 vertebra fracture, 1 CVD and 2 high level of HbA1c) in N group and 4 cases (2 vertebra fracture and 2 high level of HbA1c) in GC group.【Conclusion】Treatment of early rheumatoid arthritis by low-dose GC enables earlier improvement and didn't worsen the rate of new complications.

W42-2

Management of prednisolone in rheumatoid arthritis after induction of biological agents; a retrospective observational study based on data from a Japanese multicenter registry study

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Conflict of interest: None

【Objective】Rheumatoid arthritis (RA) patients were treated with prednisolone (PSL), but it is recommended to decrease or stop taking PSL as possible because of some complications. Indeed, we continuously kept using PSL, so we investigated the management of PSL in a retrospective observational study based on data from a Japanese multicenter registry study.【Methods】A total of 757 RA patients who were treated with PSL and without biological agents was treated with 1st biological agents by a retrospective observational study based on data from a Japanese multicenter registry study (TBCR). Endpoints were stop taking PSL after one year of the induction of biological agents, and we analyze baseline characteristic of the induction of biological agents by multivariate logistic regression analysis.【Results】209 RA patients (27.6%) were possible of stop taking PSL after the induction of biological agents. Multivariate logistic regression analysis revealed that age, ACPA, concomitant MTX, dose of PSL were independently associated with stop taking PSL.【Conclusion】We investigated the baseline characteristic of stopping taking PSL after the induction of 1st biological agents in RA patients. This study shows that age, ACPA, concomitant MTX, dose of PSL was associated with stop taking PSL.

W42-3

The impact of the combination therapy of conventional synthetic disease-modifying antirheumatic drug with anchor drug, MTX in the Japanese large cohort, NinJa2015(National Database of Rheumatic Diseases by iR-net in Japan)

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Conflict of interest: None

(Material and methods) In 15101 RA patients registered in Japanese large cohort of NinJa (National Database of Rheumatic Diseases by iR-net in Japan), 30% of the patients had been medicated MTX monotherapy, 14% had the combination therapy with MTX + bDMARD, 14% had combination therapy with MTX + csDMARD. (RESULTS) Extraction of combinations with Boolean remission rate higher than 20% from these therapies showed MTX+BUC+TAC, MTX+SSZ+BUC, MTX+SSZ, MTX+TAC, MTX+IGU that had high efficacy. In addition, from the point of view of safety, the hospitalization rate of each combination was generally around 5%, which was not much different from the rate in the overall NinJa. (Discussion) On the whole, in NinJa2015, combination therapy with DMARD in which 2 or 3 drugs are selected from 5 drugs of SSZ, BUC, TAC, IGU and mainly MTX, the anchor drug, has been actively performed also in Japan, and csDMARD, MTX, and SSZ evaluated as strongly recommended in Guidelines for the management of rheumatoid arthritis, Japan College of Rheumatology 2014 have already played the central roll. Iguratimod is increasing as new DMARD as combination drug in RA.

W42-4

Allele frequency of polymorphisms of *folylpolyglutamate synthase*, major determinant of intracellular methotrexate polyglutamates, is different between Japanese population and Caucasian

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Conflict of interest: None

Objectives: We previously showed that polymorphisms of *folylpolyglutamate synthase (FPGS)*, but not *solute carrier family 19, member 1 (SLC19A1)* or *gamma-glutamyl hydrolase (GGH)*, affect methotrexate polyglutamates (MTXPGs) in patients with rheumatoid arthritis (RA). In this study, we compared the allele frequencies between the patients and general population of Japanese or Caucasian. **Patients and Methods:** Relation of the polymorphisms of *SLC19A1, FPGS*, *or GGH* and clinical parameters (CRP, MMP-3, total Sharp score and DAS28-ESR) of 271 RA patients was examined. Allele frequencies between the patients and general population of Japanese or Caucasian cited from the International HapMap project were compared. **Results:** There were no significant association between polymorphisms of the genes and clinical parameters. Allele frequencies of the genes were not different between the RA patients and Japanese general population. The allele frequencies of *FPGS*(A at 1994A>G, C at 2572C>T) were significantly increased in our patients compared with Caucasian population. **Conclusion:** Polymorphisms of *FPGS*, major determinants of intracellular MTXPGs, may contribute the difference of tolerability or dosage of MTX between Japanese RA patients and Caucasian patients.

W42-5

Correlation between Elevation of Mean Corpuscular Volume and Concentration of Methotrexate in Red Blood Cell among Rheumatoid Arthritis Patients with Methotrexate

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Conflict of interest: None

[Object] Methotrexate polyglutamate (MTX-PG) in RBC correlates with efficacy of methotrexate (MTX) and efficacy-predictor. Elevations of mean corpuscular volume (MCV) are often seen during using MTX, correlations between rate of MCV-change, MTX-PG, and efficacy were discussed. [Methods] MTX-PG was measured with high performance liquid chromatography. Rate of MCV-change {(post MCV – pre MCV) / pre MCV} was compared with MTX-PG and efficacy among 42 patients who were administered MTX for 24 weeks. [Results] Correlation between rate of MCV-change and MTX-PG1-5 (total MTX-PG) was as follow, 8 weeks: r = 0.28, p = 0.095; 12 weeks: r = 0.39, p = 0.010; 24 weeks: r = 0.32, p = 0.042. Median of rate of MCV-change among total MTX-PG > 68.7 nM and those among ≤ 68.7 nM, which was demonstrated as cutoff of ΔDAS28 > 1.2 in our past report, was 6.5% vs. 2.8%, p = 0.006. Rates of MCV-change among who achieved DAS28 > 1.2 and those among failed were as follow, 8 weeks: 2.3% vs. 0.8%, p = 0.260; 12 weeks: 1.5% vs. 2.3%, p = 0.930; 24 weeks: 5.9% vs. 2.7%, p = 0.118. [Conclusions] MCV-change reflects total MTX-PG and significantly higher rate of MCV-change was observed when total MTX-PG reached more than 68.7 nM. There was no correlation between rate of MCV-change and clinical efficacy.

W42-6

Analysis of the safety of methotrexate at doses of over 8mg/week in 108 Japanese patients with active rheumatoid arthritis

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Conflict of interest: None

OBJECTIVES: To evaluate adverse events (AEs) for safety of methotrexate (MTX) at doses of over 8mg/week for rheumatoid arthritis (RA) **METHODS:** A retrospective observational study for one year was performed using medical records from 108 RA patients. Safety was evaluated by the relation between AEs and their prognosis. **RESULTS:** Disease Activity Score 28-joint assessment using erythrocyte sedimentation rate (DAS28-ESR) decreased significantly (P <0.0001) from 4.3±1.4 to 3.4±1.5 over the one-year observation period with modified Health Assessment Questionnaire (mHAQ) changing from 0.69±0.65 to 0.55±0.58 (P < 0.01), and annual progression of modified total Sharp score (mTSS) from 8.2±12.1 to 1.02±2.35 (P < 0.01). The AEs, such as liver dysfunction, fever, vomiting, pneumonia and shingles, were observed in 48 cases (44.4%). Low body weight (P = 0.0011), low MMP-3 value (P = 0.026), max MTX dose (P =0.031) were predictors of AE. Frequency of severe AE was related with age (p=0.02) and combination with DMARDs (p<0.001). **CONCLUSIONS:** Increasing the dose of MTX to over 8 mg/week showed clinical improvement and effected suppression of joint destruction. However, we need to consider AEs, especially focusing on body weight, age and combination with DMARDS.

W43-1

Efficacy, safety and drug retention rate of Abatacept in elderly patients with rheumatoid arthritis

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Conflict of interest: None

【**Objective**】The elderly patients with rheumatoid arthritis (RA) have some physical performance decline and various complications. The aim of this study was to examine the efficacy, safety and drug retention rate of Abatacept (ABT) in elderly patients with rheumatoid arthritis. 【**Methods**】66 patients who had received ABT between Oct. 2010 and Jul. 2016 were divided into 2 groups (under64/over65). We examined the retrospective evaluation of the patients' disease activity, physical disability, reduction of MTX or PSL dose, safety and drug retention rate. 【**Result**】 In the elderly group, the dose of MTX was significantly lower and HAQ was significantly higher than in younger group. DAS28-ESR4 was improved significantly in both groups. In the elderly group, HAQ was improved significantly at the period of 6M and 1year. In the younger group, improved significantly throughout 1 year. There was significant reduction of MTX in the elderly group. Reduction of the PSL was observed in both groups. There are no significant differences in the drug retention rate in both groups. 【**Conclusion**】The ABT treatment in elderly patients with RA was suggested useful as much as the younger patients regarding the effectiveness, the reduction of MTX, PSL, and drug retention rate.

W43-2

The efficacy of tocilizumab in elderly patients with rheumatoid arthritis in our institution

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Conflict of interest: None

[Object] To assess the efficacy and safety of tocilizumab (TCZ) in patients with elderly rheumatoid arthritis age 65 or over. [Methods] Sixty-eight RA patients were initiated TCZ in our institution from May 2008 to May 2015, and 58 of them were continued TCZ over three months. We divided them into 2 groups; group A is under 65 y.o. (n=28), group B is over 65 y.o. (n=30). DAS28-ESR and CDAI were assessed at the point of 0,1,2,3,6,12months. And we investigated about adverse events within the 12 months. [Results] DAS28-ESR / CDAI after initiation of TCZ decreased as follows; A: A:5.03±1.25→2.75±1.23 (p<0.01)/17.96±9.83→

7.82±6.16 (p<0.001), B:5.47±1.20→2.66±1.25 (p<0.001)/21.16±10.26→8.45±6.52 (p<0.001). There were no significant changes between groups on remission rate. The incidence of adverse events (AEs) and serious AEs rates were A:70.6%/14.7%, B:79.4%/8.8% and there were no dead case because of AEs. Persistence rate at 12 months was A:82.1%, B:96.6%. [Conclusion] These data indicate that TCZ therapy is safe and effective for even elderly RA patients.

W43-3

Efficacy and safety of Abatacept in patients with rheumatoid arthritis over the age of eighty

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Conflict of interest: None

(Objective)To evaluate the efficacy and safety of Abatacept in patients with very elderly (≧80 years)RA patients. (Methods) We reviewed medical records of RA patients who were treated with abatacept in our center since January 2011. We examined clinical features, including efficacy, retention rate and safety, and compared the very elderly group (≧80 years) with the remaining group (<80 years). (Results)28 patients of very elderly RA were enrolled. Patients profiles; female 78.6%, the mean age:82.6 years old, the mean disease duration 12.5 years, stage1,2 54%, class1,2 64%, MTX combination cases 50%, PSL combination cases 39%, bio naive cases 61%, concomitant with respiratory diseases 54%. The decrease in DAS28-ESR (4.5→3.7; p<0.05) and the cumulative retention rates (86%) did not differ in the two groups at 1 year. There was difference in the incidence of severe infections in the two groups (per 100 patient-years: 8.9 in the very elderly group, 4.1 in the remaining group. (Conculusion)The effectiveness of abatacept is not affected by age, but the increased rate of severe infections, in the elderly must be taken into account.

W43-4

Efficacy and safety of biologic agents in elderly patients with rheumatoid arthritis (RA)

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Conflict of interest: None

Objective: To clarify the efficacy and safety of biologic agents (BIO) in elderly patients with RA. Methods: Eighty elderly (≥65 yrs old) patients previously untreated with BIO were evaluated retrospectively for BIO efficacy, in terms of DAS28-CRP and safety, from treatment initiation until the last injection of BIO. Results: Forty-eight of the patients were started on a TNF inhibitor, 26 on abatacept, and 6 on tocilizumab. Twenty-two of the patients (27.5%) were aged ≥75 yr (older elderly group). Complications occurred in 62.5% of the patients, and the most frequent was pulmonary disease (38.7%). Methotrexate and prednisolone were used respectively in 57.5%. The median DAS28-CRP decreased from 4.45 at initiation to 2.07 at the last injection of BIO (p=0.000), and 60.0% of the patients achieved remission. The BIO retention rate was 71.3% at 104 weeks, and 11 patients (13.7%) had to discontinue BIO because of adverse events (AE). Discontinuation of BIO due to AE was more frequent in patients with complications (20.0%; p=0.033), but no difference was found between the older elderly and other patients. Conclusion: BIO significantly reduce disease activity with a good retention rate. Attention should be paid to AE of biologic agents in elderly patients with complications.

W43-5

The efficacy, safety and drug retention rate of Infliximab (IFX) in elderly patients with rheumatoid arthritis

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Conflict of interest: None

Objective: Elderly patients with rheumatoid arthritis (RA) may have lack of efficacy due to in sufficient dose of MTX, and increased risk of infection. Therefore, we evaluated the efficacy, safety and drug retention rate in elderly patients with RA. Method: The cases were RA patients who could observe over 1 year and have started IFX therapy between Sep. 2003 and Mer. 2015. Patients with RA (n=169) were divided into 2 groups of elderly patients ≧ 65 years (n=51) and younger patients < 65 years (n=118). We investigated the patients' disease activity, safety, and drug retention rate, retrospectively. Results: In backgrounds, longer duration of disease and lower doe of MTX were significant in elderly patients with RA than younger patients. There were not significant difference in DAS28-ESR, HAQ score and dose of PSL between the groups. The drug retention rate in elderly group wans not inferior to younger group Prevalence of lack of efficacy was lower in elderly group than younger group (29.4% v.s. 33.0%, p<0.001). Conclusion: We suggest that the efficacy and drug retention rate of IFX would not be affected by age.

W43-6

Tolerance and effectiveness of biologic agents in elderly patients with rheumatoid arthritis

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Conflict of interest: None

【Objective】In recent years, aging of the rheumatoid arthritis (RA) patient is advanced, and side effects of biologic agents for elderly patients with RA are of concern. The purpose of this study was to evaluate the tolerance to and effectiveness of biologic agents in elderly patients (>70 years old) with RA (ERA) in comparison with younger patients (YRA). 【Method】All patients who had received at least 1 dose of biologic agents between September 2010 and September 2016 were included and categorized according to their age. 【Result】Among 182 patients with RA treated with biologic agents, 47 were >70 years of age at treatment initiation. Although, the mean SDAI score at the initiation of biologic agent was higher in ERA, these difference became identical after one month treatment. Discontinuation due to adverse events was more common in ERA. Drug discontinuation rates were higher in ERA than those of YRA (one-year discontinuation rate: 27.2% vs 18.0%). But these rates were identical in ERA and YRA which have no comorbidities. 【Conclusion】Age in itself should not interfere with the decision to treat elderly patients with RA with biologic agents. In a subset of patients ages >70 years, concomitants comorbidities should be paid attention in the treatment of biologic agents.

W44-1

A new surgical procedure for extensor tendon dislocation at the MP joint with RA patient

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Conflict of interest: None

Extensor tendon dislocation at the MP joint is often occurred in RA and will disturb ADL due to limiting active extension of the MP joint. Flexion motion of the MP joint often limit by shortening of the extensor tendon and muscle in rheumatoid arthritis. We developed a new surgical procedure for extensor tendon dislocation. We assessed 5 patients 7 fingers had extensor tendon dislocation and the limit of flexion motion due to degeneration of sagittal band in RA. We cut extensor tendon in step shape and repair sagittal band with half-slip of the step-cut tendon. Another half-slip of the tendon is sutured to distal step-cut tendon with elongation without limit of motion of MP joint. Postoperative ROM exercise

was performed using buddy bandage as soon as possible. The follow-up period was 9 to 39 months, and the average is 21 months. Postoperative results were excellent with no recurrence and no limit of ROM in MP joint. Our novel surgical procedure can repair the degenerative sagittal band and elongate the shortening extensor tendon simultaneously is useful for extensor tendon dislocation at the MP joint with RA patient.

W44-2

A new device for arthroplasty of the MP joints using Swanson silicone implant for the rheumatoid hand - Determination of bone cut length using a gap spacer -

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Conflict of interest: None

Objectives: The critical factors of determining the mobility of a silicone finger MP joint arthroplasty (Swanson, etc.) are not only the design of the implant but also the length of bone resection and the tension of soft tissue supporting structures. We devised a gap spacer for inserting the implant in a proper tension at the MP joint of the rheumatoid hand. Methods: Generally, if the osteotomy length is too long, implant subluxation is easy to occur, and if it is too short, movement will be restrained. This spacer is made based on “Joint relationship and spacer concept”(Trail IA, 2006). To get the appropriate gap (12~13mm) between the two bones after bone resection, soft tissue release and aligning them, the spacer is used. There are 6 sized spacers with the thickness of 8 to 14mm. By inserting the spacer, tightness of the joint is measured and the final cut of bone is determined. Results: The arthroplasty using this spacer was performed at 13 MP joints in 3 patients. In all of the operated joint could get about 60 degrees of flexion postoperatively. A stable well-balanced MP joint was provided by combining soft tissue release and reconstruction. Conclusion: This gap spacer is a useful device for determining an appropriate length of bone cut, and producing a favorable result.

W44-3

Comparison between a modified gap technique and a measured resection technique in TKA in RA

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Conflict of interest: None

Controversy exists regarding the best surgical technique to utilize to obtain gap balance. we investigated the intraoperatve measurements and clinical results in TKA in RA with a modified gap technique (MG) and a measured resection technique (MR). This study involved 31 knees in RA who underwent primary PS TKA (16 in MG group, 15 in MR group). 424 knees in OA were treated as control (249 in MG group, 175 in MR group). Gap length with the femoral trial component and clinical resultss were studied. There were no significant differences in gap length, gap angle, ROM and JOA score between MG group and MR group in RA. But MR group had a tendency of greater gap length in flexion than one in extension. This result suggests that MG might provide superior gap balance to MR.

W44-4

Postoperative component alignment in total knee arthroplasty using three dimensional CT-based preoperative planning

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Conflict of interest: None

[Object] The purpose of this study was to determine the accuracy of postoperative component alignment in total knee arthroplasty (TKA) performed after the three-dimensional (3D) preoperative planning. [Methods] We investigated 53 consecutive knees underwent TKA with 3D preoperative planning. We have used 3D preoperative planning computer software and special surgical supporting jigs for accurate positioning of TKA implants. Postoperative component alignment was compared with the preoperative planning by the postoperative evaluation function of the software. The accuracy of the postoperative component alignment were compared with accelerator-based navigation TKAs (41 tibial and 42 femorla components). [Results] 94.5% and 92.7%of femoral components and 94.5% and 100% of tibial components had an alignment within 3º in coronal and sagittal plane, respectively. In TKAs with accelerator-based navigation, 80.1% and 73.8% of femoral components and 95.1% and 82.5% of tibial components had an alignment within 3º in coronal and sagittal plane, respectively. [Conclusions] Current study showed that postoperative component alignment using 3D preoperative planning compares favorably to the accelerator-based navigation system in the coronal plane and is even more accurate for the sagittal plane.

W44-5

A comparative analysis between lumbar spinal fusion and non-fusion in patients with rheumatoid arthritis

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Conflict of interest: None

Methods. A total of 52 patients who underwent surgery for lumbar spinal disorders in patients with RA were included. All patients underwent preoperative lumbar x-ray followed by lumbar spinal decompression with or without spinal fusion, and postoperative follow up for at least 2 years (mean follow up periods 5.1 years). Pre- and postoperative JOA scores were recorded. The pre- and postoperative x-ray was taken by every year during follow up periods. The adjacent intervertebral disc narrowing and slippage of surgical level by x-ray was evaluated. The relationship between ASD and the data of RA disease activity was examined. Results Revision surgery was significantly higher in the fusion group than those in the non-fusion group. Average adjacent intervertebral disc space and vertebral slip were significantly greater in the fusion group than those in the non-fusion group at the final follow up period. Average adjacent Both MMP3 and DAS28CRP were significantly associated with ASD. Conclusion Revision surgery and ASD were significantly higher in fusion group than those in the non-fusion group. A preoperative high MMP3 and DAS28CRP are likely to be ASD after surgery.

W44-6

C1-2 transarticular fixation using canulated pedicle screw for atlantoaxial instability due to rheumatoid arthritis

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Conflict of interest: None

A combination of C1-2 transarticular screw fixation and posterior wiring (Magerl-Brooks procedure) is one of the established procedures of posterior atlantoaxial fixation. Recently, cannulated cervical pedicle screw (CCPS) became available in Japan. We tried to use CCPS for Magerl technique, and connected the screw heads with rod transversely (modified Magerl technique). Consecutive 7 patients (3 males and 4 females) who underwent this procedure for atlantoaxial instability due to rheumatoid arthritis in our institute were employed for the present study. Mean age at the surgery was 66 years old and mean follow-up period was 29 months, respectively. Surgical, clinical, and radiological outcomes were evaluated. No complication related to this surgical procedure was found. ADL and occiput-cervical pain were improved in all patients. Neurological deterioration was not confirmed. During the follow-up term, neither loss of correction nor instability more than 3 mm were observed. Complete bone union was confirmed in all cases. Transverse rod between two transarticular screws reinforce posterior atlantoaxial fixation without sacrificing adequate bone-graft area in Brooks procedure. We believe that

this procedure might be an option of Magerl technique for atlantoaxial fixation.

W45-1

Surgical indication of forefoot reconstruction by evaluating plantar pressure in the patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To clarify the surgical indication for rheumatoid forefoot deformity. [Methods] Patients with RA were divided into two groups: the surgical group (SG) and the non-surgical group (NG). They consisted of 125 feet and 250 feet. DAS28, HVA, M1/2 and M1/5 were evaluated as background characteristics. Distribution of peak pressure (PP) as plantar pressure was measured at nine sections. Maximum PP, minimum PP and Δ pressure (the difference value between maximum and minimum PP) were also measured. Cut-off values were calculated for each item which differed significantly. [Results] In the SG and NG, DAS28 was 3.0 and 3.7 ($p<0.001$), HVA was 35.5° and 19.4° ($P<0.001$), M1/2 was 14.3° and 11.5° ($P<0.001$), and M1/5 was 33.8° and 30.3°. PP of SG at the 1st, 2nd, 3rd MPJ and hind foot was significantly higher than PP of the NG. Significant difference was also seen in Δ pressure. The cut-off values of HVA was 22.8° (sensitivity 78.7%, specificity 71.2%) and the cut-off value of Δ pressure was 4.51 kg/cm^2 (66.4%, 60.8%). Assessing these two items in combination, sensitivity was 49.4%, and specificity was 87.2%. [Conclusions] The assessment of Δ pressure was useful for determining surgical treatment of the rheumatoid forefoot deformity.

W45-2

The analysis of the factors for recurrence of valgus deformity or varus deformity after joint-preserving surgery for hallux valgus deformity

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Conflict of interest: None

[Object] We analyzed the factors of recurrence of valgus deformity or varus deformity after the joint-preserving surgery for hallux valgus deformity (HV). [Methods] We enrolled 72 HVs (RA/non-RA: 27/45) followed for minimum 12 months after the joint-preserving surgery. The mean age at the surgery, and the follow-up period were 62 years, and 33 months. We defined hallux valgus angle (HVA) ≥ 20° / HVA ≤ 5° / -5° < HVA < 20° at the final follow-up as recurrence group (RG)/varus deformity group (VG)/normal group (NG). We evaluated pre and postoperative HVA·M1M2 angle, ΔHVA, preoperative 1st MTP joint narrowing or erosion, age, sex, BMI, disease, and with or without surgery to the lessor toes in the 3 groups. [Results] The mean preoperative/postoperative/final follow-up HVA were 42°/4°/10°, respectively. The number (rate) of RG, VG, and NG were 14 (19%), 7 (10%), and 51 (71%), respectively. There were significant differences (RG/VG/NG) in preoperative HVA (48°/53°/39°: $p=0.00011$), postoperative HVA (8°/0°/4°: $p=0.011$), and ΔHVA (-41°/-53°/-34°: $p=0.00011$), respectively. [Conclusions] The risk of HV recurrence, and varus deformity after joint-preserving surgery were preoperative high HVA, and the preoperative high HVA or hypercorrection of HVA in this study.

W45-3

Relationship between foot and ankle surgery and depressive condition in patients with rheumatoid arthritis

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Conflict of interest: None

Object: To examine the relationship between foot and ankle surgery and depressive condition in patients with rheumatoid arthritis (RA). **Methods:** This study included 28 patients with RA who underwent foot and ankle surgery. They were evaluated by JSSF, SAFE-Q and BDI-II before and after surgery. Patients were divided into two groups; Depressive group (D group; BDI-II ≧ 14 points) and Minimal depressive group (M group; BDI-II ≦ 13 points), and examined the correlation with each component of JSSF and SAFE-Q. **Results:** JSSF, SAFE-Q (except shoes) and BDI-II, were all improved significantly after surgery ($p<0.05$). Preoperative scores of JSSF (ADL) and SAFE-Q (pain, physical function) were significantly lower in D group than the scores in M group ($p<0.05$). However, the differences disappeared after surgery. In patients who showed decreased SAFE-Q despite improved JSSF, preoperative BDI-II was higher than in patients who showed improved SAFE-Q as well as JSSF after the surgery. **Conclusion:** RA patients with ADL disorder and foot and ankle pain have depressive condition before surgery, and JSSF, SAFE-Q and BDI-II were improved by the surgery. In addition, it is suggested that depressive condition might be a factor to explain the dissociation between objective and subjective evaluation.

W45-4

Surgical procedures and clinical outcomes for forefoot deformity of Rheumatoid arthritis (RA) patients

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Conflict of interest: None

[Object] The aim of this study was to evaluate the clinical outcome of foot surgery for RA patients. [Methods] 21 feet of 19 RA patients underwent forefoot surgery, who were divided into three groups according to the surgical procedures; Group A (n=9): corrective osteotomy of first metatarsal bone with shortening osteotomy of lesser toe, Group B (n=6): arthrodesis of first metatarsophalangeal (MTP) joint with shortening osteotomy of lesser toe, and Group C (n=6): arthrodesis of first MTP joint with resection osteotomy of lesser toe. Pain VAS (0-100), disease activity (DAS28-CRP), Japanese Society for Surgery of the Foot (JSSF) scale, timed “up and go”(TUG) test were evaluated pre- and post-operatively in each groups. [Results] JSSF scale and times for TUG were significantly improved in all groups. Pre- and post-operative times for TUG of Group A was significantly shortest among all groups ($p<0.05$). However, there was no difference in its amount of improvement between groups. There was no difference in pain VAS and disease activity between groups. [Conclusions] Treatment outcomes of foot surgery for RA patients were satisfactory regardless surgical procedure when indicated properly in consideration of the extent of deformation of the joints, age and patients’ activity.

W45-5

The middle-term results of Swanson implant arthroplasty with grommets of the first metatarsophalangeal (MTP) joint in patients with rheumatoid arthritis (RA)

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Conflict of interest: None

【Objectives】To evaluate the middle-term results of Swanson type silicone prosthesis with grommets of the first MTP joints in RA patients. 【Methods】Swanson implant arthroplasty with grommets of the first MTP joint were performed on 23 feet in 14 patients (all female) with RA. The mean age at the operation was 58 (38-76) years old. Average follow-up period was 6 years. Patient characteristics, clinical outcomes using JSSF hallux scale, HVA, M1/2 angle, implant breakage, recurrence of deformity, and complications were examined. 【Results】JSSF hallux scale improved significantly from 45 points preoperatively to 76 points at the last follow-up. HVA decreased significantly from 42° preoperatively to 28° at the last follow-up. M1/2 angle was slight decreased (15° to 11°), not significantly. Recurrence of hallux valgus deformity occurred in three joints. Three implants were removed because of a surgical site infection in one patient and silicone synovitis in two patients. 【Conclusions】Swanson implant arthroplasty improved the clinical outcome, despite the high failure rate (13%). Two cases resulted in a silicone synovitis were middle-aged (38 and 43 years old) at the operation. Swanson implant arthroplasty should be carefully indicated in relatively high activity generation.

W45-6

Metatarusus primus elevatus in rheumatoid forefoot deformities

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Conflict of interest: None

Objective: To clarify the radiographic characteristics of metatarsus primus elevatus in rheumatoid forefoot deformities. Methods: A retrospective study was performed of standing AP and lateral radiographs of 51 feet (37 patients; average age 65 years) who underwent toeplasty in our hospital. The elevation of the first metatarsal bone in relation to the second metatarsal was measured as MPE. Results: MPE was 2.9+/-4.1mm (mean+/-standard deviation). Comparative study was performed between the group with MPE>5mm (N=10 feet) and that with MPE<2mm (N=26 feet). There were no significant difference in hallux valgus angle and intermetatarsal angle between two groups. In the group with MPE>5mm, calcaneal pitch, the height of talo-calcaneal and talonavicular joint were significantly greater. Conclusion: Some patients represent metatarsus primus elevates in rheumatoid forefoot deformities and greater calcaneal pitch.

W46-1

Comparison of the risk of comorbidities between patients with and without rheumatoid arthritis using Japanese health insurance database

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Conflict of interest: None

Objective: To evaluate risk of hospitalized infection (HI), cardiovascular disease and stroke (CVD), and fracture in rheumatoid arthritis (RA) patients compared to non-RA patients using Japanese health insurance database. **Method:** Among individuals > 18 years who had at least 6 months of continuous enrollment in the database, RA cases were defined to have one RA diagnostic code and prescription of disease-modifying antirheumatic drugs > 1 between 2005 and 2013 (n=6,712). We selected age-, gender-, calendar year of the observation start-, and observation length-matched non-RA cases at 1:5 ratio (n=33,560). Odds ratios (ORs) of each comorbidity of RA versus non-RA cases were calculated using the generalized estimating equation. **Results:** The incidence rates of HI, CVD, and fracture in the RA cases were 20.42, 6.79, and 10.50/1,000 person-years (PY) and incidence rate ratios [95% confidence interval, 95% CI](RA vs non-RA) of the comorbidities were significantly elevated (HI, 2.47 [2.20-2.77]; CVD, 1.63 [1.33-1.99]; and fracture, 3.35 [2.80-4.02]). The odds ratio of RA for HI, CVD, and fracture was 1.67 [1.42-1.96], 1.44 [1.14-1.82], 1.73 [1.31-2.28]. **Conclusions:** This study revealed RA cases had significantly higher risks of these comorbidities than non-RA cases.

W46-2

Hospitalization risk factor for cerebral and cardiovascular disease with rheumatoid arthlitis

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Conflict of interest: None

[Objectives] To elucidate hospitalization risk factor for cerebral and cardiovascular disease in patients with rheumatoid arthlitis (RA) on NinJa. [Methods] The patients who were enrolled in RA database NinJa in 2014 were retrospectively examined about hospitalization risk factor for cerebral and cardiovascular disease (CVD) based on their medical background in the previous year. [Results and Conclusion] Total 15032 patients were registered for NinJa in 2014. Of them 96 patients were hospitalized for CVD, namely, angina, myocardial infarction, heart failure, cerebral infarction and cerebral hemorrhage. Medical background of CVD hospitalized 77 patients (CVD group) were compared with non-CVD group (10835 patients). With univariate analysis, CVD group were statistically significantly older, more males, had longer RA disease duration, higher RA stage, lower QOL, higher patient's VAS, higher DAS28, smoking history, operation history, cancer, more steroid usage rate, lower MTX usage rate, more dose of tacrolimus than non-CVD group. With multivariate analysis, higher age, male, low QOL (EQ-5D), positivity of RF were detected as significant factors.

W46-3

Transition of incidence, clinical features and prognosis of AA amyloidosis complicating rheumatic diseases –based on the results of upper gastro-intestinal biopsy screening for AA amyloidosis of rheumatic diseases during consecutive 25 years

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Conflict of interest: None

Objective. To investigate transition of the incidence, clinical features and the prognosis of AA amyloidosis (AA) complicating rheumatic diseases. Methods. We conducted Gastro-intestinal (GI) biopsy AA screening for a total of 6441 patients who were undiagnosed AA from 1990 to 2014 and all of the above were investigated in 391cases of diagnosed AA. We divided the patients into half a decade interval groups and compared. Results. 1. Incidence of AA was significantly decreased in recent onset groups, 2. Interval from rheumatic diseases onset to AA diagnosis was significantly prolonged in recent onset groups ($p=0.0004$). 3. CRP values were significantly decreased with lapse of time ($p<0.0001$). 4. Long-term prognosis significantly improved in recent decade group (Log-rank test $p<0.001$). Conclusion. Decreased incidence and improved prog-

nosis of AA were demonstrated probably due to progress of treatment of rheumatic diseases in our cohort study.

W46-4

Dry mouth symptom is associated with the exacerbation of disease activity, pain, fatigue, mental state and use of glucocoticoids in rheumatoid arthritis

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Conflict of interest: None

【Objective】In rheumatoid arthritis (RA) patients, dry mouth symptom could be caused not only by secondary Sjogren syndrome (SS) but also by iatrogenic, psychogenic causes. The aim of this study is to examine the correlation between dry mouth symptom and RA activity, physical function, pain, mental state and fatigue.【Methods】The presence or absence of dry eye, dry mouth and anti-SSA / SSB antibodies (Ab) were examined in 218 consecutive RA patients. We defined possible SS as anti-SSA / SSB-positive and with dry mouth or dry eye symptoms. Wilcoxon test was used to study if dry mouth, dry eye, anti-SSA / SSB Ab and possible SS could correlate with age, gender, disease duration, Stage, RA activity (DASESR, TJC, SJC), physical dysfunction (HAQ), pain (PtVAS, DrVAS), treatments, anxiety, depression (HADS), and fatigue (VAS fatigue).【Results】DASESR, HAQ, PtVAS, DrVAS, anxiety, VAS fatigue was significantly higher in patients with dry mouth than without dry mouth. There was no significant difference with dry eye, anti-SSA / SSBAb and the possible SS. Glucocorticoids was significantly higher in patients with dry mouth.【Conclusions】Dry mouth symptom was suggested to correlate with disease activity, physical function, pain, fatigue mental state and use of glucocoticoids in RA patients.

W46-5

Fracture surgeries in rheumatoid arthritis patients: from the "NinJa" registry

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Conflict of interest: None

[Objectives] The aim of this study was to investigate for drug use of rheumatoid arthritis (RA) patients who injured the fracture of limbs requiring surgery using National Database of Rheumatic Diseases by iRnet in Japan (NinJa). [Methods] Presence or absence, injury site, drug use, etc. of fracture surgeries examines in 15101 patients registered in 2015. [Results] There were 51 females patients 8 males patients (Stage I: 9, II: 11, III: 12, IV: 22. Class 1: 6, 2: 29, 3: 16, 4: 4), with a mean age of 71.8years. 10 RA patients were drug free. Of the remaining 49 RA patients, there were 26 (44%) patients treated methotrexate, 9 (15%) patients treated biologic agent (Bio), 10 (17%) patients treated DMARDs. The mean oral steroid dose was 3.0mg/day prednisolone. In the no fracture group, the dose was 1.5mg/day. [Conclusion] There was a trend for a MTX a Bio group have low fracture rate. Fracture group had oral many steroid than no fracture group.

W46-6

Analysis of Treatment of Rheumatoid Arthritis in each prefecture in Japan using National Database

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Conflict of interest: None

[Object] To analyse RA treatment in each prefecture throughout Japan using the 1st National Database open data. [Method] The Ministry of Health, Labor and Welfare of Japan disclosed in Oct 2016 the data of the top 30 most-frequently prescribed drugs during a 1-year period from Apr 2014 to Mar 2015 in each prefecture in Japan along with the patients' sex and age. It does not include all drugs used in RA treatment. [Results] The total number of prescriptions of DMARDs was correlated with the population in each prefecture. However, the total expenditure on DMARDs and biologics administered to one patient during the 1-year period was correlated with four factors: the number of rainy days a year, the number of RA specialist per RA patient and the patient's age. The number of rainy days and the number of RA specialist were positively, and the patient age was inversely correlated. [Conclusions] The meteorological factors may be affecting the way of RA-treatment. RA specialists may be using more expensive drugs such as biologics. The younger patients may be being treated by more expensive drugs such as biologics, which seems very favorable seeing they have longer duration of RA pathology.

W47-1

Analysis of renal functional change in patients with rheumatoid arthritis using NinJa 2012-2015

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Conflict of interest: None

[Objectives] To evaluate the risk factors of kidney function impairment in patients with rheumatoid arthritis (RA). [Methods] Extracted were 2319 RA patients with estimated glomerular filtration rate (eGFR) less than 120 mL/min./1.73m^2 in 2012 and 2015, and with eGFR 60 mL/min./1.73m^2 and more in the year 2012, who were registered in NinJa every year from 2012 to 2015. eGFR in 2012 and eGFR in 2015 were compared, and risk factors for eGFR decline were evaluated by multivariate logistic regression analysis. [Results] eGFR in 2015 was significantly declined from eGFR in 2012 (P<0.0001), and eGFR in 555 patients (23.9%) newly declined to less than 60 mL/min./1.73m^2, and eGFR in 151 patients (6.5%) newly declined to less than 45 mL/min./1.73m^2. Age, Body Mass Index (BMI), steroid use were significantly associated with eGFR < 60 mL/min./1.73m^2(odds ratio, 95%CI, age: 1.09 1.08-1.11, BMI: 1.06, 1.02-1.10, steroid use: 1.40, 1.08- 1.81) and age, disease duration, NSAIDs and steroid use were significantly associated with eGFR <45 mL/min./1.73m^2(age: 1.11, 1.08-1.14, disease duration: 1.02, 1.00-1.04, NSAIDs: 0.55, 0.34-0.89, steroid use: 2.19, 1.41-3.40). [Conclusions] Age, BMI, disease duration, and steroid use were significant risk factors of eGFR decline in NinJa 2012-2015 cohort.

W47-2

Association of Human T Lymphotropic Virus Type I with Rheumatoid Arthritis

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Conflict of interest: None

Objectives: The present and previous results demonstrated that might act human T-lymphotropic virus type I (HTLV-I) as a pathogen in rheumatoid arthritis (RA). We studied whether HTLV-I was a pathogen for RA among Nagasaki atomic-bomb survivors cohort. **Methods:** We measured anti-HTLV-I antibody (Ab) levels by chemiluminescent enzyme immunoassay in the sera of atomic-bomb survivors who participated in biennial health examination in 2006 through 2010. When results were positive, we confirmed infection by Western blotting. The diagnosis of RA was performed by 2010 classification criteria. **Results:** Among 2094 participants (females 61.4%, average age 73 years), 217 (10.4%) had anti-HTLV-I Abs. The prevalence in females was calculated significantly higher than that in males (13.1%, 6.1%, p<0.001). Among all, 22 participants (1.1%) were diagnosed with RA. The prevalence of RA in HTLV-I positive group was significantly higher than that in HTLV-I negative group (2.8%, 0.9%, p=0.02). Age, gender-adjusted odds ratio for RA prevalence was also significant (2.92, 95% confidential interval, 1.12, 7.63). The prevalence of HTLV-I and RA was not associated with radiation dose. **Conclusions:** HTLV-I is suggested to be one of causes of RA in epidemiological study.

W47-3

Characteristics of Elderly onset rheumatoid arthritis patients In *NinJa* 2015 database

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Conflict of interest: None

[Objectives] The ratio of male patients in rheumatoid arthritis was increased in elderly-onset rheumatoid arthritis (EORA) compared with younger-onset RA (YORA). The characteristics of differentiation between men and women in EORA were investigated. [Methods] We investigated 15100 patients (2996 men and 12140 women) in *NinJa* 2015 registry. The patients were classified into three groups according with the age of onset, namely Group A (less than 65 years old), Group B (from 65 to 74), and Group C (more than 75). Each group was divided to two subgroup by men and women. [Results] In the Group C, the frequencies of medication with glucocorticoid, DMARDs, MTX, and biological drugs were 41.2%, 83.1%, 40.2%, and 13.3% in the subgroup of men, respectively, whereas 46.5%, 85.2%, 40.2%, and 15.2% in the subgroup of women. The disease activity score of mHAQ, DAS28-ESR and SDAI were 0.42, 2.19, and 7.37 in men, and 0.59, 3.29, and 8.27 in women, respectively, in Group C. The SIR of overall malignancy among men and women were 1.09 and 1.22 in Group A, respectively, 1.07 and 0.97 in Group B, and 1.26 and 0.61 in Group C. [Conclusion] In the group of EORA, disease activity was lower in men than in women. The SIR overall malignancy was lower in women of the Group C.

W47-4

The association between latent components underlying a set of measures and the quality of life of patients with rheumatoid arthritis; an approach through analytical dimension reduction to the National Database of Rheumatic Disease in Japan

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Conflict of interest: None

Aim: To identify analysis-derived components underlying a set of wide-ranging assessment measures of the RA patient status, examining also relative importance of the components as the determinant of the quality of life. **Methods:** A total of 1455 patients with moderate disease activity were recruited from the National Database of Rheumatic Diseases in Japan (*NinJa*) between 2012 and 2014. Components explaining patient status of RA were derived from principal component analysis of 13 assessment measures. The multivariate-linear regression analysis was used to examine the relative contribution of each identified component on the variation of EuroQOL-5 Dimension Questionnaire score. **Results:** Four components were detected and labeled as current symptoms, physical disability, patient distress, and laboratory findings, respectively, in order. In the multivariate analysis, the relative contribution of the first to forth components on the variation of EuroQOL score were accounted for 19.9%, 16.4%, 57.7%, and 2.1%, respectively. **Conclusion:** In the patient quality of life, psychological distress was more important than subjective/objective symptoms or physical disability. For the purpose of the achievement of improved QOL in RA patients, psychological distress should be more focused on.

W47-5

Trends in Mortality of Patients with Rheumatoid Arthritis:2000-2015

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Conflict of interest: None

[Object] To investigate whether mortality of RA patients has declined in accordance with advancements in treatment [Methods] RA patients who participated in the IORRA study were assessed during the observation period from October 1, 2000 to September 30, 2015. Based on the survival information from each of the survey, mail inquiry and etc., the standardized mortality ratio (SMR) was calculated, assuming that patients who were lost to follow-up (unknown patients) were all alive. Then, sensitivity analysis was performed to evaluated the effect of unknown patients using multiple imputation methods. The changes in SMRs within each of different time periods, 2000-2005, 2006-2010, and 2011-2015, were analyzed. [Results] A total of 10,880 patients constructed 91,020.7 person-years observation. When assuming that unknown patients all alive, the SMR was 1.12 (95%CI 1.05-1.20) for overall period and 1.09 (95%CI 0.94-1.25), 1.14 (95%CI 1.02-1.27) and 1.13 (95%CI 1.02-1.25) for each of successive time intervals. The sensitivity analysis considering risk for death in unknown patients, the SMR was 1.45 for overall and 1.59, 1.43 and 1.32 for each of intervals. [Conclusions] Mortality of RA patients compared to the general population across time may have improved over this 15-year time span.

W47-6

Early arthritis cohort study for prediction of rheumatoid arthritis in healthy islanders

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Conflict of interest: None

Background: It is important to diagnose early for early rheumatoid arthritis (RA). Autoantibodies have been observed in healthy subjects up to 10 years before they developed RA. Aim: We have attempted screening healthy population for early arthritis to measure ACPA in serum. Methods: Since 2014, we have tried to screen healthy islanders for RA in Nagasaki Prefecture. Screening for the early RA, ACPA measuring, questionnaires about arthralgia with fingers/wrists, family history with rheumatic diseases were done, 2 out of 3 were defined the high-risk subjects for RA. High-risk subjects were recommended to visit the rheumatologist for further exams. After 2015, only ACPA positive subjects were included in high-risk group. Results: We had obtained informed consents from 3617 subjects, % ACPA positivity was 1.7%. Eighty-nine subjects were required for further exams. Only 43 subjects (48.3%) visited the rheumatologist, and final diagnoses were as 6 RA, 27 non RA (16 Osteoarthritis, 6 undifferentiated arthritis, 3 Spondyloarthropathy, 11 others). Current and past smoking rate was 31.0%. Conclusions: ACPA positivity was 1.7 % in healthy islanders. Long-term follow-up is necessary to clarify the course of early arthritis.

W48-1

Profiling 14-3-3η in Human Primary Cell Based BioMAP Disease Models Reveals a Unique Pro-Inflammatory Phenotypic Signature Consistent with rheumatoid arthritis (RA)-Inflammation Biology

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Conflict of interest: Yes

Aim: 14-3-3 proteins are intracellular chaperones and are elevated in synovial fluid and serum from patients with RA. We evaluate the impact of 14-3-3η across a panel of human primary cell-based disease models in BioMAP platform. **Methods:** Phenotypic activity profiles were generated for 14-3-3η across BioMAP systems and were analyzed and compared with more than 3000 compounds in the BioMAP database. **Results:** 14-3-3η mRNA is highly expressed in all BioMAP Diversity Plus Systems in B cell and Fibroblast based systems, compared to vehicle control. The activity profile for 14-3-3η in BioMAP shows highly selective effects in two systems: HPNo, a vascular endothelial cell-PBMC co-culture; and BT, a stimulated co-culture of B and T cells. 14-3-3η increases VCAM-1 and TNFα in HPNo and sIL-6 production in BT. Comparison of the profile to the BioMAP database identified mechanistic matches with pro-inflammatory TLR-like agonists including Pam3CSK4, Flagellin and HKLM, whereas the BioMAP profile of 14-3-3η was not similar to LPS, a potential bacterial endotoxin contaminant. **Conclusion:** The BioMAP profile for 14-3-3η is consistent with B cell activation that correlates with pro-inflammatory activity and disease-relevant biomarkers, indicating the role of 14-3-3η in the pathogenesis of RA.

W48-2

Gene modules correlated with disease activity and treatment identified from CD4$^+$ T cell subsets of Rheumatoid Arthritis

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Conflict of interest: Yes

[Object] The aim of this study was to analyze the transcriptome of CD4$^+$ T cell subsets in rheumatoid arthritis (RA) and identify gene modules correlated with clinical traits and therapy. [Methods] PBMC were taken from 10 RA patients and 10 healthy controls (HC). Samples were repeatedly taken from three RA patients 6 months after abatacept (ABT) treatment. Seven CD4$^+$ T cell subsets (Naive, Treg, Tfh, Th1, Th17, Th17.1, Th2) were sorted, and paired-end RNA sequencing was performed using HiSeq 2500. [Results] The overview of a total of 149 samples revealed that administration of ABT exerted a large shift toward the expression pattern of HC. Knowledge-based pathway analysis revealed that ABT substantially ameliorated transcriptomic changes in RA CD4$^+$ T cell subsets. Weighted gene co-expression network analysis (WGCNA) of all CD4$^+$ subsets identified a common gene module that consisted of 227 genes and was correlated with DAS28-CRP (Spearman's rho = 0.46, $p = 4 \times 10^{-9}$). The most highly connected 30 genes of this module included *JAK3* and *ZAP70*, and pathway analysis revealed that ABT treatment suppressed the TCR signaling pathway network. [Conclusions] Dysregulation of the TCR signaling pathway in RA CD4$^+$ T cells is associated with disease activity and ameliorated by ABT treatment.

W48-3

Pathogenesis role of resistin in rheumatoid arthritis

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Conflict of interest: None

[Objectives] The aim of this study is to elucidate the effects of resistin on rheumatoid synovial fibroblasts (RSFs). [Methods] Expression of resistin and the receptor, adenylyl cyclase-associated protein 1 (CAP1), in the synovial tissue from rheumatoid arthritis (RA) and osteoarthritis (OA) was examined by immunohistochemistry. RSFs were established from RA synovial tissue. RSFs were treated with resistin for 18 hours. Then, total RNA was extracted, and the gene expression profile was analyzed by RNA sequencing. Concentration of chemokines in the culture supernatant was determined by ELISA. Expression of CAP1 was examined by RT-PCR and Western blotting. [Results] Resistin and CAP1 was highly expressed in the RA synovial tissue compared to OA. Resistin was expressed by macrophages in the RA synovium. RNA sequencing revealed that expressions of 18 genes, including 7 chemokines (CXCL1, CXCL2, CXCL3, CXCL5, CXCL6, CXCL8 and CCL2), from RSFs were increased more than 2 fold by stimulation with resistin. Production of CXCL8 and CCL2 in the culture supernatant of RSFs was increased by resistin. CAP1 was expressed by RSFs. [Conclusion] Resistin might play an important role in the pathogenesis of RA via up-regulation of chemokine expression in the synovial tissue.

W48-4

The dysregulation of chemokine gene trasnscription by histone H3 lysine 4 methyltransferases in rheumatoid arthritis synovial fibroblasts

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Conflict of interest: None

[Object] The activation of synovial fibroblasts (SF) plays an important role in rheumatoid arthritis (RA) pathogenesis. We examined whether the epigenetic mechanisms, such as histone modifications, were involved in the activation of RASF. [Methods] The mRNA levels of histone methyltransferases (HMT) that catalyze an active histone marker histone H3 lysine 4 (H3K4) methylation were investigated in RASF and osteoarthritis (OA) SF. Genes whose expression decreased in HMT siRNA-treated RASF were examined. The change in expression of the identified genes after TNFα stimulation and H3K4me3 in the promoters after HMT siRNA treatment was examined in RASF and OASF. [Results] MLL1 and MLL3 mRNA levels were high after TNFα stimulation in RASF.

CXCL10, CXCL11 and CCL5 mRNA levels were repressed with the silencing of MLL1 or MLL3 in RASF. The gene expression of the chemokines after TNFα stimulation and H3K4me3 in the promoters were high in RASF. H3K4me3 in the promoters decreased with the depletion of MLL1 but not MLL3. In the chemokine genes, it is suggested that MLL1 regulates H3K4me3 at the promoters and that MLL3 regulates H3K4 methylation in other sites, such as enhancers. [Conclusions] H3K4-specific HMT may be involved in the activation of RASF through upregulation of chemokines.

W48-5

Phenotype of Platelets is Altered in Circulation of Patients with Rheumatoid Arthritis

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Conflict of interest: None

Background: Platelets play an important role in hemostasis. On the other hand, platelets have various surface molecules and can induce activation of other cells through cell-to-cell contact and may contribute to the pathogenesis of systemic diseases such as RA. To examine this hypothesis, we investigated the phenotype of circulating platelets and the association with clinical characteristics. Methods: Eight RA and 9 scleroderma and 13 healthy controls were examined. Expression of CD62P, membrane-bound TGF-b, CD147, CD142, and CD31 on platelets was examined using flow cytometry. Correlation between proportion of platelet subsets and clinical parameters were examined. Results: Proportion of $CD62P^+$ platelets were higher in both RA and SSc compared to HC ($P < 0.0005$, $P < 0.0002$, respectively). Interestingly, proportion of $CD147^+$ platelets were significantly higher in RA ($P < 0.0004$), whereas both proportions of $CD147^+$ and $TGF\text{-}b^+$ platelets were higher in SSc, respectively. In patients with RA, proportion of $CD62P^+$ platelets was positively correlated with CRP or ESR and composite disease markers such as SDAI and was decreased in 6 RA patients after treatment ($P < 0.03$). Conclusions: In patients with RA, platelets have altered phenotype and might be involved in the pathogenesis.

W48-6

MMP3 high titer is a high risk of sarcopenia in RA patients

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Conflict of interest: Yes

[Objectives] RA patients have lower muscle and higher prevalence of sarcopenia than healthy individuals. We investigated the relationship between sarcopenia and disease activity at baseline of prospective observational study (CHIKARA study, UMIN000023744). [Methods] Muscle mass, body fat mass, total body water, bone mass, and basal metabolic rate were measured by body composition analyzer MC-780A (TANITA). We investigated the correlation between sarcopenia and disease activity, physical function, and laboratory data by uni- and multivariate analysis. [Results] 100 RA patients (female:78%, age: 66.1 years) were entry. Mean disease duration was 5.5 years, DAS28-ESR was 3.55, and sarcopenia was 28%. Sarcopenia correlated with weight, BMI, body fat mass, muscle mass, basal metabolic rate, Steinbrocker stage, CRP, bone mass, and MMP3 by univariate analysis. Glucocorticoid dosage, RF, and ACPA did not correlated. BMI, body fat mass, and MMP3 were independent risk factor by multivariate analysis. The odds ratio of sarcopenia was 3.09 compared MMP3 over and under 90.7 ng/ml by ROC curve analysis ($p=0.023$). [Conclusion] Sarcopenia was 28% in RA. Low BMI, high body fat mass, and high MMP3 were independent risk factor of sarcopenia. The relationship of MMP3 and sarcopenia was indicated.

W49-1

The association between methotrexate polyglutamate concentration in erythrocyte and liver dysfunction in rheumatoid arthritis patients

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Conflict of interest: None

[Objectives] We investigated the association between methotrexate polyglutamate (MTX-PG) concentration in erythrocytes and liver dysfunction in rheumatoid arthritis patients treated with MTX. [Methods] Sixty-two patients with abnormal AST or ALT were enrolled. We studied the correlation between MTX-PG (1, 2, 3, 1-5) concentrations in erythrocytes and the ratios of AST (S ratio) or ALT (L ratio) to the upper limits. Also we stratified patients with folic acid (FA) or fatty liver (FL). [Results] More than 80% of liver dysfunction was within 3 times of upper limit level. There was no correlation between MTX-PG1-5 concentrations and S or L ratio ($r<0.3$, $p>0.05$), even when stratified with FA or FL ($r<0.3$, $p>0.05$). The mean MTX-PG1-5 concentration in FA group tended to be higher than in non-FA group (94.8 vs. 85.3 nmol/L, $p<0.05$, the mean MTX dose was significantly higher in FA group). The mean MTX-PG1-5 concentration in FL group tended to be lower than in non-FL group (86.2 vs. 99.4 nmol/L, $p>0.05$). [Discussion] There was no correlation between MTX-PG concentrations and liver dysfunction. However, there was a tendency toward higher MTX concentration in patients with FA or FL, indicating that MTX-PG concentrations might be influenced by these factors in developing liver dysfunction.

W49-2

Tapering or stopping of metotrexate in non-tumor necrosis factor therapy (tocilizumab and abatacept) in patients with rheumatoid arthritis

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Conflict of interest: Yes

[Objectives] To evaluate tapering or stopping of MTX in non TNF therapy (TCZ and ABT) and impact of it to RA treatment. [Methods] 35 RA patients who initiated TCZ or ABT with concomitant MTX and continued non-TNF agents for 2 years were used. Time course of disease activity, activity of daily living, joint destruction and tapering concomitant drug (MTX and PSL) were investigated. [Results] 28 females and 7 males with mean age of 59 years. TCZ was continued for 2 years in 23 cases and ABT in 12 cases. Mean DAS28-CRP was 4.6 at baseline, 2.1 at 1 year and 1.9 at 2 years. Significant decrease and sustainment were also observed in CDAI, serum MMP3 and mHAQ. Although ΔmTSS at baseline was 7.3, it was significantly improved to 0.5 from 1 year to 2 years. Mean MTX dosage was significantly decreased from 9.4mg/w at baseline to 3.0 mg/w at 2 years. There was a significant difference of MTX dosage. Although MTX was concomitant in all patients at baseline, it was used in only 42.9% at 2 year. PSL was also tapered from 3.5mg/day at baseline to 0.9mg/d at 2 years. More baseline MTX dosage was observed in MTX-continuing group at 2 years than in MTX-stopping group at 2 years. [Conclusions] This study suggested that concomitant MTX can be tapered or stopped in RA patients treated with TCZ or ABT.

W49-3

Analyze of the reducing of methotrexate in rheumatoid arthritis with abatacept at early treatment stage

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Conflict of interest: None

Objective: To assess the clinical characteristics of rheumatoid arthritis (RA) patients treated with abatacept (ABT) and achieved clinical remission and reducing the dose of methotrexate at 3 months after treated with ABT. Methods: Efficacy was evaluated by CDAI. Results: 90 (8men, 82women, average age 57.7 years old) of RA patients were treated with ABT and enrolled in this study. Overall remission rate was 25.6% at early treatment stage (CDAI ave. 27.5+/-15.4→11.2+/-9.1, mHAQ ave.6.2+/-9.6→2.2+/-4.0. 41 patients (55.4%) were able to decrease the dose of MTX (ave.dose 11.2 +/-2.6 mg/week→9.1 +/-2.3mg/week). There were

no significant differences in ACPA positive or negative. Results: ABT is able to achieve reduction of MTX at early treatment stage.

W49-4

Methotrexate dosage reduction in patients with rheumatoid arthritis who achieved remission with TNF inhibitors

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Conflict of interest: None

[Objective] To investigate adjustment of dose of concomitant methotrexate (MTX) in patients with rheumatoid arthritis (RA) who achieved remission with TNF inhibitors in clinical practice. [Methods] A total of 89 patients with RA achieved clinical remission (DAS28-CRP<2.6) with their first TNF inhibitor with concomitant MTX. Of these, 85 patients who had ≥ 3-year follow-up were included in this retrospective study. [Results] The mean time from starting TNF inhibitors to achieving remission (baseline) was 16 weeks, and the mean DAS at baseline was 1.93. The proportion of patients maintaining remission at 1, 2, 3 years was 97, 90, 82%, respectively. MTX dose was reduced significantly from baseline to 1, 2, and 3 years (8.7, 7.8, 7.0, and 6.7 mg/week, respectively). Thirty-five (41%) patients maintained remission with reducing MTX dose at 3 years. Multivariate logistic regression revealed that DAS at baseline (OR: 0.13, 95% CI: 0.03-0.51), time from starting TNF inhibitors to baseline (OR: 0.94 per 1 week, 95% CI: 0.90-0.99), and MTX dose at baseline (OR: 1.39, 95% CI: 1.12-1.73) predicted maintaining remission with reducing MTX dose at 3 years. [Conclusions] Reducing dose of concomitant MTX can be one of the treatment options in patients who achieved remission with TNF inhibitors.

W49-5

Clinical features of treatment resistant patients with multiple biologic-DMARDs: from FIRST registry

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Conflict of interest: None

Objectives: To characterize patients with rheumatoid arthritis (RA) refractory to multiple bDMARDs. **Methods:** We retrospectively analyzed data from 1852 bDMARD-naïve RA patients who started bDMARDs from 2003 to 2016 in our institution. Patients who had not achieved low disease activity (LDA) despite treatment with more than four biologics were defined as refractory cases. The primary endpoint was the rate of refractory cases, and we compared baseline characteristics between refractory cases and the patients who achieved LDA with the first bDMARDs, using multivariate analysis. **Results:** Of the 1852 patients, 54 (2.9%) were refractory cases and 723 (39%) achieved LDA with the first bDMARDs. Statistically significance were observed in the baseline characteristics of refractory cases as follows: mean age 54.4 (vs 59.4), MTX 6.7mg/W (vs 9.8mg/W), tenderness joints 14 (vs 11), pain-VAS 64 mm (vs 50), and DAS28-ESR 6.1 (vs 5.4). **Conclusions:** Our results suggested that refractory cases were the use of low dose MTX, even as young and high DAS28-ESR. Improved pain management would be able to complement disease suppression in RA.

W49-6

The RA female cases using MTX with pregnancy hope

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Conflict of interest: None

【Object】MTX is an anchor drug. It is using many cases. It is necessary to discontinue MTX, but problems such as exacerbation occur by doing so. To stop MTX, we planned the pregnancy and the delivery of the RA females who used MTX with hope of the pregnancy.【Method】From 2010 through 2015, there were six RA female patients who had pregnancy hope and used MTX.【Result】The states of 6 RA female patients with pregnancy hope ware all remission or low disease activity in DAS28. 3 patients in these cases, we could control their RA by use ETN. They were able to pregnancy, delivery and nurse. A patient did not have symptom exacerbation after stopped MTX. Growth of their fetus and babies did not have any problem. There was a case that a patient who treated by MTX+ENT gave up to conceive because of RA exacerbated after stopped MTX. Another case, though the patient had freeze fertilized ovum, she gave up to conceive because RA was not able to be controlled after stopped MTX.【Conclusion】Four of six casas with pregnancy hope became pregnant. Three of four cases were used MTX+ETN and stopped only MTX. Two of one case was used only MTX and stopped it. For the pregnancy and the delivery while they used ETN, the complications did not occur.

W50-1

The role of SH3BP2 in lupus-prone (BL6/*lpr*) mice

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Conflict of interest: Yes

[Objectives] SH3BP2 is an adaptor protein which is dominantly expressed in immune cells and regulates intracellular signaling pathways such as Syk and PLCγ. We have previously reported that SH3BP2 deficiency suppresses autoantibody production in a murine collagen-induced arthritis model. In this study, we investigated the effect of SH3BP2 gain-of-function mutation on the phenotype of lupus-prone mice. [Methods] SH3BP2 P416R gain-of-function mutant mice and lupus-prone (BL6/lpr) mice were crossed to yield the double mutant mice. Skin rash and proteinuria were assessed until 12 months of age. At the end of the observation, mice were euthanized, and serum and organs were collected. Anti-dsDNA antibody levels in sera were measured by ELISA. B-cell and T-cell subsets were analyzed by flow cytometry. [Results] Skin rash and proteinuria were alleviated in the double mutant mice compared to the BL6/lpr mice. Anti-dsDNA antibodies production and splenic B220+ T cell population were decreased in the double mutant mice. [Conclusion] Contrary to our initial hypothesis, SH3BP2 gain-of-function mutation ameliorated clinical and immunological phenotypes of the lupus-prone mice. Further analyses are required to reveal the unexpected role of SH3BP2 in the autoimmune disease.

W50-2

Repertoire analysis and genetic association study of B cell receptors in SLE by RNA sequencing

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Conflict of interest: Yes

Objective: Although various autoantibodies are observed in SLE, the precise etiologies underlying them are unclear. We tried to investigate the B cell receptor CDR3 amino acid sequence characteristics of SLE patients and to unveil the genetic regulation of them. **Method**: We performed RNA-sequencing of peripheral blood plasmablasts from 50 SLE cases and 30 healthy donors. Sequenced reads were mapped to BCR genes; IGH, IGK and IGL, and CDR3 amino acid sequences were determined. **Result**: We defined “public sequence” as CDR3 amino acid se-

quences which were shared between individuals. Among CDR3 sequences of IGk and IGl, 618 and 355 public sequences were observed. The expression patterns of public sequences were different between SLE cases and controls, and could differentiate them based on CDR3 data alone. The expression level of public sequences predominantly expressed in SLE cases partially correlated with anti-ds DNA antibody titer. eQTL analysis suggested the genetic association with the expression of public sequences predominantly expressed in SLE. **Conclusion**: Difference in CDR3 amino acid sequence was observed between SLE and healthy donors, and it was presumed to be associated with autoantibody. The expression of these sequences was suggested to be under genetic control.

W50-3

Endoplasmic reticulum stress induces lupus kidney disease by facilitating antigen cross-presentation

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Conflict of interest: None

Objective: Our 'self-organized criticality theory' explains that SLE is induced after repeated immunization with antigen in mice normally not prone to SLE, where cytotoxic T lymphocyte generated *via* antigen cross-presentation induces lupus tissue injury. Here we examine the contribution of endoplasmic reticulum (ER) stress to antigen cross-presentation and the induction of lupus nephritis. **Methods:** Mice were repeatedly immunized with ovalbumin (OVA), and unfolded protein response (UPR)-related molecule in splenic DC (spDC) was detected. Bone marrow-derived DC (BMDC) was cultured with OVA and/or an inducer of ER stress Tunicamycin, and EEA1, Sec61 or OVA was immunoprecipitated and detected. **Results:** Expression of UPR-related protein including Bip, PERK, IRE1 alpha, XBP1 and phosphorylated eIF2 alpha was increased in the spDC of the mice that developed glomerular injury. In BMDC, co-culture with Tunicamycin increased both the amounts of Sec61 co-precipitated with EEA1 and OVA in the cytoplasm. **Conclusion:** ER stress increased not only endosomal Sec61 but also the export of antigen from endosome to cytoplasm, suggesting that antigen cross-presentation can be increased in proportion to the amount of antigen accumulated in the cytoplasm of DC, thereby leading to lupus kidney injury.

W50-4

Expression and functional analysis of Deooxyrinonuclease 1-like-3 in immune cells

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Conflict of interest: None

Deoxynuclease 1-like-3 (DNase1L3) belongs to DNase1 family. It is reported that DNase1L3 digests nuclear DNA in apoptotic or necrotic cells. Mutations of *DNase1L3* gene that cause loss of function are reported in murine models of Systemic Lupus Erythematosus (SLE) and familial SLE with an autosomal recessive pattern of inheritance. Although it is suggested DNase1L3 plays a protective role in SLE, the mechanism how loss-of-function of DNase1L3 cause SLE has been largely unknown. We analyzed expression levels of DNase1L3 mRNA in human white blood cells by real-time-PCR. At steady states, plasmacytoid dendritic cells had the highest expression of DNase1L3. We next examined the condition to up-regulate expression of DNase1L3. Interleukin-4 induced markedly high DNase1L3 expression in monocytes, monocyte-derived dendritic cells and monocyte-derived macrophages. DNase1L3 protein was distributed in cytosol, and was secreted into extracellular space. The secreted DNase1L3 protein could digest naked DNA. Furthermore, the secreted DNase1L3 protein could also degrade lipid-DNA complexes and protein-DNA complexes, which are resistant to DNase1. We suggest DNase1L3 is secreted by innate immune cells and may play a critical role in the tissue homeostasis by degrading various forms of DNA.

W50-5

Platelets increase IL-1β production of monocytes via NLRP3 inflammasome activation

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Conflict of interest: None

[Objectives] To discover the mechanism that platelets increase IL-1β production of monocytes. [Methods] We compared IL-1β production in coculture with platelets among THP-1 cell lines, NLRP3 and caspase-1 knocked down by shRNA and scramble control. We analyzed the influence to IL-1β production of monocytes cocultured with platelets by stimulating factors from platelets and signaling blockers. We compared CD16+ monocytes with CD16- monocytes in IL-1β productivities, mRNA expressions of NLRP3 and caspase-1 and platelets-monocytes-aggregates ratios. [Results] NLRP3-knockdown THP-1 and caspase-1-knockdown THP-1 had lower IL-1β productivities in coculture with platelets than control. CCR5 inhibitor and ATP inhibitor attenuated IL-1β production of monocytes cocultured with platelets. CD16+ monocytes had higher IL-1β productibity in coculture with platelets than CD16- monocytes. CD16+ monocytes had higher NLRP3 mRNA expression and higher platelets-monocytes-aggregates ratio than CD16- monocytes. [Conclusions] Platelets increase IL-1β production of monocytes with CCL5 and ATP released from platelets via NF-kB and NLRP3 inflammasome activation.

W51-1

Predictive factors for poor prognosis and indication of plasma exchange in anti-MDA5-positive dermatomyositis with interstitial lung disease under the combined immunosuppressive treatment

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Conflict of interest: None

【Object】Anti-MDA5 (+) dermatomyositis (DM) often accompanies rapidly progressive interstitial lung disease (RP-ILD) with poor prognosis. Combined immunosuppressive therapy such as glucocorticoids, calcineurin inhibitors and intravenous cyclophosphamide, has been suggested to be effective in DM with RP-ILD, but some are still resistant to the therapy. We examined the utility of plasma exchange (PE) in resistant cases and investigated the good indication for PE.【Methods】We evaluated clinical features and the serum cytokines before treatment in 32 anti-MDA5 (+) DM patients who received combined therapy. The patients were divided into 3 groups; the survivors without PE (n=22, group A), the survivors with PE (n=4, group B) and the deceased (n=6, group C).【Results】Among B+C groups, PE was underwent in 5 patients and 4 were survived. 5 patients without PE were all deceased. Hypoxemia was more frequent and serum IL6, IL10, IL12p70, and IFNα levels were significantly higher in group B than in group A. The group B+C had more increased numbers of monocyte and neutrophil and higher serum ferritin level than group A.【Conclusions】Good prediction of disease severity using several clinical parameters and prompt indication of PE will deliver a favorable outcome in anti-MDA5 (+) DM patients.

W51-2

Serum ferritin levels, distribution of ground glass opacities and new development of Lung infiltration during therapy predict prognosis of interstitial lung disease in anti-MDA5Ab positive dermatomyositis

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Conflict of interest: None

Object) The aim of the present study is to identify poor prognostic factors in RP-ILD in DM positive for anti-MDA5 Ab. Method) Retrospective analysis was performed on consecutive 15 anti-MDA5+ patients with RP-ILD among 63 inflammatory myositis who admitted our department from 2007 to 2015. These patients were treated with a combination of high dose glucocorticoid, cyclosporine and intravenous cyclophosphamide as a first line therapy. Results) Subjects were 15patients of 8 males and 7 females. 14 of them were amyopathic DM. Eight of them died within 6 month. Poor prognostic factors in patients with ILD positive for anti-MDA5 Ab were older age, elevation of serum ferritin levels (>1000ng/ml) before treatment and increase during therapy, extent and distribution of GGO (number of lung fields >5) and worsening / emerging lung infiltration. We developed score to predict the prognosis. Conclusion) When serum ferritin levels are elevated before treatment, ferritin levels are increased during therapy, many lung fields are affected by GGO and new lung infiltration emerged during the therapy, the prognosis of ILD of DM patients with anti-MDA5 Ab is poor.

W51-3

Long Term Prognosis and Relapse of Dermatomyositis Complicated with Interstitial Pneumonia: Comparision between Anti-ARS Antibodies and Anti-MDA5 Antibodies

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Conflict of interest: None

[Objects] The aims are to compare long term prognosis and relapse of dermatomyositis complicated by interstitial pneumonia (DMIP) between anti ARS antibodies positive (ARS+) and anti MDA5 antibodies positive (MDA5+). [Methods] This study comprised DMIP patients admitted to Yodogawa Christian Hospital or Osaka Medical College after October, 2011. We divided the patients to two groups: MDA5+ and ARS+, and compared prognosis and relapse for 2 years between the two groups. [Results] Of the 35 patients, 12 were ARS+, 11 were MDA5+ and 1 and 11 were positive and negative (ARS-/MDA5-) for both. KL-6 at the start, 1 and 2 year after of therapy initiation were higher in ARS+ than in MDA5+(P = 0.008, 0.028. 0.013, respectively). Though serum ferritin level at the start of therapy was higher in MDA5+ than in ARS+(P = 0.003), that of 2 year after were higher in ARS+ than in MDA5+(P = 0.018). One of ARS+ and 5 of MDA5+ died 24 weeks after the therapy initiation (P = 0.004), and only 1 of ARS-/MDA5- died from 24 to 104 weeks. Four of 11 ARS+, 1 of 5 MDA5+ relapsed 104 weeks after the therapy initiation (P = 0.044). [Discussion] Short time prognosis was worse in MDA5+ than in ARS+, and long term prognosis was not significant. We suggested that disease activity of ARS+ lasted for long time.

W51-4

Intravenous Immunoglobulins for Steroid and immune suppressive agents refractory anti –SRP antibody positive myositis

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Conflict of interest: None

[Objective] To analyze the outcomes of the anti –SRP antibody positive myopathy receiving Intravenous Immunoglobulins (IVIG). [Methods] We analyzed 4 patients who were diagnosed anti –SRP antibody positive myopathy and received IVIG because of immune suppressive agents. [Results] Two patients received IVIG because of the induction therapy and two patients received because of the exacerbation. The median age was 54.5 years old and median CPK was 1696 before the initiation of IVIG. One patient developed severe dysphagia. No patients had malignancy and active interstitial pneumonia. After IVIG, all patients led to remission and CPK became normal. The median interval between the initiation of the IVIG and normal CPK was 40 days. Two patients with IVIG induction therapy still remained remission. But, two patients with exacerbation developed recurrence. [Conclusions] Our findings indicated that IVIG **I**VIG should be considered in resistant anti –SRP antibody positive myopathy.

W51-5

Intravenous Immunoglobulins for Steroid refractory polymyositis and dermatomyositis with dysphagia

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Conflict of interest: None

[Objective] To analyze the swallowing outcomes of steroid refractory polymyositis and dermatomyositis with dysphagia receiving Intravenous Immunoglobulins (IVIG). [Methods] We analyzed eight patients who were diagnosed PM/DM and received IVIG because of the steroid refractory dysphagia [Results] Five patients were female. The median age was 54 years old. Seven patients received induction therapy and one patient received treated because of the exacerbation. Two patients had malignancy. All patients received prednisolone and seven of them received immunosuppressive drugs. Before the initiation of the IVIG, five patients required tubal feeding and three patients required dysphagia diet. After IVIG, although six patients improved their swallowing ability, two patients did not improved and required cancer treatment. Finally, all patients improved their swallowing ability and could eat food, including tubal feeding or dysphagia diet. The median interval between the onset of dysphagia and eating normal food was 19.5 weeks. Two patients did baloon dilation because of swallowing rehabilitation. One patient developed aspiration pneumonia. [Conclusions] Our findings indicated that IVIG should be considered in steroid resistant PM/DM with dysphagia.

W51-6

In-vitro analysis of cytotoxic T lymphocyte-mediated muscle injury in polymyositis

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Conflict of interest: None

Objectives: It is recognized that muscle fibers are injured by cytotoxic T lymphocytes (CTLs) with their cytotoxic molecules (perforin and granzymes) in polymyositis (PM). Although the image of CTL invasion into non-necrotic fibers is the definitive finding of PM, it is uncertain whether CTL can penetrate the cell membrane of muscle fibers. Moreover, the function of CTL invaded in fibers remains unclear. We reproduced CTL muscle injury *in vitro* to reveal a new cytotoxic mechanism accompanied by CTL invasion into muscle fibers and to develop a novel therapy targeting its process. Methods: To generate H2KbOVA-expressing C2C12 cells (H2Kb-OVA-C2C12), C2C12 cells were transfected with a gene encoding OVA peptide and MHC class I molecule (H2-Kb). H2Kb-OVA-C2C12 were co-cultured with OVA peptide-stimulated spleen cells of OT-I mouse expressing T-cell receptors that recognize OVA specifically. CTL function was analyzed by a chromium-51 release assay. Fixed cells were stained immunohistochemically for actin and CD45 and visualized with confocal microscopy. Results: OVA peptide-dependent cytotoxicity was detected. Cell imaging revealed myotubes containing CD45-positive-cells. Conclusions: We generated an in vitro

model of CTL muscle injury that emulates CTL invasion in myofibers.

W52-1

***Pseudomonas aeruginosa* pneumonia was increased in RA patients with underlying lung diseases**

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Conflict of interest: None

We studied 61 rheumatoid arthritis (RA) patients who had admitted to our hospital for bacterial pneumonia. The mean age of the patients was 72.0±10.4 years and 67.2% were female. The mean duration of the disease was 13.7±11.6 years. Forty-four patients (72.1%) had received glucocorticoids, 18 patients (29.5%) had received methotrexate, and 10 patients had received biologics for the treatment with RA. Forty-nine (77%) of the patients had underlying lung diseases such as interstitial pneumonia or bronchiectasis. We detected the causative pathogens of the pneumonia for 35 (57.4%) patients. Among these patients, *Pseudomonas aeruginosa* was the most common cause of pneumonia (18% of the RA patients). *Streptococcus pneumoniae* was detected in 7 patients (11.5%), *Haemophilus influenzae* was detected in 4 patients (6.6%). In general, *Pseudomonas aeruginosa* was rare causative pathogen for community-acquired pneumonia. Interestingly, we found that all the patients who had been detected *Pseudomonas aeruginosa* had underlying lung diseases. Thus, underlying lung diseases could be one of the risk factors for bacterial pneumonia, especially *Pseudomonas aeruginosa* infection in RA patients.

W52-2

Opsonic and Antibody Responses to Pneumococcal Polysaccharide in Rheumatoid Arthritis Patients Receiving Golimumab Plus Methotrexate

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Conflict of interest: None

The objective of this study was to evaluate the humoral response to 23-valent pneumococcal polysaccharide vaccination (PPSV23) in RA patients receiving methotrexate (MTX) alone or in combination with a tumor necrosis factor inhibitor, golimumab (GOM). PPSV23 was given to 114 RA patients, who were classified into three groups: RA control (n = 35), MTX alone (n = 55), and GOM + MTX (n = 24). Concentrations of antibodies against pneumococcal serotypes 6B and 23F were measured using ELISA and antibody functionality was determined using a multiplexed opsonophagocytic killing assay, reported as the opsonization index (OI). In the GOM + MTX group, the IgG responses were lower than those in the MTX alone or control groups, whereas the OI responses were similar to those in the other 2 groups. Furthermore, discrepancies between the IgG and OI responses were found in GOM + MTX group. No severe adverse effect was observed in any treatment groups. The similarity of these measurements between all 3 groups suggests that RA patients receiving MTX + GOM still benefit from receiving the PPSV23 vaccination, even though they produce less IgG in response to it. These results can help clinicians to better schedule and evaluate pneumococcal vaccination for RA patients.

W52-3

Risk and prognostic factors of *Pneumocystis* pneumonia in rheumatoid arthritis

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Conflict of interest: None

[Background] *Pneumocystis* pneumonia (PCP) prophylaxis is effective, though the tolerability is low. Adaptation criteria of the prophylaxis in RA is not fully provided. To know that, it is important to investigate the risk factors of PCP. [Methods] The subjects were RA patients visited to our institute from September 2009 to August 2016. All subjects were full-filled with the 1987 ACR criteria or the 2010 ACR/EULAR classification for RA. PCP was defied as *Pneumocystis jirovecii* detection by sputum PCR. Medical records were analyzed retrospectively. [Results] There were 9 RA patients suffered from PCP. All of them were treated with PSL at the onset of PCP, and 8 of them were treated with MTX, and two of them were treated with biologic DMARDs. Seven were complicated with lung disease. Lymphocytes number were 830/μL at the last arrival. There are five survivors after one month from the onset. Lymphocytes number at the post-treatment day 6 was significantly lower in non-survivors (1600 [434-2410]/μL vs. 335 [97-648]/μL, $p<0.05$). [Conclusion] The patients treated with corticosteroid or complicated with lung diseases may be good indicators for the PCP prophylaxis. After the treatment, you should check the lymphocytes count.

W52-4

Retrospective study of the continuation rate between different administrations of sulfamethoxazole/trimethoprim for prophylaxis of pneumocystis pneumonia in patients with rheumatic disease

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Conflict of interest: None

Objective: The aim of this study was to investigate the continuation rate between different administrations of sulfamethoxazole/trimethoprim (ST) for prophylaxis of pneumocystis pneumonia (PCP) in patients with rheumatic disease. Methods: Fifty-one patients recruited into this study were divided into two groups, a continuation group (continuation of ST treatment for at least 8 weeks) and a discontinuation group (ST treatment for less than 8 weeks). The baseline characteristics of patients and administration of ST were compared between the two groups. Results: Nineteen patients (19/51; 37%) discontinued ST treatment. The median of age tended to be older in the discontinuation group than in the continuation group (68 vs.59, P=0.32). The value of eGFR tended to be lower in the discontinuation group than in the continuation group (54 vs.75.5, P= 0.04). The percentage of daily oral administration of ST tended to be higher in the discontinuation group than in the continuation group (53 vs. 34%). Conclusion: Results suggested the necessity of evaluating baseline characteristics of patients, such as age and renal function, before the start of ST for prophylaxis of PCP. The continuation rate seems to be lower for daily oral administration than in other types of ST administration.

W52-5

Risk Factors of Pneumocystis Jirovecii Pneumonia (PJP) in Patients with RA and Salazosulfapyridine (SASP) as a Possible Protective Agent

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Conflict of interest: None

Background: Pneumocystis jirovecii pneumonia (PJP) is a serious complication during the treatment in patients with variety of rheumatic disease. There are several reports that indicate the risk factors for the development of PJP during the treatment with bDMARDS. We again tried to find risk factors of PJP and also possible protective factors. Methods: Subjects were 413 patients with RA. Out of 413 patients, PJP developed in 29 patients. Diagnosis of PJP was done according to the report of Harigai, et al (N Engl J Med 2007). We picked up 14 variables that may relate to the development of PJP, such as age, presence of interstitial lung disease (ILD), and drugs for the treatment of RA. Univariate and multivariate analysis were done to find out risk and protective factors. Results: By

univariate analysis, 10 variables including advanced age and class, high dose of PSL, the presence of ILD, and others were significantly related to the development of PJP. By logistic regression analysis, class 3/4, more than 6mg/day of PSL, non-use of SASP, and less than 1500/mcl of peripheral blood lymphocytes were significant risk factors. Conclusion: We obtained several risk factors of PJP, and a significance of SASP as a protective agent should further be studied.

W52-6

The prophylactic effect of TMP-SMX against acute-onset diffuse interstitial lung diseases with connective tissue disease

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Conflict of interest: None

Objective) Acute-onset diffuse interstitial lung diseases (AoDILD) are highly mortal condition and their cause are often difficult to discriminate. The aim of this study is to examine hypothesis that taking trimethoprim/sulfamethoxazole (TMP-SMX) for Pneumocystis Pneumonia (PCP) prophylaxis with connective tissue disease also have prophylactic effect against AoDILD. Methods) We retrospectively investigated data from 621 patients with TMP-SMX for PCP prophylaxis and 43 patients who admitted for either acute respiratory failure/acute interstitial pneumonia/PCP/drug induced pneumonitis during 2004-2016. Results) There was no single case who admitted to hospital due to AoDILD with TMP-SMX prophylaxis. There were 25 cases admitted for AoDILD and 7 cases8 (28%) were dead. Among 25 cases, 5 cases developed AoDILD after TMP-SMX cessation. 70 cases ware taking under dose prophylaxis for some reasons but there was also no AoDILD case. Conclusions) Taking TMP-SMX for PCP prophylaxis may also have prophylactic effect against AoDILD. And those effect may also exist even with under dose.

W53-1

Clinical features and chest radiographic findings of RA patients with non-tuberculosis mycobacterium (NTM) in our institution

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Conflict of interest: None

[Objectives] In RA patients, there are very little reports concerning about non-tuberculosis mycobacterium (NTM). We aimed to analyze clinical features and chest radiographic findings of RA patients with NTM using the database of our institution. [Methods] We investigated RA patients with NTM registered in our database from 2008 to 2015 retrospectively. We surveyed patient profiles, associated other diseases, detecting bacterial species and thoracic CT findings. [Results] We confirmed 16 RA patients with NTM. Mean age was 68 years. Out of 16 patient, 14 cases were detected *M.avium* and 2 cases were detected *M.intracellulare*. As for thoracic CT findings, 12 cases were nodular bronchiectatic type while 3 were fibrocavitary type. In 16 RA patients with NTM, 7 patients showed exacerbation of chest CT findings. All of 3 patients with fibrocavitary type revealed deterioration of chest abnormalities. RA disease activities were likely to be higher in "exacerbation" group. [Conclusion] Disease activity of RA patients and chest radiographic findings are sometimes influenced by chronic inflammation with NTM. When we evaluate RA disease activities and chest radiographic findings, conditions of NTM are needed to be considered.

W53-2

Clinical course of nontuberculous mycobacteriosis (NTM) in patients with collagen disease

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Conflict of interest: None

Objective: To identify the risk factors of the development and exacerbation of NTM infection in patients with rheumatic diseases. Methods: 20 patients were enrolled in this study by meeting the diagnostic criteria of NTM infection. The medical records of enrolled patients were retrospectively reviewed. Results: Eleven patients with RA, 4 patients with vasculitis, 3 patients with Sjögren's syndrome and 1 patient with DM and SLE for each. MAC was detected in 13 patients. Notably, bronchiectasis was the predominant pulmonary complication which was observed in 13 patients. Although a total of 7 patients ever experienced the exacerbation of NTM, immunological state including peripheral blood leukocyte and lymphocyte counts and the serum IgG level were comparable between ever and never exacerbated patients, respectively. Conclusion: NTM infection in patients with rheumatic diseases is likely to develop on the dysfunction of pulmonary barrier rather than the systemic immune state.

W53-3

Factors associated with *Mycobacterium avium* complex pulmonary disease in patients with rheumatoid arthritis:results from a cross-sectional observational study

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Conflict of interest: None

[Objective] To investigate factors associated with *Mycobacterium avium* complex pulmonary disease in patients with rheumatoid arthritis (RA). [Methods] We cross-sectionally investigated radiographs of 396 RA patients. MAC pulmonary disease (MAC-PD) was diagnosed by criteria of American Thoracic Society. RA patients with abnormal shadow on chest x-rays underwent chest CT. Bronchoscopy was performed on patients with negative for MAC by sputum and positive CT findings compatible with MAC-PD. RA patients with MAC-PD were compared with those without MAC-PD. Relevance was analyzed by univariate and multivariate logistic method. [Results] Eight who had MAC-PD at entry and 15 who refused bronchoscopy were excluded from the analysis. Fourteen patients were newly diagnosed with MAC-PD. Six out of them were diagnosed by expectorated sputum cultures and eight were diagnosed by cultures of bronchoalveolar lavage fluids (BALF). Multiple regression models showed that low BMI (adjusted OR (aOR) = 0.671, $p < 0.001$) and decrease in the number of peripheral blood lymphocytes (aOR = 0.998, $p < 0.001$) significantly correlated with MAC-PD in patients with RA. [Conclusion] Clinicians should be alert to this pulmonary comorbidity, when managing RA patients with the associated factors.

W53-4

Risk Factors of Pulmonary Mycobacterium Avium-comlex (MAC) Disease and the Significance of Anti-MAC Antibody in Patients with Rheumatic Diseases

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Conflict of interest: None

Background: The incidence of pulmonary MAC disease (PMD) is increasing in Japan, and it is becoming a great concern in the field of rheumatology. We aimed to detect risk factors for PMD in patients with rheu-

matic diseases and evaluate the significance of the measurement anti-MAC antibody (AMA). Methods: Subjects were 94 patients (mean age, 70.2 years) with various rheumatic diseases whose chest CT findings are difficult to distinguish from pulmonary lesions due to rheumatic diseases itself. Sputum culture was done more than twice, and blood was drawn for AMA detection. Various clinical factors were collected and multivariate analysis was done to find risk factors of PMD. Results: Out of 94 patients, 14 patients were diagnosed as PMD. Multivariate analysis found only one significant risk factor, low BMI. The mean BMI with and without pulmonary MAC disease were 17.5 +/- 2.3 and 21.3 +/- 3.7, respectively ($p < 0.0005$). In patients with BMI less than 18.5, OR of developing PMD was 14. AMA was positive in 12 patients. The sensitivity, specificity, PPV and NPV of AMA for PMD were 64.3%, 96.3%, 75.0%, and 94.0%, respectively. Conclusion: Low BMI was only one risk factor of developing PMD. Measurement of AMA can be a replacement of one positive sputum culture.

W53-5

The usefulness of QFT-Plus for the diagnosis of latent TB in rheumatoid arthritis patients - comparison with T-Spot

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Conflict of interest: None

【Background · Objective】Interferon gamma release test (IGRA) is an examination aimed to aid for diagnosis of M. tuberculosis infection. Currently in Japan two types of test are used, QFT-TB gold (QFT-GIF) and T-spot. In recent years, next generation of QFT-GIT kit called QFT-Plus is used in Europe. QFT-Plus is more sensitive than QFT-GIT, and its specificity is said to be equal. We studied the usefulness of QFT-Plus in the diagnosis of latent TB in rheumatoid arthritis patients.【METHODS】QFT-Plus and T-spot were held and compared with 156 patients undergoing rheumatoid arthritis treatment.【Results】There were only one case with QFT-Plus and 4 cases with T-spot for undecidable case, but there was no statistically significant difference. The positive cases were significantly higher in 16 QFT-Plus, 7 T-spot. Negative cases were QFT-Plus 145 cases, T-spot 139 cases. There were 6 cases of positive concordance and 136 cases of negative concordance in both tests.【Conclusion】There is no Gold standard of infection in latent tuberculosis and true positive negative predictive value remains unknown. But, using QFT - Plus may further improve the detection sensitivity of latent tuberculosis in rheumatoid arthritis patients.

W53-6

A prospective study of the standardized incidence ratio (SIR) of tuberculosis (TB) in patients with RA by *NinJa* cohort data for 13 years

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Conflict of interest: None

Objective: To evaluate the characteristics of the newly developed tuberculosis (TB) in the registered patients in **NinJa** cohort study for rheumatoid arthritis (RA). **Methods:** We calculated the standardized incidence ratio (SIR) of TB from the clinical data on National Database of Rheumatic Disease by iR-net in Japan (**NinJa**) prospectively from 45 facilities for 13 years. **Results:** Among 110,521 RA patients registered from 2003 to 2015, 67 patients developed TB and the SIR of TB was 2.58 (95%CI:1.96-3.20). 8 patients (11.9%) were treated with biologic agents, and 22 patients (32.8%) were treated with MTX. The mean age of them was 71.3 years old and the mean duration of RA before the onset of TB was 11.9 years. **Conclusion:** Similarly our last reports, the incidence of TB in RA patients was in the downward trend. By this study, in elderly, in patients with RA of long-term morbidity is the high risk of the newly developed TB.

W54-1

Identification of risk factor for severe complication of lung disease in RA patients with pre-existing pulmonary lesions who were treated with biologics

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Conflict of interest: None

Objective: To clarify risk factors for severe complication of lung disease in rheumatoid arthritis (RA) patients with pre-existing pulmonary lesions who were treated with biological DMARDs (bDMARDs). **Methods:**We consecutively enrolled 107 RA patients with pre-existing pulmonary lesions. We compared clinical characteristics and incidence of hospitalization due to severe lung complication between a bDMARDs therapy subset (n=44) and a non-bDMARDs therapy subset (n=63). **Results:**Female and high disease activity were revealed much more in the bDMARDs subset than in the other subset. There was no difference in age at disease-onset, positivity rate of RF/ACPA, prevalence of smoking, steroid use and methotrexate (MTX) use between the two subsets. Patients in the bDMARDs subset tended to be hospitalized more frequently than the non-bDMARDs subset (20%vs.10%). Our multiple logistic regression analysis found out that female, but not bDMARDs use, was the risk factor for the hospitalization due to severe lung complications in all of these RA patients. Moreover, MTX use was also the risk factor in patients treated with bDMARDs. **Conclusions:**In RA patients with pre-existing pulmonary lesions, female and MTX use could be the risk factors for the deterioration of lung disease during treatment of bDMARDs.

W54-2

Predictive value of chest HRCT findings for respiratory adverse event among RA patients treated with biological therapy: long-term results from an observational study

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Conflict of interest: None

Objectives: The aim of this study was to assess the risk for respiratory adverse events (RAEs) in RA patients with intestinal lung disease (ILD) or airway disease (AD) treated with biologics evaluating their chest HRCT findings. Methods: This is an observational study including 241 patients with RA who underwent biological therapy from 2005 to 2011. We assessed chest HRCT at the induction of biological therapy and grouped 237 patients according to the presence of ILD or/and AD. Next we assessed the emergence of respiratory infection and IP (onset or worsening), which was referred to as RAEs. Cox regression models estimated the risk for incidence of RAEs and explored predictors for RAEs. Results: HRCT abnormalities were found in 35.8% of the all patients. ILD features were found in 27.8%, AD in 11%. We identified 27 RAEs cases including bacterial pneumonia (10), IP (7), PCP (2), bronchitis (2), organized pneumonia (2), NTM (1), empyema (1), pleuritic (1). The incident rate of RAEs was 15.7 cases per 1000 patient-years in all patients, 20.1 in ILD group, 49.5 in AD group. AD, honeycombing, bronchiectasis were identified as risk factors for RAEs. Conclusions: Pre-existence of AD was associated with higher risk for development of RAEs especially in ILD/AD coexisting cases.

W54-3

Risk Factors for Acute Exacerbation of Interstitial Pneumonia associated with Rheumatoid Arthritis

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Conflict of interest: None

Objectives: To investigate the risk factors associated with acute exacerbation (AE) and its survival in patients with rheumatoid arthritis-associated interstitial pneumonia (RA-IP). **Methods:**We examined the clinical features of 60 RA-IP patients admitted to our hospital between July 2010 and September 2016 to identify variables significantly associated with AE occurrence and survival using Cox hazards analysis. **Results:**The mean patient age was 73.2±10.7 and 36 (60%) were female. 22 (36.7%) developed AE and 7 of them (11.7%) died (with the mean follow-up period of 2.7 years). Methotrexate use was associated with occurrence of AE (Hazard ratio 1.09, 95% confidence interval 1.01-1.18). Age (median 70 vs. 82 years, p=0.002) and MMP-3 level (median 84.8 vs. 205.6 ng/mL, p=0.033) on admission were significantly higher in patients who died of AE. Univariate analyses revealed that age over 75 years, MMP-3 level over 200 ng/mL, and 3L or more oxygen use on admission were associated with death **Conclusion:**Our data suggest that methotrexate use relates to the occurrence of AE, and age, MMP-3 level, and oxygen volume relate to AE survival in patients with RA-IP.

W54-4

Efficacy of tacrolimus (TAC) on rheumatoid arthritis-related interstitial lung disease (RA-ILD)

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Conflict of interest: Yes

[Object] To confirm efficacy of TAC on RA-ILD. **[Methods]** In bDMARD-naïve RA patients who initiated TAC but not MTX due to ILD during 2005-2015, activity indices including DAS28-ESR4 (DAS28), respiratory symptoms [RS; cough, dyspnea on effort], KL-6, and chest CT score at baseline (BL) and Week 24 (W24) were retrospectively assessed. ΔDAS28≧0.6, lack of RS, %ΔKL-6≧20%, and reduction in CT score were defined as "improved". **[Results]** BL characters (n=40) were; age 66±11 years, female 70%, duration 64±73 months, concomitant drugs were GC 45%, SASP 3%, and none 51%. At W24, DAS28 decreased from 4.91±1.57 to 3.61±1.21 (p<0.0001), RS were positive in 25 to 7 (62.5 to 17.5%), KL-6 1006±1025 to 830±630 U/ml (p=0.0386), CT score 1.44±0.77 to 1.42±0.78 (p=0.0039). Improvement in RS, KL-6, CT score were observed in 48, 43, 53%, and count of improved items (0, 1, 2, 3) were in 10, 11, 11, 8 patients (25, 28, 28, 20%), respectively. %ΔKL-6 (n=35) was higher in patients with improved DAS28 (n=23) than the others; 28±31% vs. -34±87%(p=0.0067). No SAE was observed. **[Conclusions]** TAC was effective on both arthritis and ILD with acceptable safely profiles. Moreover, patients who acquired a better disease control in arthritis had a higher % reduction in KL-6.

W54-5

Prevalence and risk of chronic interstitial pneumonia in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To reveal prevalence and risk of chronic interstitial pneumonia (C-IP) in patients with rheumatoid arthritis (RA). [Methods] Subjects were RA patients who attended our hospital from 2009 to 2013. In those, C-IP found with CT were retrospectively analyzed using multivariate logistic regression in association with their background factors including age, sex, disease duration and activity of RA, serological factors, Steinbrocker stage, functional disorder, and renal function. [Results] Total subjects were 9330 patient-yrs consisted of 2702 patients (female 82.3%). Their median age was 65.0 yrs and disease duration was 9 yrs. Their mean DAS28ESR was 3.22. Ratio of patients with functional disorder was 14.9%. Rate of patients who received lung CT was 35.8% and patients without CT were recognized as those without C-IP. Prevalence of C-IP was 10.5%, which consisted of 41.5% UIP and 58.5% NSIP. C-IP tended to develop early after the onset of RA and NSIP was more in female. Significant factors related to C-IP were higher age, male (odds ratio (OR) 2.9), positive rheumatoid factor (OR 1.7), functional disorder (OR 1.7) and high disease activity (DAS28ESR≧3.2; OR 2.0). [Conclusions] To detect complicated C-IP in RA patients, CT should be performed in those who have above factors.

W54-6

Prognosis of and treatment selection for each disease type of chronic interstitial pneumonia (CIP) with Rheumatoid arthritis (RA) patients

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Conflict of interest: Yes

Background: We aim to know the influence on prognosis and treatment selection of each disease type of CIP. Methods: We reviewed clinical data of RA-CIP patients in August, 2011 and those of RA-CIP patients in August, 2016. HRCT findings are categorized as UIP (usual interstitial pneumonia) and NSIP (nonspecific interstitial pneumonia) and others. Results: Total RA-CIP patients in 2011 were 83 (34males), those in 2016 were 124 (51males). Among those in 2011 (in 2016), UIP were 16 (22), NSIP 25 (46), others 41 (56). During 5 years, 17 patients died. Mortality rate of UIP is 57%, NSIP 5%, others 25%. Among death cases, 5 patients died from LK and 3 patients died from acute exacerbation of IP. MTX, Corticosteroid, Biologics, Tacrolimus are prescribed for 9,9,27%, 32,57,50%, 32,33,34%, 64,63,46% of each type of CIP patients respectively. Conclusions: Among RA-CIP, UIP had bad prognosis, and NSIP had good prognosis. Treatement selection of each type of CIP was not so differ from each other.

W55-1

Pregnancy outcome and its relevant factors in patients with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA)

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Conflict of interest: None

【Objective】To elucidate the factors affecting the pregnancy outcome in patients with SLE and RA.【Methods】Patients with SLE and RA in our university between 2012 and 2016 who experienced pregnancy were retrospectively reviewed. Medical information was collected from their chart.【Results】Nineteen pregnancies in 14 SLE patients and 26 pregnancies in 21 RA patients were identified. Among SLE pregnancies, the mean age, disease duration and prednisolone dose were 33.4±3.2, 11.5±8.2 years and 6.2±4.2 mg/day, respectively. The disease activity was well controlled (the mean SLEDAI, 2.8±2.0). Live birth pregnancies were 15 (78.9%) and fetal loss occurred in 4 pregnancies. The mean dose of prednisolone was significantly lower in the pregnancies with live birth than those with fetal loss (4.9±3.4 vs 11.3±3.3mg/day, p=0.02). Among RA patients, the mean age and disease duration were 33.5±5.6 and 9.9±7.4 years. The mean DAS28-ESR and HAQ were 2.18±0.88 and 0.30±0.50. All 26 pregnancies were live birth.【Conclusions】High live birth rates were observed in both SLE and RA pregnancies on the condition of well-controlled disease activity. In SLE pregnancies, prednisolone dose at the time of conception may also be associated with live birth

pregnancy.

W55-2

Fertility of women with connective tissue disease

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Conflict of interest: None

[Object] The aim is to evaluate the fertility and infertility treatment of women with collagen disease at our center. [Methods] We conducted a retrospective study. 62 women with connective tissue disease who received infertility treatment from 2002 to 2016 were included. We assessed the type of infertility treatment, the outcome of fertility, the age at the treatment and the treatment of onnective tissue disease. [Results] 25 cases (40.3%) resulted in ongoing pregnancy and 13 cases (21.0%) resulted in abortion. 21 cases underwent artificial reproductive technology (ART). We had 31 oocyte pick up (OPU) cycles and 38 embryo transfer (ET) cycles. Median age at ART was 37.0 years. The pregnancy rate and ongoing pregnancy rate per OPU cycle were 29.0%(9/31) and 16.1%(5/31), respectively. The pregnancy rate per ET cycle was 23.7%(9/38). In all women who received ART at 37 years old in Japan, the pregnancy rate and ongoing pregnancy rate per OPU cycle were 34.0% and 14.9%(5/31), respectively and the pregnancy rate per ET cycle was 21.2%. The pregnancy rate of women with connective tissue disease was similar to all women who underwent ART in Japan. [Conclusions] The pregnancy rate of women with connective tissue disease was no less than women with no complications.

W55-3

Pregnancy outcomes after maternal exposure to tacrolimus

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Conflict of interest: None

[Objective] Tacrolimus is generally used in patients with systemic lupus erythematosus. It is recommended for use for pregnant patients if the benefit is greater than the risk. In Japan, it is contraindicated to pregnant patients on the basis of pre-clinical studies. Our goal is to analyze the clinical outcome of pregnancy in which the mother has been given Tacrolimus. [Method] Patients who took tacrolimus during pregnancy were analyzed in this study (Cohort A). We also retrospectively analyzed all patients who were given tacrolimus and delivered their child during 2002 to 2016 (Cohort B). [Results] In cohort A, 45 women were studied. The original diseases were autoimmune disease in 31 patients, post-organ transplantation in 13 patients, and the other in 1 patient. Pregnant outcomes were live births for 25 patients, spontaneous abortions for 7, elective termination for 1, stillbirth for 1. One fetuse with congenital anomalies were observed. In cohort B, 12 women were studied. Pregnant outcome was live birth for 11 patients, and stillbirth for 1. One patient was diagnosed as having a congenital abnormality. [Conclusions] Based on our study, it may be suspected that use of tacrolimus during pregnancy does not increase the risk of spontaneous abortion or congenital malformations.

W55-4

The efficacy of ovarian preservation therapy in patients with systemic lupus erythematosus (SLE) using recent cyclophosphamide pulse therapy (IVCY) regimen – preliminary study

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Conflict of interest: None

[Objectives] To assess the efficacy of monthly GnRH against premenopausal ovarian impairment (POI) induced by IVCY in patients with SLE [Methods] This is a case-control study. Patients treated with IVCY (84cases) were divided into two groups; preserved and control groups. The incidence of POI was compared between two groups. Risk factors of POI in preserved group were also examined. [Results] Disease duration (8.9±2.1 vs 6.2±2.9 yr), cumulated dose of cyclophosphamide (4.4±0.3 vs 4.6±0.9g), anti ss-A antibody prevalence (57.1% vs 42.8%) were similar between two groups. However, the age at the beginning of IVCY in preserved group were younger (27.4±1.5 vs 39.5±2.3yr) and the dose of prednisolone higher (43.8±3.0 vs 38.8±3.6mg/d) than those in control group. Although the rate of parity and pregnancy after IVCY was higher in preserved group than in control group, the incidence of POI of both groups were almost same (25% vs 22.2%). Patients with POI in preserved group showed higher IVCY induction age (24.0±1.3 vs 35.2±1.8yr), longer disease duration (6.3±2.2 vs 14.7±4.2 yr) and higher induction dose of prednisolone (50.3±3.0 vs 30.0±2.7mg/d) compared with patients without POI. [Conclusion] Ovarian preserved therapy might have a limited impact in recent IVCY regimen.

W55-5

The effects of surgical intervention on body image in patients with rheumatoid arthritis (RA)

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Conflict of interest: None

【Objectives】The current study aimed to investigate the effects of surgical treatments on body image in patients with rheumatoid arthritis. 【Method】90 patients with RA were divided into four groups of patients who underwent the surgical intervention for large and small joints of the **upper** and lower limbs. The pain VAS, HAQ-DI, body image assessed by body image assessment tool (BIAT), and depression assessed by Beck Depression Inventory-II(BDI-II) were investigated before and 6 months after the surgery in each groups. 【Result】Pain VAS, HAQ-DI, BIAT and BDI-II significantly improved at six months after the surgery. In the large joints of the **upper** and lower limbs groups, the body-cathexis significantly improved. The low body-esteem significantly improved in the small joints of the **upper** and lower limbs groups. 【Discussion】In the large joints group, the improvement of pain VAS and ADL associated with the improvement of BI and depression. The improvement of cosmetic appearance contributed to improved BI in the small joints group. The surgical intervention resulted in satisfactory clinical outcomes in terms of BI and depression.

W55-6

Polymyositis complicated with interstitial pneumonia during pregnancy: A case report

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Conflict of interest: None

A 27-year-old pregnant woman was referred to our division at 15 weeks of gestation because of an elevation of her serum muscle enzyme. Her last pregnancy was terminated with spontaneous abortion at 21 weeks of gestation a year ago. She had been aware of muscle weakness and dyspnea on exertion since then. At 10 weeks of gestation, her dyspnea was exacerbated and fever appeared. A chest CT scan showed interstitial reticular shadow in her both whole lung fields. An electromyogram revealed myogenic change and anti-Jo1 body was detected with a blood test, then She was diagnosed as polymyositis with interstitial pneumonia (IP) based on these findings. High-dose corticosteroids treatment was administered with successful improvement of her serum muscle enzyme. As the serologic marker of IP got worse, cyclosporine was added to her treatment. At 30 weeks of gestation, the bloodstream resistance in the umbilical cord artery was found. Simultaneously, hypertension was presented. Her pregnancy was terminated at 34 weeks and 1day. A male baby weighing 1594 g was delivered without asphyxia. The case with polymyositis complicated with IP during pregnancy and successful delivery was very rare in the literatures. We report the course of this case in detail and discuss pathophysiology of the case.

W56-1

The frequency of fibromyalgia in the RA patients

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Conflict of interest: None

[Object] To research the frequency of fibromyalgia (FM) in RA patients, and clinical features, effect to the disease activity. [Method] The subject are RA patients with Biologics or JAK kinase. We evaluated DAS28-CRP4, SDAI, pain VAS, disease duration as RA assessment. ACR 1990 criteria and ACR 2010 preliminary diagnostic criteria were used for the diagnosis of FM. We also used FIM for ADL, CES-D for self-assessment of depression. The main endpoint was the frequency of FM in RA patients. The secondary was the relation of disease activity of RA, ADL (FIM), and depression (CES-D). The study was approved by the ethics review board of Matsubara Mayflower Hospital and written informed consent was given. [Results] We conducted 89 RA patients. There were 3 cases (3.4%) defined FM using ACR 1990, 7 cases (7.9%) using ACR 2010 and 2 cases using both criteria. As compared the groups with above ACR 2010 with below criteria, DAS28-CRP4 3.82 vs 2.26, SDAI 21.03 vs 7.05, pain VAS 50.7 vs 24.0, FIM 109.2 vs 116.9, CED-S 14.5 vs 12.6, age 72.3 vs 68.2, disease duration 16.7 yrs vs 20.0 yrs. [Conclusion] In RA patients treated with biologics and JAK kinase, 3.4% patients had a diagnosis of FM using ACR 1990 criteria, 7.9% using ACR 2010 criteria.

W56-2

Examination about outbreak peak of the symptom in HPV vaccine associated neuro-immunopathic sydrome (HANS)

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Conflict of interest: None

Background: HANS is central nervous disease around the hypothalamus, and various symptoms become multilayer in a going process and cannot send normal life. We assumed this point in time outbreak peak of HANS. Objective: I intended for HANS 32 girls first vaccination 14.3±2.7 years old, first symptom appearance 15.4±3.1 years old. A period to outbreak peak classified it after the first inoculation more than within 1 through 2, within 2 through 3, three years for less than one year from six months for less than six months from 30th for first inoculation less than 30 days Result: Less than three years are 16 people (50%) and 69% of past when is most allergic from Outbreak peak2 year It was 25% of antinuclear antibody positives. Then, less than one year was 60% of allergies, antinuclear antibody 60% in five people (16%) from six months, and subsequently within 1 through 2 were allergy 25%, antinuclear antibody 25% in four people (13%). Discussion: There were the most within 2 through 3 in Outbreak Peak which various kinds of symptoms of HANS made multilayer from the first inoculation. In addition, there were many things which had an allergy for an inoculation, and it was thought that control abnormality of some kind of immune system participated in HANS.

W56-3

The relationship between the patient characteristics of rheumatoid arthritis and locomotive syndrome

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Conflict of interest: None

[Object] There were few reports showing the relationship between Rheumatoid arthritis (RA) and locomotive syndrome. In this study, we demonstrated the associations of the RA patient characteristics with Locomo 25, a 25-question risk assessment questionnaire. [Methods] There were a total of 661 patients with RA whose Locomo 25 we investigated from 2012 to 2016. The associations of patients' baseline characteristics with Locomo 25 were analyzed with Pearson's correlation coefficient. Subsequently, cutoff values of locomotive syndrome (Locomo 25 ≧16 points) were calculated by regression linear models of patients' parameters. [Results] The mean age of 661 patients (female 501patients, 75.8%) was 64.5±12.8 years and the duration was 11.2±9.0 years. The stronger correlated parameters were HAQ-DI (r=0.851), PGA (r=0.680), DAS28-CRP (r=0.607). The cutoff values were 0.25 (HAQ-DI), 20 (PGA), 2.3 (DAS28-CRP). [Conclusions] We demonstrated the stronger correlation between Locomo 25 and HAQ-DI, PGA and DAS28-CRP. It was considered important to perform tight control of RA and suppress patients' pain and RA disease activity and prevent functional disability for the purpose of preventing development and progression of locomotive syndrome.

W56-4

Methotrexate adherence in patients with rheumatoid arthritis treated in private practice for rheumatic disease is excellent

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Conflict of interest: None

[Objective] Medication non-adherence to MTX is a widely recognized problem that leads to unfavorable outcomes including adverse reactions. We aimed to investigate adherence to MTX, which is an anchor drug for RA treatment. **[Methods]** RA patients being treated at 30 facilities in Japan rheumatism association in private practice enrolled in this survey from January to September 2016. An anonymous questionnaire was used to know patients' background and factors affecting MTX adherence. **[Results]** Of 4,446 RA patients, 94% had knowledge of MTX while 4.5% answered they did not. The reasons for no knowledge of MTX are as follows: 1) no problem even they did not know, 2) MTX information was too difficult to understand. While 0.5% of the patients almost never took MTX, 81% took MTX as prescribed. In case of not taking MTX, approximately 50% of them informed their personal doctors of the fact. **[Conclusion]** MTX adherence is excellent in the patients of this research group since most of the patients took MTX properly. Medical staff should take efforts to understand patients' background and their knowledge of MTX in order to increase their medication adherence. An

increase in medication adherence leads to higher therapeutic effects.

W56-5

The medical partnership in Sasebo city, Nagasaki for patients with rheumatoid arthritis (RA)

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Conflict of interest: None

(Introduction) To treat the RA patients for long time, there is needed the hospital with the specialists of RA and community clinics. We created the medical partnership for the RA patients between our hospital and community clinics in Sasebo City, Nagasaki. (Methods) Patients visited our hospital every 3-6 months for some examinations, and get advice from the nurse who specialized in RA. Rheumatologists examine and decide the treatment plan supported by the treat to target (T2T). Patients take the notebook which was written the treatment plan to clinics, and get the medicine. (Results) Between August 2010 and June 2015, we enrolled 177 patients at 75 clinics. At the entry, the average age was 63.9 years old. At June 2015, MTX usage rate was 66.9%, the biologic usage rate was 9.0%, and PSL usage rate was 14.2%. At the entry, the average DAS-28ESR 2.90, DAS-28CRP 2.09, S-DAI 5.6. Persistency rate of the patients with the partnership was 75.1%. The 36.4% patients stopped the partnership for other illness, and the 20.5% patients returned to our hospital for remission therapy. The 22.7% patients visit community clinics only, because they (included 4 drug free patients) keep the remission and low disease activity. (Conclusions) The partnership is important to treat the RA patients.

W56-6

Rheumatism clinical care support system and joint echo combined rheumatism clinical practice

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Conflict of interest: None

【Purpose】Rheumatism patients have different comprehension skills to the medical condition, and efficient medical treatment and sufficient explanation are difficult in many cases. We report on the use of tools to facilitate medical treatment and facilitate accurate explanation.【Method】DAS 28 etc using Smart Device. Jjoint echo was performed on the tjc/sjc. We conducted a questionnaire survey on 70 people who enforced the law and investigated the degree of understanding of the condition.【Result】The time required for SD inquiries was 4' 24 seconds on arage for the first time. SD can collect information such as evaluation of joints necessary for examination, differences may occur between patients and doctors and nurses regarding swollen joints. In that respect, joint echoes can be checked for synovial thickening / signal, and X - P can confirm ambiguous bone erosion, clearly explain the condition. the degree of comprehension of the patient's condition before and after using the tool increased from 66% -/86% "well understood", " I got an explanation.【Conclusion】2010 Rheumatology White Paper is "I want you to shorten the waiting time (23.5%)" and "I want you to listen to more (12.2%)", but Medical information can be provided to the doctor.

W57-1

Association of *SIRT1* (*sirtuin 1*) gene polymorphism with systemic sclerosis (SSc) in Japanese population

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Conflict of interest: None

<Purpose> SIRT1 encodes a Sirtuin family of protein, and known to associate with aging. SIRT1 is NAD-dependent deacetylase and works through action to intracellular target protein. SIRT1 deacetylate hypoxia inducible factor (HIF) in a hypoxia state and activates HIF2A leading to increase activity of HIF2A target. In addition, SIRT1 knock out mouse exhibits activation of macrophage and inflammation at liver and adipose tissue. This phenotype suggests association of SITRT1 with autoimmunity. SSc is autoimmune diseases associated with peripheral hypoxia. Association between SSc development or phenotype and SIRT1 polymorphism was investigated. <Methods> 195 Japanese SSc patients and 544 healthy controls were recruited in this study. Five SNPs, rs7895833, rs12778366, rs3758391, rs7069102 and rs2273773 on the Sirt 1 gene were genotyped using Taqman assay. <Results> Haplotype of rs2273773 was susceptible polymorphism for Japanese SSc development. (OR 0.77 (95% CI 0.59-0.98) P=0.04). rs7895833, rs12778366 and rs3758391 was associated with development of skin ulcer and pulmonary hypertension (PH) ($p<0.05$). < Conclusions > SIRT1 gene polymorphism was associated with SSC development in Japanese cohort. Some of SIRT1 gene polymorphism was also associated with skin ulcer and PH phenotype.

W57-2

YKL-40 and cutaneous immunohistochemistry (IHC) in systemic scleroderma (SSc)

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Conflict of interest: None

Object: YKL-40 is a chitinase-like protein induced during processes including angiogenesis and tissue remodeling. We investigated serum YKL-40 values and IHC of cutaneous tissue in SSc patients. Method: Between Aug. 2014 and Mar. 2016, we treated 77 SSc patients in our department. The patients were divided into 4 groups depending on whether suffered IP or PAH, which can affect the prognosis. Group1 (n=41) did not suffer from either IP or PAH, Group2 (n=18) suffered from IP, Group3 (n=4) suffered from PAH, and Group4 (n=14) suffered from both IP and PAH. YKL-40 values in 4 groups and a control group of healthy individuals (n=18) were measured by ELISA. IHC of skin biopsy tissue from patients and controls was performed to investigate YKL-40 expression. Result: YKL-40 levels were elevated in Group1 compared to controls (66.1±40.0 vs 41.5±21.4ng/ml), and were elevated due to complications (Group2,3,4:102.0±68.9, 183.5±120.4, 225.9±161.0ng/ml), with a tendency for PAH to cause greater elevation. IHC revealed staining of the vessels in the superficial dermis, suggesting that YKL-40 may be further elevated by angiogenesis caused by microcirculatory damage in SSc. Conclusion: Our results suggest that YKL-40 may be useful for diagnosing complications associated with microvascular lesions.

W57-3

The cellular origins of circulating microparticles and their relationship to clinical features in systemic sclerosis

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Conflict of interest: None

[Purpose] To clarify the cellular origins of circulating microparticles (MP) and pursue the relationship to the pathogenesis in systemic sclerosis (SSc). [Methods] Seventeen patients with SSc, 20 patients with RA, and 13 healthy controls were involved. Platelet-rich plasma was isolated from whole blood by using gradient centrifugation, and analysed by flow cytometer. We defined MP as particles smaller than 1.0μm diameter, and identified by staining with cell type specific surface antibodies. We analyzed correlation between the proportion of MP origin subsets and clinical information, retrospectively collected from clinical records. [Results] The mean age was 64.5±9.5 years, 89% were female, and the mean dis-

ease duration was 6.8±10.1 years. Platelet-derived MP was the largest population in SSc, RA, and healthy controls. In SSc, the proportion of endothelial cell-derived MP (EMP) was higher than those in RA or healthy controls ($p<0.01$, $p<0.001$, respectively). On the other hand, that of immune cell-derived MP was tended to be higher in SSc and RA as compared with healthy controls. [Conclusion] The distributions of MP subpopulations in SSc, especially EMP, were different from those in RA and healthy controls. It may have relations with underlying pathogenesis in SSc.

W57-4

The Relation between anti-activin type IIB receptor intracellular domain (ACVRIIB-id) Ab and Subtypes of Systemic Sclerosis (SSc)

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Conflict of interest: None

To identify new autoantibodies for SSc, we conducted protein array assays. Using statistical approaches and considering clinical relevance, we identified anti-ACVRIIB-id Ab as a new candidate autoantibody for SSc. ACVRIIB is a receptor of TGF-β superfamily, which are thought to have close relationship with SSc. Next, we measured the serum activin A and anti-ACVRIIB-id Ab in SSc patients (n= 20) and healthy controls (n= 20) with ELISA. We found the elevations of activin A ($p< 0.001$) and anti-ACVRIIB-id Ab titer ($p= 0.012$) in SSc patients. Then, we measured anti-MHC class II DR/ACVRIIB-id complex (DR/ACVRIIB-id) Ab titer with flow cytometry in patients with SSc and compare the Ab titer and clinical manifestations. We found that DR/ACVRIIB-id Ab titers were high in anti-topoisomerase I Ab (ATA)+ patients and low in anti-RNA polymerase III Ab (ARA)+ patients ($p < 0.001$). Those of anti-centromere Ab+ were middle (vs. ATA+ $p= 0.012$, vs. ARA+ $p= 0.003$). There is no knowledge of relationships between topoisomerase-I and ACVRIIB and no amino acid sequence homologies between them. Investigation of relationship between SSc and DR/ACVRIIB-id Ab may give a new insight of SSc.

W57-5

Serum Level of KL-6, a Biomarker of Interstitial Lung Disease (ILD), is Higher in Diffuse SSc than in Limited SSc and RA even When the Activity of ILD is Low

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Conflict of interest: None

Background: Measurements of serum levels of KL-6 have been reported to be useful to speculate the activity of interstitial lung disease (ILD). However, we have noticed that in some patients, serum KL-6 levels are sustained in high levels even when the activity of ILD deceased. We tried to detect the factors that contribute in sustaining serum KL-6 levels high. Methods: Subjects were 100 patients including 54 RA, 19 d-SSc, and 27 l-SSc. They had stable ILD for more than 2 years in terms of chest CT images and %VC. Serum KL-6 levels were checked periodically from the first visit. Variables were checked including diagnosis, age, gender, ILD pattern, ILD grade, % VC, peak and last serum KL-6 levels, and others. These variables were statistically analyzed. Results; Last serum KL-6 value was highest in d-SSc followed by l-SSc and RA ($p < 0.0001$). % VC were lowest in d-SSc followed by l-SSc and RA ($p < 0.02$). Multivariate analysis was done to extract factors that contribute to discriminate 2 groups, i.e. a very high KL-6 group (KL-6 >= 900 U/ml, n=10) and another group (KL6 < 900 U/ml, n=90). These factors were diagnosis, and peak serum KL-6 values. Conclusion: Patients with d-SSc and high peak KL-6 values tend to show high serum KL-6 values even when ILD became stable.

W57-6

Effectiveness of the triple therapy glucocorticoid + intravenous cyclophosphamide + double filtration plasmapheresis for skin sclerosis in patients with diffuse cutaneous systemic scleroderma

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Conflict of interest: None

Objectives; Patients with diffuse cutaneous systemic scleroderma (dcSSc) experience severe skin sclerosis in the early stage. Although the severity of skin thickening is an independent prognostic factor, there is no established treatment for this symptom. We performed triple therapy (glucocorticoid + intravenous cyclophosphamide + double filtration plasmapheresis) for the skin thickening. We retrospectively analyzed the effectiveness of this treatment. **Methods;** We enrolled eight patients with dcSSc who received the triple therapy at our hospital from 2008 to 2016. We analyzed the difference in the mean change from baseline in modified Rodnan skin score (mRSS), KL-6, %FVC, and %DLCO. **Result;** The mean patient age was 56.0 ± 11.1 years. The mean disease duration at therapy initiation was 5.9 ± 5.4 months. The mRSS decreased significantly from 27.0 ± 9.4 to 15.8 ± 9.8 ($p = 0.03$). The percentage change of mRSS was 42.2%. KL-6 decreased from 578.9 ± 414.4 U/mL to 205.3 ± 114.1 U/mL ($p = 0.02$). The results of pulmonary function tests at baseline and at the end of the therapy revealed no difference in the mean %FVC and %DLCO. **Conclusion;** The triple therapy may improve skin sclerosis in patients with dcSSc; however, prospective studies are required to determine its role.

W58-1

Evaluation of vascular lesions in systemic sclerosis patients using nailfold videocapillaroscopy

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Conflict of interest: None

Purpose: Density of capillaries (DOC) was compared in various connective tissue diseases. The relationship between DOC and vascular endothelial cell function in pulmonary vascular disease and medium arteries in systemic sclerosis (SSc) patients was also investigated. **Subjects and Methods:** Subjects comprised 55 patients, with SSc in 25 patients, systemic lupus erythematosus (SLE) in 11, mixed connective tissue disease in 13, and polymyositis/dermatomyositis (PM/DM) in 6. DOC was measured with nailfold videocapillaroscopy (NVC). Tricuspid regurgitation pressure gradient (TRPG) was measured in SSc patients at rest and and after exercise load. Brachial artery flow-mediated dilatation (FMD) was also measured in SSc patients. **Results:** DOC was significantly lower in SSc than in SLE and PM/DM. No correlation was found between DOC and TRPG at rest in SSc, but a negative correlation with TRPG was seen after exercise load. No correlations were seen between FMD and DOC or between FMD and TRPG after exercise load. **Discussion:** Microangiopathy was shown to be present in SSc. DOC in SSc may be correlated with the pulmonary vascular bed. In SSc, the mechanisms of injury for microangiopathy and endothelial cell disorder in medium arteries may differ.

W58-2

The characteristics of capillary abnormalities observed by Nailfold Videocapillaroscopy in Japanese patients with Systemic Sclerosis

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Conflict of interest: None

Objective: Capillary abnormalities observed by nailfold videocapillaroscopy (NVC) are useful for the diagnosis of systemic sclerosis (SSc). However, there are few reports about NVC in Japan. In the present study, we aim to estimate whether NVC may contribute to the discrimination of SSc from other connective tissue diseases (CTDs). **Methods:** NVC findings were collected from 67 adult Japanese patients with CTDs, including 24 SSc patients. We observed NVC abnormalities were assessed in 6 aspects: enlarged capillaries, giant capillaries, hemorrhages, loss of capillaries, ramified capillaries, and disorganization of the vascular array. The association between clinical manifestations and NVC patterns were assessed. **Results:** Sixty-three patients (94%) had irregular NVC patterns. There were no differences in the frequency of patients who had irregular NVC patterns between SSc and non-SSc. However, SSc patients had more fingers with irregular NVC patterns than non-SSc (5.5 +/- 1.9 fingers vs. 4.1 +/- 2.5, p= 0.03), especially in the aspect of loss of capillary. **Conclusion:** NVC may contribute to the diagnosis of SSc in the Japanese patients as reported in other ethnicities.

W58-3

Introduction of Raynaud Clinic using nailfold videocapillaroscopy to promote early diagnosis of connective tissue diseases

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Conflict of interest: None

[Object] Raynaud's phenomenon (RP) is known to be early sign of connective tissue diseases (CTD), especially in systemic sclerosis (SSc). We started "Raynaud Clinic" using NVC to promote early diagnosis of CTD. [Methods] Two rheumatologists evaluated patients by NVC at Raynaud Clinic from 2016/2/17 to 2016/11/16. [Results] 49 patients were included. 42 were female and the age was 59.1±19.1. The reasons of consultation were as follows: RP 39, puffy fingers 3, positive autoantibodies 6, and skin sclerosis 1. Final diagnoses were as follows: CTD 35 dcSSc 2, lcSSc 15, sine-SSc 1, MCTD 3, SS 4, SLE 5, UCTD 5, None 12, eosinophilic fasciitis 1, and multiple myeloma 1. Among 7 patients with RP of less than a year, 5 were diagnosed with CTD. Abnormal NVC were observed in 30 (61.2%). The sensitivity of RP, ANA, and abnormal NVC for the diagnosis of CTD were 88.6%, 91.4%, and 82.9%, respectively, and the specificity of those were 42.9%, 64.3%, and 92.9%, respectively. In patients with RP, abnormal NVC yielded sensitivity of 80.7% and specificity of 87.5%. In 12 patients referred from outside, 3 were diagnosed as CTD and abnormal NVC yielded sensitivity of 100% and specificity of 88.9%. [Conclusions] Raynaud Clinic using NVC may promote early diagnosis of CTD.

W58-4

Investigation of pseudo-obstruction and prognosis in patients with systemic sclerosis

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Conflict of interest: None

<Objectives> Pseudo-obstruction is one of the gastrointestinal involvements with systemic sclerosis (SSc), and it is associated with a poor prognosis. Disease-specific antibodies are often correlated with some organ involvement and mortality, we investigated the relevance of disease-specific antibodies in pseudo-obstruction cases. <Method> Twenty-eight SSc patients out of 281 hospitalized patients were investigated. The relationship among disease-specific antibodies, pseudo-obstruction, and prognosis of these patients were analyzed. <Results> Positive rate of anti- topoisomerase I antibodies, anti-centromere antibodies (ACA), anti-U1 RNP antibodies were 14.3%, 35.7, and 14.3%. Disease duration is significantly long in ACA positive patients. SSc patients needed to implant CV access port more than the other rheumatic disease patients. The prognosis of patients with pseudo-obstruction was poor. <Conclusion> Our study suggested that SSc with ANA positive cases showed close relation with pseudo-obstruction, and they had poor prognosis. We also found the relationship between pseudo-obstruction and anti-U1 RNP antibody. We have to be careful about gastrointestinal involvement with ACA positive SSc patients.

W58-5

Ten years follow-up of small intestinal clearance in patients with systemic sclerosis

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Conflict of interest: None

Object: GI tract involvement is commonly accompanied in SSc patients. We previously reported a close correlation between the small intestinal clearance (SIC) and esophageal diameter. The aim of this study was to evaluate a correlation between the SIC and clinical features in SSc patients during ten years follow-up. Methods: Fifty-five patients with a definite diagnosis of SSc were included in the study. The SIC was classified according to barium meal reach at 30 min after intake; grade1 (>2/3 of the whole small intestine), grade2 (1/3~2/3), grade3 (<1/3), grade4 (the duodenum). The SIC change grade1 and 2 was classified as "invariant", and grade increase or grade3 and 4 during follow-up as "decrease". Results: The mean durations of follow-up period were 9.5 years. The SIC grade was increased in 40.0% of SSc patients during follow-up. The frequency of SIC "decrease" in anti-centromere antibodies (ACA) positive SSc patients was significantly higher than that in ACA negative SSc patients (61.9 vs 26.5%, $p<0.05$). The esophageal diameters at initial evaluation were significantly wider in SIC "decrease" group than in "invariance" group (21.8 ± 6.5 vs 30.9 ± 8.6 mm, $p<0.01$). Conclusion: The present study strongly support that ACA is an important factor of the SIC in SSc patients.

W58-6

Challenges in revised classification criteria for systemic autoimmune rheumatic diseases and their overlap syndrome

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Conflict of interest: None

[Purpose] To elucidate the challenges in revised classfication criteria for systemic autoimmune rheumatic diseases and their overlap syndrome. [Methods] A total of 792 patients with systemic autoimmune rheumatic diseases are included in this study. The following criteria were used: 1997 revised ACR criteria and 2012 SLICC criteria for SLE, 1980 ACR criteria and 2013 ACR/EULAR criteria for SSc, 1987 revised ACR criteria and 2011 ACR/EULAR criteria for RA, and the criteria by Bohan and Peter (definite or probable) for PM/DM. [Results] 84 and 100 patients fulfilled the old and the new SLE criteria, respectively. Similarly, 33 (old) and 45 (new) patients met SSc criteria, 235 (old) and 319 (new) patients met RA criteria, and 10 (PM) and 7 (DM) patients fulfilled the Bohan and Peter criteria. Fifteen and 31 patients were identified as overlap syndrome by the old and the new criteria, and the number reduced to 6 (old; 3 SLE-SSc and 3 SLE-PM) and 11 (new; 7 SLE-SSc and 4 SLE-PM). [Conclusion] Although the revised classification criteria showed and improved sensitivity, the handling of RA-overlap syndrome was a criticle challenge. In addition, SLE-SSc overlap syndrome has been still predominant except for RA-overlap.

W59-1

Dysregulated FOXO transcription factors in articular cartilage in aging and osteoarthritis

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Conflict of interest: None

[Object] Forkhead box O (FOXO) transcription factors play an essential role in regulating antioxidants and protein quality control. In the present study, we investigated the expression of FOXO transcription factors in OA cartilage and the function of FOXO in human chondrocytes. [**Methods]** Knee joints from humans were analyzed for expression of FOXO. siRNAs and plasmids targeting FOXO1 and FOXO3 were transfected into human articular chondrocytes. Protein expression of antioxidant proteins and autophagy-related proteins were assessed. **[Results]** FOXO mRNA expression was significantly lower in OA cartilage than in normal cartilage. In OA cartilage, chondrocyte clusters showed strong FOXO phosphorylation and cytoplasmic localization. Cell viability was significantly reduced by siFOXO after treatment with tBHP. Knockdown of FOXO1 resulted in significant reductions in levels of antioxidants and autophagy-related proteins. In contrast, the constitutive active form of FOXO3 increased cell viability in response to tBHP. **[Conclusions]** Reduced expression of FOXO transcription factors in chondrocytes increased susceptibility to cell death induced by oxidative stress. This was associated with reduced levels of antioxidant proteins and autophagy-related proteins.

W59-2

Comparison of gene expression in synovial tissues between osteoarthritis and rheumatoid arthritis

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Conflict of interest: None

【Purpose】This study was conducted to investigate the etiology of synovial pathology in osteoarthritis (OA) through the comparison of gene expression with rheumatoid arthritis (RA) synovium.【Methods】Synovial tissues were collected from 64 OA knees and 40 RA knees at prosthetic surgery, and expression levels of MMP-1, 2, 3, 9, 14, uPA, TNF-α, IL-1β, VEGF-A, IL-6, TNFR1, TNFR2, IL-1R1, VEGFR2, IL-6R and gp130 was determined by qPCR. Gene expression levels as well as correlations in gene expression were compared between OA and RA.【Results】Expression of MMP-2, 14, uPA, VEGFR2 was more enhanced in OA synovium, while the expression of MMP-1, 3, 9, TNF-α, IL-1β, VEGF-A, TNFR2 and IL-1R was greater in RA synovium. In OA synovium, expression of MMP-2, 14, uPA was significantly correlated with that of VEGF-A, while any of these correlations were not observed in RA synovium.【Discussion】The result of this study revealed that in OA synovium, several proteinases were expressed at the levels higher than those in the RA synovium, possibly as a result of induced angiogenesis.【Conclusion】Comparison with RA synovium indicated a possibility that the expression of several proteinases may be induced by angiogenesis in OA synovium.

W59-3

Preparation for anatomic variations in Japanese cases with medial osteoarthritis of the knee

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Conflict of interest: Yes

Based on our previous studies, anatomic variations of the lower extremities in Japanese patients with medial osteoarthritis of the knee were summarized. Then, preparations for the anatomic variations were assessed. The characteristics of Japanese patients are lateral and anterior bowing of the femoral shaft, proximal tibia vara with medial shift of the articular surface, and medial torsion of the tibia. During total knee arthroplasty, distal femur should not be cut perpendicular to the mechanical axis when the femur has bowing. In knees with medial shift of the tibial articular surface, hip-knee-ankle angle under-estimates the varus deformity. Femoro-tibial angle cannot express the loading condition in the medial joint, either. Discrepancy between the anatomical and mechanical axes should be assessed preoperatively. Reduction osteotomy can correct the varus deformity, and the anatomical axis would match the new mechanical axis after the reduction osteotomy. The second toe should not be used for the landmark of alignment of the tibial component. If the shape of the patella does not fit the patellar groove of the femoral component, the patella should be resurfaced.

W59-4

Changes of Coronal Lower Limb Alignment in Standing Position after Total Knee Arthroplasty for Patients with Varus Osteoarthrits of the Knee

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Conflict of interest: None

The aim of this study was to examine the changes of coronal lower limb joint alignment in standing position after total knee arthroplasty (TKA) for patients with varus osteoarthritis of the knee (knee OA). One hundred patients with varus knee OA (HKA Angle $\geq 4^\circ$) who underwent primary TKA were included in this study. We divided patients into three groups in terms of ankle joint line straightness for tibial functional axis; Group A (11 patients, valgus more than 3°), Group B (65 patients, straight) and Group C (24 patients, varus more than 3°). We measured HKA Angle, tibial knee joint line varus angle (TKV Angle), tibial functional axis angle (TF Angle), tibial knee joint line angle (TK Angle), tibial ankle joint line angle (TA Angle) and talus ankle joint line angle (TaA Angle) on radiographs of the whole leg in standing position 3 weeks after TKA, and then we compared each measurement value within three groups. There were not significant differences in HKA Angle, TKV Angle, TF Angle and TK Angle. Whereas, there were significant differences between groups in TA Angle and TaA Angle ($p < 0.01$). The shape of distal tibia influences coronal ankle alignment in standing position after TKA, so we should consider it in patients with severe varus or valgus deformity.

W59-5

Relationship between calcium pyrophosphate dihydrate crystal and operated osteoarthritis of the knee -gender specific analyses-

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Conflict of interest: None

[Objectives] To investigate the relationship between CPPD crystal and operated knee OA separated by gender. [Methods] Three hundred sixty-six UKA, TKA and HTO (average age 73.3: male 59: female 307) were performed for over Kellgren-Lawrence grade III knee OA. At the operation, joint fluids were collected and elucidated the CPPD crystal. We evaluated the relationship between CPPD crystals and age, BMI, CRP, ESR, MMP-3, osteophyte formation degree (OFD), FTA, and leg alignment. [Results] CPPD crystals were detected from 101 OA knees (27.6%). CPPD (+) rate in female (30.0%: 92/307) was significantly higher than that in male (15.3%: 9/59). There was a significant difference only between CPPD (+) and (-) about FTA (186.9°/182.0°) in male. There were significant differences between CPPD (+) and (-) about age (76.3/72.4), FTA (182.7°/183.2°), BMI (24.9/26.6) in female. The more severe OFD became, the higher CPPD (+) rate was in female, significantly. CPPD (+) rate in valgus knees (60.9%) was higher than that in varus knees (29.6%) in female significantly. [Conclusions] CPPD (+) rate in fe-

male was significantly higher than that in male and significantly different items in male and female were different. These results may suggest that the mechanism of CPPD deposition is different by gender.

W59-6

Joint arthroplasty with osteochondral graft from the knee for hand joint osteoarthritis

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Conflict of interest: None

Purpose To evaluate the clinical outcomes of articular surface reconstruction for hand joint osteoarthritis (OA) using autologous osteochondral grafts from the knee. **Methods** Five patients underwent joint arthroplasty for hand osteoarthritis with autologous osteochondral grafts from the patellofemoral joint. Mean patient age was 53 years (range 48-58y). The patients were followed for an average of 48 months (range 16-89 m). Metacarpophalangeal joint arthroplasty was performed in 2 cases (OA 1, gout 1), and proximal interphalangeal joint in 3 cases (OA 2, RA 1). The patients' clinical outcomes were evaluated with radiographic images, joint range of motion, visual analog scale, and DASH score. **Results** Graft union was confirmed in all cases without radiographic evidence of resorption or necrosis. Follow-up radiographic examinations showed good graft incorporation without signs of osteoarthritis. The finger flexion-extension arc improved from an average of 21˚ to 61˚. The mean visual analog scale also improved from 7.0 to 1.5. Mean DASH score improved from 33 to 12. **Conclusion** Autologous osteochondral grafting from the patellofemoral joint provided satisfactory outcomes and may be a useful option for joint surface reconstruction of hand joint osteoarthritis.

W60-1

Efficacy and safety at 24 weeks of daily clinical use of tofacitinib in patients with rheumatoid arthritis

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Conflict of interest: None

Objective: To evaluate the efficacy and safety of tofacitinib (Tofa). Method; 70 patients with RA who were treated with Tofa were enrolled. DAS 28ESR and the AEs were evaluated during Tofa treatment of 24 weeks. In addition, the factors contributed to achievement of LDA at 24 weeks were investigated. Result: 49 patients had been treated with biologics prior to tofa. 49 patients received concomitant MTX. The mean DAS28ESR decreased from 5.08 to 3.53 at 24 weeks. Univariate analysis showed that the number of previous use of bDMADs, DAS28ESR at baseline and positivity of ACPA were associated with achievement of DASLDA. Multivariable logistic analysis showed that the number of bDMARDs previously used was independently associated with achievement of LDA. 12 patients experienced AEs and herpes zoster were most frequently seen. In the concomitant MTX (+) and (-), the Δ values of DAS28ESR were -1.78, -1.18, respectively. bDMARDS-naïve patients showed better efficacy as compared with bDMARDS experienced patients (Δ DAS28-ESR;-2.46, -1.21, respectively.) Conclusion: Tofa treatment was more effective in MTX-concomitant use and bDMARDs-naïve patients. Analysis of factor contributed to good response suggested that efficacy of tofa diminishes if started after use of multiple bDMARDs.

W60-2

The impact of the combination therapy of Tofacitinib (TOF) add on or switch MTX in the Japanese large cohort, NinJa2015(National Database of Rheumatic Diseases by iR-net in Japan)

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Conflict of interest: None

(Material and methods) In 15101 RA patients registered in Japanese large cohort of NinJa (National Database of Rheumatic Diseases by iR-net in Japan), 1% of the patients had been medicated TOF. 68 patients had the combination therapy with MTX + TOF, but 49 patients had not combination therapy, TOF only. (Results) Extraction of combinations with Boolean remission rate, MTX + TOF had high efficacy. In addition, from the point of view of safety, the hospitalization rate of each combination was generally around 5%, TOF without MTX group had the hospitalization rate, especially for pneumonia and herpes zoster. (Discussion) In this current study, we recommended TOF add on MTX because of efficacy and safety.

W60-3

Prevalence and risk factors of reactivation of resolved hepatitis B virus in rheumatoid arthritis patients treated with biological disease-modifying anti-rheumatic drugs

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Conflict of interest: None

[Object] To identify the prevalence and risk factors for HBV reactivation in RA patients with resolved HBV who received bDMARDs. [Methods] RA patients initiated with bDMARDs from April 2009 to October 2016 were reviewed. Of these patients, registered were the patients who had been diagnosed as resolved HBV and whose HBV-DNA were repeatedly measured. The endpoint was reactivation of HBV. The frequency and risk factors of HBV reactivation were retrospectively analyzed. [Results] 152 RA patients with resolved HBV were included and 132 patients had anti-HBs. Abatacept (ABT) was administered in 29 patients, golimumab (GLM) in 26, etanercept in 25, tocilizumab (TCZ) in 25, adalimumab in 19, infliximab (IFX) in 17 and certolizumab pegol in 11. Seven (4.6%) patients developed HBV reactivation. In 5 out of 7 patients, HBV-DNA levels remained < 2.1 log copies/ml. HBV-DNA level over 2.1 log copies/ml was observed in 2 patients, however HBV-DNA became negative after the initiation of entecavir. The prevalence of HBV reactivation was significantly higher in the patients negative for anti-HBs ($p = 0.008$, Log-rank test). [Conclusions] HBV reactivation occurred in 4.6% of RA patients with resolved HBV during the bDMARDs therapy. Absence of anti-HBs can be risk for reactivation of resolved HBV.

W60-4

Can the infants receive live vaccine, whose mothers with rheumatoid arthritis treated by etanercept?

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Conflict of interest: None

[Background] We reported that patients with rheumatoid arthritis (RA) under control by etanercept can perform the pregnancy, delivery and breast-feeding without aggravation of RA. However, a fatal case of disseminated mycobacterial infection has been reported in an infant who received BCG vaccine, whose mother was treated with infliximab throughout her pregnancy. Discontinuing infliximab in the third trimester of pregnancy should be considered in order to minimize fetal exposure. Etanercept is an anti-TNF inhibitor, but is a fusion protein not an antibody. The association between etanercept and live vaccine inoculation to infants is unclear. [Objectives] To evaluate the live vaccine incoulation of the infants whom mothers was treated by etanercept. [Result] 12 infants received BCG vaccine and three received rotavirus vaccine. All infants were breast-fed. One case vomited after rotavirus vaccination. [Discussions] Etanercept is a fusion protein, and it is TNF receptor antagonist. Etanercept has a short half-life time and a low rate of transplacental passage and mother's milk secretion. So, it is thought that the adverse effect is less in live vaccine inoculation. [Conclusion] The breast-fed infants can receive live vaccine, whose mothers with RA treated by etanercept.

W60-5

Incidence and Risk Stratification of Reactivation of Hepatitis B Virus (HBV) in Patients with Resolved HBV Infection on Immunosuppressive Therapy for Rheumatoid Arthritis The Third Report of a Multicenter Prospective Observational Study by the sixteen hos

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Conflict of interest: None

[Objectives] We are performing multicenter observational, prospective study to clarify the incidence and stratify the risk of HBV reactivation in rheumatoid arthritis (RA) patients. We report the results of one to three years observation in the patients with resolved HBV infection. [Methods] Patients with RA, treated with steroids, and/or synthetic or biological immunosuppressive drugs (ISD), with negative HBs antigen and positive anti HBs and/or HBc antibody (Ab) were enrolled. HBV-DNA (RT-PCR) and related data were registered regularly. [Results] Among 1126 patients, 2708 person-years, detection of HBV-DNA were found in 46 patients, 1.72/100 person-years, and positivity more than 2.1 log copy/ml were seen in six cases, 0.22/100 person-years. None of reactivated patients showed clinical hepatitis. Reactivation was seen more frequently in patients with negative HBs Ab and positive HBc Ab than in patients with both Ab positive, 9.26% vs 2.9%, $p<0.001$. In ROC analysis of HBs Ab titer in HBV reactivation, area under the curve was 0.608. [Conclusions] HBV reactivation with ISD was 1.72/100 person-years in RA patients with resolved HBV infection. Risk stratification using HBs Ab titer was possible but sensitivity and specificity was not enough for clinical use.

W60-6

A case of severe enteritis with sporadic punched out ulcers which pathogen needed to distinguish Epstein-Barr virus from cytomegalovirus in the cryopyrin-association periodic syndrome patient under treatment with canakinumab

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Conflict of interest: None

A 20 y.o. woman diagnosed CAPS with NLRP3 point mutation was hospitalized due to abdominal pain and fever. She was initiated canakinumab (CAN) when she was 15 y.o,, and fixed treatment with 450mg of CAN for every 6 weeks and 10mg of PSL for everyday since she was 17 y.o.. When she was hospitalized, her WBC and CRP were elevated. We performed colon fiber (CF) and observed sporadic punched out ulcers. We started ganciclovir (GCV) because the findings were characteristic of cytomegalovirus (CMV) colitis. After 5-week of GCV treatment, her symptom got better. However, 2weeks after the end of GCV, her abdominal pain got worse and we performed CF again. Colon ulcers were relapsed. We performed PCR for CMV and EBV, and only EBV was detected. Her symptom disappeared after 2 weeks of GCV injection. [Discussion] Although the CF findings were similar to CMV colitis, there was the evidence of EBV infection, not CMV. Because CMV and EBV were members of the herpes family of viruses, GCV is also effective for EBV. [Clinical significance] CAPS is one of the rare diseases of autoinflammatory diseases. The treatment complication of CAN is valuable in clinical medicine. In the case of prolonged diarrhea in the patients treated with CAN, severe viral enteritis, like this case, should be considered.

W61-1

Myocardial fatty acid metabolism and perfusion mismatch in scintigraphy predicts worse prognosis in systemic sclerosis patients with asymptomatic cardiac involvement

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Conflict of interest: None

Objectives: To evaluate clinical utility of myocardial fatty acid metabolism and perfusion mismatch in SSc patients without cardiac failure. **Methods**: All patients who visited St. Marianna University Hospital from 2009 to 2015 and performed cardiac scintigraphy using ^{99m}Tl and ^{123}I-BMIPP were retrospectively evaluated. Patients who fulfilled ACR classification criteria of SSc and SLE were selected. We subtracted %uptake of metaboism (^{123}I-BMIPP) from that of perfusion (^{99m}Tl) and semi-quantitatively scored from 0 to 5 on each 17 myocardial segments standardized by American Heart Association. We compared sum of all the scores and each score in 3 coronary artery regions between patients with SSc and SLE. **Results**: Among 177 patients, we analyzed the data in 25 cases with SSc and 23 with SLE. The sum of all mismatch scores was not significantly different between the 2 groups ($p=0.82$). The mismatch score of right coronary artery (RCA) region was significantly higher in SSc than SLE ($p=0.03$). The SSc patients with higher RCA mismatch score had higher incidence of cardiac death ($p=0.19$) and lower of PH development ($p<0.01$). **Conclusions**: The higher mismatch score in RCA region of cardiac scintigraphy could be associated with cardiac death but not with PH development in SSc patients.

W61-2

Condition factors affecting achievement of discontinuation of high dose infliximab in patients with rheumatoid arthritis

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Conflict of interest: Yes

[**Objective**] We investigated the condition factors affecting achievement of discontinuation criterion of high dose infliximab (HD-IFX) in patients with the rheumatoid arthritis (RA). [**Methods**] Fifty patients (4 males and 46 female) treated with HD-IFX were examined. We compared the patient backgrounds between the group of achieved discontinue criterion (group A) and that of non- achieved criterion (B group). [**Results**] Sixteen (32%) of 50 patients fulfilled a criterion of drug holidays for HD-IFX. Compared with group B, dosage of MTX at the onset of treatment was significantly higher (A; 11.1 vs. B; 8.3 mg/week, $p<0.01$). HAQ-DI (A; 0.25 vs. B; 0.59, $p<0.05$) and SDAI (A; 10.2 vs. B; 17.1, $p<0.05$) was significantly lower at the time of escalation. [**Conclusion**] To achieve HD-IFX discontinuation criteria, higher MTX dose at the onset of IFX, and lower HAQ-DI and SDAI at the time of escalation.

W61-3

Examination of golimumab treatment response in patients with rheumatoid arthritis by determination of rheumatoid factor and anti-citrulline peptide antibody levels

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Conflict of interest: None

[Objectives and Methods] We investigated the treatment response using rheumatoid factor (RF) and anti-citrulline peptide antibody (ACPA) levels in 126 patients with rheumatoid arthritis who had started golimumab (GLM) treatment by October 2015. The study focused on 78 patients who had been treated with GLM for more than 52 weeks and whose DAS28-CRP could be evaluated pre- and post-treatment. We compared the treatment response between the high RF ($RF \geq 160$; $n = 11$) and low RF groups ($RF<160$; $n = 60$), and between the high ACPA ($ACPA \geq 100$; $n = 14$) and low ACPA groups ($ACPA<100$; $n = 14$). [Results] DAS28-CRP improved from 4.24 to 2.73 in all GLM-treated patients; specifically, it was found to be lower in the high RF group (4.70→2.44) than in the low RF group (4.20→2.71), a pattern which was also observed in the high ACPA group (4.79→1.92) compared with the low ACPA group (3.81→2.66). In particular, GLM (100 mg; escalating dose)-treated patients showed a remarkable decreasing tendency in DAS28-CRP scores [high RF group (4.79→2.32) and low RF group (4.44→2.99) and high ACPA group (4.86→1.81) and low ACPA group (4.35→3.12)]. [Conclusion] At week 0, DAS28-CRP scores were greater in the high RF or ACPA groups, but GLM 100 mg treatment was highly effective among these patients.

W61-4

Fast-acting property of Certolizumab pegol (CZP) in treatment of rheumatoid arthritis : from FIRST registry

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Conflict of interest: None

Purpose: Dose escalation of Infliximab (IFX) was approved in 2009, whereas CZP, the latest TNF-inhibitor was approved in 2013. Because both bDMARDs are considered to be fast-acting drugs, we here compared the fast-acting property of IFX with CZP. **Methods:** The efficacy of IFX in patients with RA before and after the approval of the dose escalation (pre- and post-approval, n=376 and 292, respectively) was compared with CZP (n = 92). Selection biases were statistically removed using propensity score (PS) matching. The primary endpoint was the rate of achievement of DAS28-ESR low disease activity (LDA) at 2 and 24 weeks. **Results:** After PS matching, there was no significant difference in the baseline characteristics. On comparing patients before and after approval of IFX dose escalation, although both groups equally achieved LDA at 2 weeks (28.0% vs 35.6%, respectively), the rate of achievement LDA at 24 weeks significantly differed between the groups (31.0% vs 66.7%, respectively). On comparing IFX post-approval and CZP groups, no differences in rates of LDA were observed at 2 and 24 weeks (IFX:CZP = 26.7%:22.2% at 2 weeks and 64.4%:62.2% at 24 weeks). **Conclusion:** These data suggest that CZP might have equal efficacy and fast-acting property of IFX dose escalation.

W61-5

The effectiveness and safety of Certolizumab pegol in the multiple center study

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Conflict of interest: None

[Objectives] To clarify the effectiveness and safety of Certolizumab pegol (CZP) for RA patients in multiple centers. [Methods] 39 RA patients in whom CZP was introduced between April 2013 and September 2014 were evaluated. We reviewed the improvement of DAS-28ESR at Week52 by LOCF method. [Results] The group of patients included 8 males and 31 females. The mean age was 61.4 years old; the disease duration was 11.5 years and the patients of receiving methotrexate was 31 cases (79.5%). The DAS-ESR improved from 4.5 at baseline to 2.8 at Week 52. Regarding with use of MTX, the DAS28-ESR at 52W were improved from 4.7 to 2.8 and from 4.3 to 3.3 with MTX group and the group without use of MTX, respectively. Comparison about the pretreatment with biologics, DAS28-ESR at 52W were improved from 4.4 to 2.8 in naive group and from 4.6 to 3.4 in switch group. [Conclusion] The clinical effect of CZP was seen in 4 weeks. CZP showed clinical efficacy in both patients without use of MTX and bio-switched patients.

W61-6

Analysis of Effectiveness of Bioshimilar Drug from CISA Data

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Conflict of interest: None

We analyzed the effectiveness of biosimilar drug by Kaplan Meier method to calculate the ratio of its administration continuity. Continuity rate of 77 cases of Infliximab-biosimilar (BS) on 300 was 68% while that was 58% in 294 cases of infliximab (INF), which was statistically significant. It was more clear when we compared in naïve cases (70% in BS vs 60% in INF). Among switch cases there is no significant differences in continuity rate between BS and INF. These results suggest that BS is as effective as INF.

W62-1

Anti-Suprabasin Antibody; novel antibodies contribute to the pathogenesis of neuropsychiatric systemic lupus erythematosus

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Conflict of interest: None

[Objectives] Neuropsychiatric systemic lupus erythematosus (NPSLE) is often difficult to diagnose and distinguish from those of other diseases, because no specific antibodies have yet been detected. **[Methods]** We identified immune complexes (ICs) of suprabasin (SBSN) in cerebrospinal fluid (CSF) of NPSLE by a novel proteomic strategy for identifying and profiling antigens. We analyzed total 129 patients (NPSLE=31, SLE=22, MS=30, NMO=26 and VM=20) of CSF for anti-SBSN antibodies using the luciferase immunoprecipitation system (LIPS) assay. We also evaluated the correlation of anti SBSN antibodies, clinical parameters and multiple cytokines. **[Results]** We found that the titer of anti-SBSN antibodies were significantly higher in CSF of NPSLE compared to that of SLE, MS and VM. According to the receiver operator characteristic (ROC) curves, we confirmed the area under the curve (AUC) was 0.78 and the sensitivity and specificity values at cut off points were 41.9% and 91.8%, respectively. Also, the titer of CSF anti SBSN antibodies was significantly correlated with CSF IL-10, IL-13, GM-CSF, IP-10 and MCP-1. **[Conclusions]** These findings indicate that SBSN could be a novel autoantibody for the evaluation of suspected NPSLE, and may help elucidate the pathogenesis underlying this disease.

W62-2

Usefulness of soluble PD-1 in patients with systemic lupus erythematosus

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Conflict of interest: None

[Objectives] Programmed cell death protein 1 (PD-1) is a immunosuppressive cell surface receptor and is expressed on T cells and pro-B cells. Soluble PD-1 (sPD-1), which is produced by the alternative splicing, can functionally block the regulatory effect of membrane-bound PD-1 on T cell activation. We aimed to retrospectively evaluate the usefulness of sPD-1 in patients with systemic lupus erythematosus (SLE). **[Methods]** We measured the levels of sPD-1 by ELISA in sera of patients with SLE (n = 59) and systemic sclerosis, and healthy controls, and compared them. We also analyzed the association between the levels of sPD-1 and clinical information in SLE patients. **[Results]** The levels of sPD-1 in SLE patients with SLEDAI-2K≥6 were significantly higher than those in SLE patients with SLEDAI-2K<6, systemic sclerosis patients, and healthy controls (p<0.05). In SLE patients, the levels of sPD-1 were moderately correlated with the titers of anti-dsDNA antibodies, levels of C3 and C4, and SLEDAI-2K. In addition, the levels of sPD-1 were significantly higher in SLE patients with arthritis, mucosal ulcers, fever, leucopenia, or anemia than those without (p<0.05). **[Conclusion]** The present study suggested that sPD-1 can serve as a new biomarker reflecting disease activity in SLE patients.

W62-3

Usefulness of soluble CD163 in patients with systemic lupus erythematosus-associated hemophagocytic syndrome: A retrospective study

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Conflict of interest: None

[Object] Extracellular portion of CD163 is shed into blood as a soluble form (sCD163) upon macrophage activation. We aimed to retrospectively study the usefulness of serum sCD163 in patients with autoimmune associated hemophagocytic syndrome (AAHS) associated with systemic lupus erythematosus (SLE). **[Methods]** The levels of sCD163 were measured in sera of SLE patients with AAHS (n=22), active SLE patients without AAHS (n=42), and healthy controls (n=68) by ELISA. Associations between sCD163 levels and clinical information were evaluated. We also compared the sCD163 levels in pre- and post-treatment sera of available patients with AAHS (n=17). **[Results]** Serum sCD163 levels in SLE patients with AAHS were significantly higher than those in SLE patients without AAHS, and healthy controls (p<0.05). SLE patients without AAHS also had significantly higher serum sCD163 levels than healthy controls (p<0.05). In SLE patients, serum sCD163 levels were moderately correlated with the titers of anti-dsDNA antibodies, levels of CH50, and SLEDAI-2K scores. In addition, serum sCD163 levels significantly decreased as disease was ameliorated following treatment in patients with AAHS (p<0.05). **[Conclusion]** The present study suggested that serum sCD163 can serve as a new biomarker for AAHS with SLE.

W62-4

Analysis of the involvement of CD26-negative T cell subsets in the pathophysiology of steroid-resistant systemic lupus erythematosus

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Conflict of interest: None

[Objectives] T cell costimulatory molecule CD26 is up-regulated following T cell activation, and the increased number of $CD26^+$ T cells has been detected in patients with autoimmune diseases including RA. Since the role of CD26 in the pathogenesis of SLE still remains to be elucidated, our objective is to characterize the CD26-positive or negative T cell subsets in SLE patients. [Methods] Human $CD4^+$ or $CD8^+$ T cells were purified from PBMCs of 50 SLE patients or 30 healthy adult volunteers. We examined the phenotypes of CD26-positive or negative subsets and explored the possibility whether these subsets were involved in the pathophysiology of SLE. [Results] In addition to $CD8^+CD26^{nega}$ T cells, $CD4^+CD26^{nega}$ T cells were also markedly increased in SLE patients, and these cells were $CD28^{nega}CD57^+Perforin^{hi}Granzyme\ B^+$ cytotoxic effector cells with high expression of both CD11a and CD11b. SLE patients with a large number of $CD4^+CD26^{nega}$ T cells are suggested to be resistant to steroid treatment, since it takes more than 24 months to reduce the daily dose of prednisolone to less than 10 mg after the initial treatment. [Conclusion] Our data strongly suggest that $CD4^+CD26^{nega}$ cytotoxic T cells may be involved in the pathophysiology of steroid-resistant SLE.

W62-5

Stimulator of interferon genes (STING) plays a crucial role in type-I IFN production induced by the sera from SLE patients

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Conflict of interest: None

[Background] Type-I interferon (IFN-I) plays important roles in the pathogenesis of SLE. It has been reported that serum IFN-I levels are high in active SLE patients and that IFN-I is produced when DNA sensors recognize DNA-containing immune complex. Stimulator of interferon genes (STING) is known as a key molecule in cytosolic DNA-sensing, which leads to IFN-I production. However, the involvement of STING in the pathogenesis of SLE has not been clarified. So we studied the role of STING in the production of IFN-I in SLE. [Methods] We evaluated both the IFN-I bioactivity in sera and the serum-mediated type-I IFN-inducing activity (IFN-I-IA) in SLE by using two different reporter cell lines. And we established the STING-deficient reporter cell lines (STING-KO) using the CRISPR/Cas9 system. [Results] IFN-I bioactivity was high in the sera from SLE compared with other autoimmune diseases and healthy controls. Serum-induced IFN-I-IA was also higher in SLE than those in other autoimmune diseases. And the enhanced IFN-I-IA in SLE was reduced in the STING-KO. [Conclusion] Our finding suggests that IFN-I bioactivity is high in the sera of SLE, and that these sera have a potential to induce IFN-I production through STING.

W62-6

Investigation of clinicopathological relationship of TCRαβ^{+}CD3^{+}CD4^{-}CD8^{-} (double negative) T cells and the features of renal pathology

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Conflict of interest: None

[Object] TCRαβ^{+}CD3^{+}CD4^{-}CD8^{-}(double negative) T cells which are known to specifically increase in ALPS. ALPS sometimes complicate autoimmune disease such as Evans syndrome and the SLE.DNT increases in patients with SLE, invades the kidney, and is known to be a new indication of the activity. [Methods] In 23 cases with SLE in October, 2015 from June, 2014, we measured DNT ratio by flow cytometry. The DNT ratio in all peripheral blood lymphocytes assumed the high level group more than 1.5% in reference to the diagnostic criteria of ALPS. [Results] Cases that had lighter glomerular lesion tended to be DNT high level group (66% vs. 6%, P= 0.008, Fisher's exact test), and cases that had high stromal lymphocytic infiltration tended to be DNT high level group (66% vs. 12%, P= 0.021). [Conclusions] In the guidelines, we determine a treatment strategy based on the ISN/RPS classification that is the classification of the glomerular lesion. In patients with SLE, DNT ratio helped the kidney pathologic finding particularly a glomerular lesion, and become the biomarker to treatment strategy.

W63-1

Initial dosage, Safety and Benefit of Hydroxychloroquine

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Conflict of interest: None

[Object] We examined the adverse events (AEs) and effect of skin lesion of HCQ. [Methods] We enrolled patients taking HCQ for SLE or CLE more than 3 months in our and related facilities from September 2015. We assessed skin lesion with CLASI at start of administration and after 3 month. We examined the serum biomarkesrs. [Results] We enrolled the 23 patients and in CLE were 2 cases, in SLE were 21 cases. HCQ dose was determined in 13 cases by ideal weight and in 10 cases by minimum. 43% cases had AEs, such as the new skin lesion in 3 cases, eye manifestation in 3 cases, pericarditis in 1 case and the others in 6 cases.3 cases eye manifestation appearing weren't indicated by ophthalmologist, 1 case stopped HCQ and eye manifestation in 2 cases disappeared for a few days without stopping. We needed glucocorticoid treatment only for pericarditis and other AEs improved by reducing or stopping HCQ. 72.7% patients improved skin lesion (change of CLASI-3.27±4.15) and 31.8% disappeared it.4casesreceived HCQ by ideal weight reduced HCQ dose due to AEs, but all cases improved skin lesion. 62.5% cases increased low complement and the other biomarkers didn't change. [Conclusions] HCQ had efficacy of skin lesion, but the AEs in half of them. We need to consider how dose is the best HCQ dose.

W63-2

The Effect of Hydroxychloroquine add-on in Patients with Systemic Lupus Erythematosus without Severe Organ Involvement

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Conflict of interest: None

OBJECTIVE: To evaluate the efficacy and safety of hydroxychloroquine (HCQ) add-on with systemic lupus erythematosus (SLE). METHODS: Laboratory data were evaluated for 49 SLE outpatient cases with HCQ in our hospital. RESULTS: Among the 49 SLE patients who were treated with HCQ, 33 patients (30 females, average age 43 years, median age of 6 years, lupus nephritis 10, NPLUPUS 8) were included in current analysis. The median of the treatment periods by HCQwas 332 days, the average of the HCQ dose was 4.0 mg/kg/day. The erythrocyte sedimentation rate (ESR) before administration, three months after, six months after administration were 20.50 mm/h [7.75 - 36.25], 11.50 [5.00 - 31.25], 12.00 [5.00 - 32.5], and urinary protein were 0.096 g/day (g / gCr) [0.048-0.16], 0.084 [0-0.28] each. Among the patients with urine protein more than 0.3 g/day, urinary protein were 1.066 [0.32-1.84], 0.3173 [0.31-0.59], 0 [0-0.4] respectively. Moreover, in the patients with low complement C3 level before HCQ administration, the median of C3 before, three months after, six after were 64 mg/dl [56-78], 68.8 [63-76], 76.50 [64 - 84] each. CONCLUSION: It was suggested that HCQ add-on might have beneficial effects even to the SLE patients without severe organ involvement.

W63-3

Evaluation of the correlation between clinical phenotype and the bio-markers in SLE

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Conflict of interest: None

【Object】Evaluation of the correlation between clinical phenotype and the bio-markers in SLE.【Methods】We classified SLE patients who admitted from April 1 2014 to October 1 2015 into three groups, lupus nephritis (LN), neuropsychiatric SLE (NPSLE) and non-serious diseases (NSD) and investigated the correlation between clinical phenotype and the bio-markers among three groups.【Results】In this term, we treated 20 active SLE patients, including 4 NPSLE, 5 LN, 8 NSD and others. In NPSLE, we couldn't find any correlations between conditions and markers. In LN and NSD, complement, one of bio-marker, indicated disease activity, but the change of leukocyte and lymphocyte counts were shown in the different manner, that suggested the late response to the treatment in LN patients.【DISCUSSION】Bio-markers can't indicate disease activity or effect of therapy in NPSLE. In LN, the improvement of leukocyte and lymphocyte count was delayed after initial therapy compared with NSD. This suggests that LN, with more intensive therapy, are probably resistant to initial therapy. We need to discuss in more cases.【Conclusions】We report our investigation of the correlation between clinical phenotype and the bio-markers in SLE.

W63-4

Mycophenolate mofetil therapy for two cases of antiphospholipid antibody-associated chorea

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Conflict of interest: None

Chorea is a hyperkinetic movement disorder characterized by rapid flowing and chaotic movement of one or more portion of the body. That could occur by autoimmune mechanism. Symptomatic therapy with dopamine antagonists is usually effective, and glucocorticoids in combination with immunosuppressive agents (e.g. azathioprine and cyclophosphamide) may be useful. We did not know the efficacy of mycophenolate mofetil (MMF) therapy for this condition. Here we reported two cases antiphospholipid antibody (aPL)-associated chorea could be cured by MMF. Measurement of aPL could help management of chorea patients. Our report provides new therapeutic approach for MMF`s beneficial effects on aPL-associated chorea.

W63-5

Two cases of systemic lupus erythematosus retinopathy with rapid progressive visual impairment treated with multiple immunosuppressants

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Conflict of interest: None

Case 1, a 16-year-old man was admitted to our hospital due to sudden decrease of visual acuity (VA) in his left eye. He was diagnosed with SLE because of malar rashes, alopecia, leukopenia and hypocomplementemia. Fundus examination showed bilateral cotton wool spots and retinal artery occlusions. After the treatment with mPSL pulse, IVCY and RTX, his VA improved (from right 0.6 and left 0.3 at admission to right 1.2 and left 0.7). Case 2, a 21-year-old woman was diagnosed as SLE on the basis of malar rashes, oral ulcer, leukopenia and positive test for anti-ds-DNA antibody and anti-phospholipid antibody. Two months later, she presented with abnormal sensation of her fingers, consciousness disorder and visual impairment. NP-SLE was diagnosed and the ophthalmological examination showed severe ischemic retinopathy in her bilateral eyes. In spite of the intensive therapies such as mPSL pulse, IVCY, plasmapheresis and RTX, there was no VA improvement (right 0.01 and left counting fingers). The incidence of retinal lesions is 7-26% of SLE patients and it is characterized by a wide variety of visual outcomes. It is suggested that SLE retinopathy is significantly associated with renal or CNS involvement, therefore critical important both visually and prognositically.

W63-6

Clinical features of systemic lupus erythematosus occurring during anti-TNF therapy

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Conflict of interest: None

Case1. A 48-year-old woman treated with infliximab for Crohn's disease suffered from alveolar hemorrhage, facial erythema, oral ulcers, alopecia, and serositis. Case2. A 66-year-old woman treated with golimumab for RA developed marked swelling in her lower legs with proteinuria and a high fever. Skin biopsy suggested lupus panniculitis. Case3. A 66-year-old woman treated with inflixmab for RA developed cytopenia and serositis. These three cases showed positive ANA and anti-double strand (ds) DNA antibodies and were diagnosed with SLE, followed by an immunosuppressive therapy based on oral prednisolone. We reviewed 13 cases of SLE diagnosed during TNF-α inhibitor therapy reported from Japan. The mean age was 53.31 (±14.2) years old, and male-to female ratio was 4:9. Underlying diseases were RA (10 patients), Crohn's disease (2 patients), and psoriasis vulgaris (one patient). ANA and anti-ds DNA antibodies were positive in all cases except two undocumented cases. Six patients showed serositis and three patients developed biopsy-proven lupus nephritis. Neuropsychiatric SLE, hemophagocytosis, and alveolar hemorrhage was reported in by one. Most cases required immunosuppressive therapy.

W64-1

Short-term result of reverse shoulder arthroplasty for patients with rheumatoid arthritis

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Conflict of interest: None

[Purpose] Reverse shoulder arthroplasty (RSA) was invented for patients with cuff tear arthropathy (CTA) and its clinical results showed excellent functional outcome. On the other hand, outcomes of RSA in patients with rheumatoid arthritis (RA) are reported in just several papers so far. Therefore, our purpose is to investigate short-term result of RSA in patients with RA. [Methods] We performed RSA in 15 rheumatic shoulders, which had joint destruction and rotator cuff tear from July 2014 to October 2016. We compared range of motion, constant score and shoulder 36 between pre- and post-operative situation. The morphology of destruction and prevalence of notch, post-operative fractures were evaluated with X-ray. [Results] Range of motion was improved from 80.7 to 118.8 degree in flexion and from 69.3 to 112.7 degree in abduction. External rotation was decreased from 26.0 to 10.6 degree. Constant score was improved from 28.2 to 53.5 and shoulder 36 increased from 7.9 to 11.2 as well. There were no dislocation, infection and loosening of the prosthesis. Only 2 cases had scapular notching. [Conclusion] RSA is one of the effective treatment methods for rheumatic shoulders, which have joint destruction and rotator cuff, tear as long as we are careful in bone fragility.

W64-2

The evaluation of total elbow arthroplasty for the patients with rheumatoid arthritis under 50 years old

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Conflict of interest: None

[Object] We evaluated the clinical outcomes of unlinked TEA for the patients with RA less than 50-years old. [Patients and method] Records of 17 women (20 elbows) aged 35 to 49 (mean, 46.0) years who underwent alumina ceramic TEA for RA were reviewed. The mean follow-up period was 11.2 (range, 3 to 22) years. Functional outcomes were assessed by range of motion (ROM), Japan Orthopedic Association Elbow Score (JOA score; 0-100), and modified version of the Mayo Elbow Performance Score (MEPS; 0-100 points). [Results] The TEA with SKC-1 prostheses were performed in 9 patients, and with the JACE prostheses in 11 elbows. The mean preoperative ROM in extension and flexion were -40.6 degrees and 108.5 degrees, respectively. The mean preoperative JOA score and MEPS were 46.9 points and 39 points, respectively. The mean postoperative ROM in extension and flexion were -16.3 degrees and 142.4 degrees, respectively. The mean postoperative JOA score and MEPS were 91.7 points and 95 points, respectively. The ROM, JOA score, and MEPS improved significantly. The implant loosening and dislocation were not identified. Two elbows required ulnar nerve neurolysis. [Conclusion] The results of unlinked alumina ceramic TEA for the patients with RA less than 50 years-old were satisfactory.

W64-3

Relationship between Larsen grade and MEPS score of RA patients underwent TEA

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Conflict of interest: None

OBJECTIVE: Total elbow arthroplasty (TEA) is an effective treatment for elbow arthrosis caused by RA. We aimed to clarify the relationship between grade of Larsen classification used as an indicator of joint destruction and the result after TEA surgery. **METHODS**: From June 1998 to June 2016, we investigated the records of 71 patients with data available among 95 patients who underwent TEA at our hospital and compared the preoperative and postoperative Mayo Elbow Performance Score (MEPS) and MEPS improvement values were compared. **RESULTS**: The average age is 64.5 years. In Larsen Grade (LG), LG 2 was 5 (6.7%), LG 3 was 12 (16.9%), LG 4 was 33 (46.5%) and LG 5 was 21 (30%). In the nonparametric correlation analysis (Spearman's rank sum correlation coefficient), weak correlation is observed between LG and MEPS improvement but there was no statistical significant. However modarate correlation was observed between MEPS improvement and

preoperative MEPS, furthermore, statistically significant. **Conclusion**: We suggest that improvement of elbow function by TEA is promising for RA patients with high LG and lower preoperative MEPS.

W64-4

Effects of Total Elbow Arthroplasty in Rheumatoid Arthritis Treated with Biologics on Disease Activity and Functional Disability

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Conflict of interest: Yes

[Objective] We examined the effect of Total Elbow Arthroplasty (TEA) in RA patients treated with biologics on the post-operational disease activities and functional disability. [Method] Subjects are 23 joints of biologically treated RA cases during the period of 2006 – 2014 that TEA was done in this hospital. They were ETN14, TCZ4, ADA2, IFX2 and ABT1. Disease activities were evaluated by CDAI, the functional disability was evaluated by the pre/post-operation HAQ, MEPS and PREE. [Results] Mean age and disease duration was 63.5 years old and 25.8 years. CDAI after TEA showed significant improvements improving from 12.9 to 6.7. Range of motion also improved significantly. PREE of 73.1 before TEA significantly improved to 16.4. HAQ-DI also showed significant improvement from 2.0 to 0.5. HAQ improved, not only in the upper limb functional items, but also in lower limb function. MEPS also improved significantly from 45.0 to 98.1. [Conclusion] TEA provided the bearing properties and good joint range of motion, and improved the upper limb functions. Also, for RA patients, the elbow joint is load-supporting joint, and TEA was effective to acquire lower limb functions. It was suggested that combined treatment with medical and surgical therapy enabled to acquire better ADL.

W64-5

Patient-Rated Elbow Evaluation (PREE) and other clinical parameters in patients with rheumatoid arthritis by total elbow arthroplasty

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Conflict of interest: None

[Objectives] We aimed to investigate the correlation between PREE and other clinical parameters in rheumatoid patients treated by TEA. [Methods] 43 elbows of 39 rheumatoid patients who underwent TEA were included in this study. The mean age of patients was 61 years, and the average follow-up period was 22 months. The clinical evaluations included DAS28-CRP, elbow and shoulder range of motion, Grip strength, the scoring system of Japanese Orthopedic Association elbow scoring system (JOA), MEPS, PREE, DASH, Hand20, and HAQ-DI pre-and post-operatively. Statistical analysis was performed using Wilcoxon matched-pairs test and Spearman's correlation coefficients. [Results] PREE significantly correlated with DASH and Hand20. Correlation between PREE and both JOA and MEPS was significant preoperatively, but not significant postoperatively. Grip strength significantly correlated with DASH, Hand20 and PREE, but no correlation was found between the shoulder ROM and the same score. [Conclusion] PREE may not only reflect the elbow joint simply but also the whole function of upper extremity, and may not correlate with the objective evaluation. Grip strength may be related to the subjective evaluation of upper limbs, and it should be considered when evaluating upper limb function using PREE.

W64-6

Clinical result of upper limb surgery for RA patients using biologics treatment

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Conflict of interest: None

【Objectves】We examined cases in which surgery was performed on joints of upper limbs (elbow joint, wrist joint, fingers) in RA patients who are using biological treatments.【Methods】There were 45 cases of RA patients (male 3 · female 42) with 80 surgical procedures, average age at surgery 57.7 years (21-76), biological agents in use were Etanercept 28cases, Infliximab 6cases, Tocilizumab 9 cases, etc. The surgical site consists 12 elbow joints (15 joints), 17 joint hand joints (17 joints), 18 thumb fingers (CM 3, MP 15, IP 7 joints), 25 fingers (MP 107, PIP 14 joints). The surgical cases were examined for the presence or absence of postoperative complications and changes in clinical course.【Results】In 2 patients using Etanercept, relapse of RA activity occurred during withdrawal. Postoperative infection was confirmed in 2 joints as a complication. In cases where synovectomy was performed, all local symptoms disappeared, and disease activity was also improved. Patients who underwent reconstruction for finger deformation / dysfunction improved overall appearance and function, resulting in high patient satisfaction.【Conclusions】Upper limb surgical therapy in RA patients with biological treatment seems to be useful for further improving drug effect and QOL.

W65-1

Clinical manifestation and DMARDs therapy after MTX-LPD in patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] The purpose of this study is to evaluate the clinical manifestation and DMARDs therapy after MTX-LPD in patients with rheumatoid arthritis [Methods] We investigated 33RA patients complicated MTX-LPD and invastigated items ware pre-medicated DMARDs before diagnosis of MTX-LPD, cellular type of MTX-LPD, chemotherapy, prognosis of these patients and post-medicated DMARDs after MTX-LPD therapy. [Results] Pre-medicated DMARDs of 33 patients were 23 MTX, 5 other cs-DMARD (BUC2, TAC2, SSZ1). 15Biologics user were IFX5, GLM4, ADA2, ETN2, ABT2 combined with MTX. Cellular type of 21patients were DLBCL. 10 patients were underwent R-CHOP chemotherapy and 22 patiets is not underwent. 1 patinets was deceased, and the others is alive. Post-medicated DMARDs after ML therapy were [Conclusion] The prognosis of MLandMTX-LPD is gettingbetter, but the selection of post-medicated DMARDs after ML is difficult and no evidense.

W65-2

The analysis of 23 cases of methotrexate-related lymphoproliferative disease

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Conflict of interest: None

<Objective> Lymphoproliferative diseases (LPD) occasionally de-

velops in patients treated with methotrexate (MTX). We examined 23 cases of MTX-LPD in patients with rheumatoid arthritis to clarify features of MTX-LPD. <Methods> From April 2006 to October 2016, 23 patients who visited our hospital were analyzed the clinical data retrospectively from medical records. <Result> The average age at the diagnosis of LPD was 72.2 years. A male: female ratio was 10: 13, and the MTX dose and duration were 8mg/week. 5 patients were treated with only MTX, and 8 patients with corticosteroids, 5 patients with biologics. 12 cases were DLBCL, and 4 were Hodgkin's lymphoma. 10 patients obtained CR after discontinuation of MTX, and 13 treated with chemotherapy. The levels of sIL-2R were significantly higher in patients who treated with chemotherapy compared with no chemotherapy. After onset of LPD, 12 patients were treated with corticosteroids, and 1 with biologics, 1 with MTX. <Conclusion> We suggest that the levels of sIL-2R were associated with prognosis of MTX-LPD.

W65-3

Clinical significance of pathological findings and EBV infection with MTX-related Lymphoproliferative disorder in RA patients

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Conflict of interest: None

MTX-associated lymphoproliferative disorders (MTX-LPD) were wide-spread clinical entity. The evaluation of histological findings and the presence of EBV infection of atypical cells were important. EBV+ mucocutaneous ulcer (EBV-MCU) is subcategorized in 2016 revised WHO classification related with aging and immunosuppressive state such as MTX. We retrospectively investigated 43 RA patients with MTX-LPD (medium age: 67 years-old, MTX duration: 6.6 years, dose: 8.5 mg/w). Positive EBV was determined EBER-ISH and LMP-1 staining of biopsy specimens. MCU-LPD with oral cavity or pharynx was seen in 14 RA patients (polymorphic B-cell 8, DLBCL 6 cases) with 71% positive EBV. DLBCL was diagnosed as 15 patients (nodal 8, extra-nodal 7) with 31% positive EBV. Among 14 MUC-LPD patients, 5 were regression by only withdrawal MTX and 4 were added Rituximab monotherapy for residual LPD. Four patients were dead caused by LPD, including 3 with complicated hemophagocytic syndrome. After regression of LPD, 17 were treated by biologics for increased RA activity. The therapeutic strategy was varied by histopathological diagnosis and positive EBV. In particular, EBV-MCU is self-limited distinct entity and these patients can achieve spontaneous regression by only withdrawal MTX.

W65-4

The clinical analysis of regressive LPDs in methotrexate associated lymphoproliferative disorder

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Conflict of interest: None

Purpose; To investigate the clinical analysis of the regressive MTX-LPD. **Methods:** Data were retrospectively collected from 62 patients with MTX-LPD in our institution. **Results:** The underlying diseases of 62 patients were RA (N=59), psoriasis vulgaris (N = 1), SLE (N = 1), and dermatomyositis (N = 1). The median durations of MTX were 5.2 years. LPD subtypes were 26 of DLBCL, 10 of HL, 9 of LPD, 4 of follicular lymphoma, 3 of Hodgkin like lymphoma, and 5 of others. The 5-year and 10-year overall survival of all patients were 81.9% and 59.6%, respectively. The patient number of the regressive LPDs was 42. Among those patients, 24 patients kept complete response (Regressive:R group), whereas 18 patients indicated relapsed/regrowth (RR group). Focusing on LPD phenotypes in both groups, DLBCL and LPD were main LPDs in R group, although 9 of 18 patients were HL in RR group. The median duration from the time of LPD diagnosis to the time of relapsed/regrowth was 10.6 months (0.7-35.6). Seven of 18 patients were dead, and 5 were HL. **Conclusion:** It was notable that the relapsed ratio was high in HL, whereas the relapsed/regrowth incidence in DLBCL and LPD was low. Based on our data, it is suggested the attention to the LPD subtypes is important to the clinical management of MTX-LPD.

W65-5

Methotrexate-related lymphoproliferative disease

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Conflict of interest: None

Objective After introduction of methotrexate (MTX) in 2001 as a first-line drug for rheumatoid arthritis (RA), its use has increased, with MTX-related lymphoproliferative disease an important adverse event. We examined 13 cases treated at our hospital. Results From 2006-2013, 13 LPD patients (5 males, 8 females) with an RA history were treated at our hospital, each of whom had a history of MTX use before LPD diagnosis. Mean age at diagnosis was 67.3 years and mean duration of RA was 31.9 years. Pathological tissue type was DLBCL in 6, CHL in 2, PTCL in 1, and polymorphic LPD in 4, while 5 of 11 tested were positive for EBER-ISH. In 7 patients who remitted following MTX withdrawal only, recurrence was confirmed in 1. Seven underwent chemotherapy, of whom 3 obtained remission, 3 died, and 1 is currently receiving treatment. Discussion and Conclusion Although RA itself can increase the risk of LPD, time to onset of LPD is known to be shortened by use of MTX. Furthermore, LPD development has been shown related to biological preparations, with use of those increasing in recent years. For RA patients using MTX or biologics, careful follow-up examinations with LPD onset in mind are necessary.

W65-6

Can we discover the onset of the iatrogenic immunodeficiency-related lymphoproliferative disorder (LPD) early with monitoring the sIL-2R of rheumatoid arthritis (RA) patients ?

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Conflict of interest: None

[Purpose] 23 RA patients had developed LPD between 2008 and 2016 in our hospital. The sIL-2R has been recognized as tumor marker of ML. In this study, we had selected the sIL-2R as the bio marker for developing LPD. [Object] As nonLPD group, 255 RA patients (65males, 220females) that measured the sIL2-R were selected from 405 RA patients without developing LPD. The average age of them was 67.6y.o (±12.5) and the average period of RA duration is 13.1 years (±11.7). In LPD group, 17 patients (1male, 17females) were selected except four with the data loss. The average age of them was 70.3y.o (±9.6) and the average period of RA duration was 20.6y (±13.3).16 cases had taken MTX. The average period of suffering MTX was 9.2y (±5.4).8 cases were administrated bDMARDs. 1 case was administrated csDMARDs only [Method] The duration, sIL-2R and LDH were assessed between LPD group and nonLPD group. [Result] The duration of RA in LPD group was significantly high compared with nonLPD ($p \leq 0.05$). The average of sIL2-R in LPD was 2044 (± 2518) and in nonLPD was 489 (± 245). The average of LDH in LPD was 354 (±262) and in nonLPD was 195 (±41). There is significantly difference in two groups ($p \leq 0.01$). [Conclusion] The sIL2-R and LDH may discover the onset of LPD early when RA patient caused abnormality.

W66-1

The effects of switching daily teriparatide to denosumab on the spine and femoral strength assessed by finite element analysis of clinical computed tomography in patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] To evaluate the quantitative effects in RA patients who are treated with desnosumab for 12 months after TPTD therapy. [Methods] 14 RA patients who were receiving TPTD for 24 months to switch to denosumab for 12 months evaluated according to changes in two bone turnover markers (P1NP, TRACP-5b). They are assessed according to bone mineral density (BMD) by dual x-ray absorptiometry (DXA) and bone strength by quantitative computed tomography (CT) at baseline. They were reevaluated after 12 months. Nonlinear finite element analysis (FEA) was performed on the CT scans to compute an estimate of spinal and femoral predicted bone strength (PBS) by FEA. [Results] Patients were aged 72.4 years, mean 28-joint Disease Activity Score, 3.0±0.8. PINP and TRACP-5b were significantly decreased from baseline. On average, BMD-spine (baseline and 12 months) was 0.99, 1.03 g/cm^2($p<0.01$) (median change 4.3%), BMD-femoral neck was 0.66, 0.67 g/cm^2($p<0.01$) (median change 8.8%), PBS-spine was 3789, 3579 N ($p<0.01$) (mean change -6.0%), and femoral PBS was 33558, 3554 N ($p=0.3$) (mean change -1.1%). [Conclusions] Our results provide that denosumab can increase BMD on RA patients. On the other hand, there were difference between BMD and FEA. We will have to follow these effects in longer term.

W66-2

Effects of Once a Week Administration of the New Synthetic Product of 1-34 Teriparatide on Glucocorticoid-Induced Osteoporosis

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Conflict of interest: None

[Object] To clarify the effect of weekly teriparatide (56.5ug, wTPTD) and bisphosphonates (BIS) on vertebral fractures (vFx) in Glucocorticoid-Induced Osteoporosis (GIO). [Methods] A oneyear cohort study recruiting 172 patients (148 women) with GIO. Means of age, disease duration, total prednisolone (PSL) dosages, and daily PSL dosages (dPSL) of the subjects were 64+/-15 (yo,+/), 11+/-11 (y), 25+/-29 (g), and 6.7+/-5.9 (mg/day), respectively. vFx were defined from Xray films with the SQ method. Lumbar BMD were measured with Lunar 3030 (GE). Prevalent vFx were seen in 170 (46%) patients. [Results] 1)The BMD was showed no difference between treatment groups at the base line. The dPSL was significantly higher ($p<0.03$) in the group of wTPTD than in the group of BIS (11.66.1, respectively). 2) Incident vertebral fractures were observed in 24 (BIS16%), 1 (wTPT4.5%). 3) A multivariate logistic regression analysis revealed that statistically significant factors for incident fractures were wTPTD (vs BIS, 0.12, 0.03-0.45), prevalent fractures (2.72, 1.03-7.24), daily PSL (1.02, 1.00-1.03), BMD (OR; 0.95, 95%CI; 0.910.99). [Conclusions] wTPTD might be more effective than BIS for prevention of osteoporotic vFx in GIO.

W66-3

The prevalence of renal deterioration after anti-osteoporosis medication

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Conflict of interest: None

[Objectives] Since kidney dysfunction is associated with an increased risk for hip fracture, of renal function deterioration should be avoided to treat osteoporosis. The aim of this study is to clarify the prevalence of decrease in eGFR occurred after anti-osteoporosis medication. [Methods] Anti-osteoporosis drugs and eGFR data of out-patients between April 2011 and December 2014 were extracted from electronic medical record. The % changes in eGFR from just before newly medication to 2 weeks - 6 months later were calculated and the prevalence of kidney function deterioration that is defined as decrease in eGFR of 20% and more. [Results] The changed in eGFR around 906 newly medications in 245 patients (primary osteoporosis 140, osteomalacia 8, rheumatoid arthritis 92, spondyloarthritis 5) were investigated. Renal deterioration were observed in 21.1% after alphacalcidol 1.0μg/day and in 9.5 – 12% after weekly alendronate *Menatetrenone, iv* alendronate, daily and weekly teriparatide, eldecalcitol. Raloxifene had only one drug without renal function deterioration. [Conclusion] The decrease in eGFR of 20% and more is often occurred after anti-osteoporosis medications except for raloxifen. Strict monitoring of renal function is required to treat osteopososis.

W66-4

Risk factors for bone loss in patients with rheumatoid arthritis treated with or without biologics over 12 months

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Conflict of interest: None

【Objective】We examined the risk factors for bone loss in RA patients with or without biologics (bio) whose onset of RA was after approval of bio in Japan.【Methods】94 patients were treated with bio and 64 patients were without bio. We examined age, sex, disease duration, BMI, average dose of methylprednisolone, the duration of bio use, the use of anti-osteoporosis drugs, changes in CRP, and DAS28-CRP.【Results】The BMD of the lumbar spine increased over 12-months in the patients with bio (median: 0.006 g/cm2) and without bio (median: 0.004 g/cm2). The BMD of the femoral neck decreased in the patients with bio (-0.004 g/cm2) and without bio (-0.007 g/cm2). There were no statistical differences. Multiple logistic regression analysis showed that the risk factors for bone loss in the lumbar spine was lack of anti-osteoporosis drug use in the patients with bio whereas low BMI without bio. The risk factors for bone loss in the femoral neck was low BMI, lack of anti-osteoporosis drug use, and the usage of high dose methylprednisolone in the patients with bio whereas long duration of disease without bios.【Conclusion】These findings suggest that patients with RA who possess these risk factors should be considered for earlier and more aggressive treatments to prevent bone loss.

W66-5

Factors that affect on raise of bone mineral density for rheumatoid arthritis patient

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Conflict of interest: None

[Objective] Factors that affect influence on bone mineral density (BMD) in osteoporosis (OP) treatment for rheumatoid arthritis (RA) were evaluated statistically. [Methods] 180 RA patients who have been treated consecutively for more than 1 year were recruited in this study. In these, 13 were male, and 167 were female, and 44 were thrown glucocorticoid (GC). Average age was 72.9. Their gain of minimum %YAM value in lumbar spine (L-S) and %YAM of greater trochanter (GT) were evaluated statistically with Linear Regression Analysis (LRA) and Binary Logistic Regression Analysis (BLR) for sex, age, GC, drug, thrown term (term),

order, %YAM value, P1NP, TRACP-5b, serum calcium (Ca), DAS28-CRP, SHS, mHAQ. Statistical significance was set as below than 5%. [Results] For LRA, use of teriparatide (TPTD), use of denosumab (d-mab), and %YAM demonstrated significant correlation with L-S, and TPTD, d-mab, %YAM, and Ca were picked up with BLR for %YAM gain in L-S. With GT, only d-mab demonstrated significant correlation for BLR, while d-mab, DAS28-CRP, mHAQ demonstrated significant regression with %YAM gain. [Conclusions] In traeting OP for RA patient, fundamental condition, BMD status, and choice of drug must be considered.

W66-6

Clinical evaluation of BMD and TBS for GIO patients

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Conflict of interest: None

Glucocorticoid (GC) therapy leads to an increase in fracture risk. We performed retrospective study to clarify the effects of alendronate or alfacalcidol on the change in the trabecular bone score (TBS) of the lumbar spine. Patients were 118 patients receving high-dose GC therapy and the mean initial daily GC dose of predonisolone was 27.9 ± 7.1 mg/day. Although the bone mineral density (BMD) of the lumbar spine continued to significantly decrease for 12 months in the alfacalcidol group, BMD increased above the baseline level at 3 and 6 months in the alendronate group. TBS was significantly decreased at 9and 12 months in the alfacalcidol group. There were no significant differences in TBS between the alfacalcidol and alendronate groups for 12 months. In conclusion, TBS at lumbar spine in patients treated with GC was able to detect bone structure changes earlier than BMD.

W67-1

Influence of oral prednisolone on effect of denosumab on osteoporosis in patients with Japanese rheumatoid arthritis ~a Multicenter Registry Study~

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Conflict of interest: None

[Objectives] We investigated the influence of oral prednisolone on the efficacy of DMB in OP patients with Japanese RA. [Methods] The final study cohort of 63 patients received continuous DMB therapy more than 24 months from Tsurumai Biologics Communication Registry (TB-CR-BONE). We reviewed the results for 12 and 24 months about the increase and decrease of bone mineral density (BMD) of lumbar spine (LS) and total hip (TH) by DEXA and bone turnover markers, PINP and TRACP-5b. [Results] In the patients receiving oral prednisolone group (n=23, group GC+) and not receiving group (n=40, group GC-), the mean age was 69.8 and 71.0 years old (p=0.622); disease duration was 16.0 and 15.7 years (p=0.592). The rate of decreased PINP and TRAC-5b from baseline to 12 and 24 months were each -8.0% vs -42.6%(p=0.031), -13.8% vs -33.8%(p=0.134) and -22.0% vs -35.1%(p=0.229), -20.6% vs -27.3%(p=0.945) in the group GC+ vs GC-. The rate of increased LS-BMD and TH-BMD from baseline to 12 and 24 months were each 5.3% vs 7.0%(p=0.361), 10.0% vs 7.7%(p=0.104) and 1.4% vs 3.8%(p=0.804), 5.7% vs 4.3%(p=0.945) in the group GC+ vs GC-. [Conclusion] DMB was effective in OP of RA patients. Oral prednisolone use did not influence the efficacy of DMB in the period of 24 months.

W67-2

Therapeutic effect of denosumab and teriparatide for steroid-induced osteoporosis that exhibit resistance to bisphosphonates

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Conflict of interest: None

【Purpose】Although bisphosphonates (BP) has been used as a first-line drug for steroid-induced osteoporosis, there are some cases with insufficient response. In such cases, denosumab (DMAB) or teriparatide (TRPD) can be alternatives to BP, but there have been no reports comparing the effects of these agents so far. We compared the effects of DMAB and TPTD on bone mineral density in patients who had been resistant to BP.【Method】Thirty patients with steroid-induced osteoporosis whose %YAM in lumbar spine and femur less than 70% were examined. They had been taking BP for more than 2 years and prednisolone 5 mg / day for more than 3 months. BP was switched to DMAB (19 cases) or TRPD (11 cases), and the changes of the %YAM before and after 54 weeks were determined.【Results】The mean baseline %YAM of DMAB and TPTD groups were not significantly different (lumbar spine, 71.2% vs. 67.5%･femur, 63.6% vs. 60.6%). There was also no difference in age, BMI, or steroid dose between the two groups. The rate of change of %YAM after 54 weeks tended to increase in TPTD group as compared with DMAB group in lumbar spine (2.8% vs. 6.8%) and in femur (0% vs 2.4%).【Conclusion】It was suggested that TPTD could be a better alternative in patients with steroid-induced osteoporosis resistant to BP.

W67-3

Use of corticosteroid decreases the effect of denosumab for the treatment of osteoporosis

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Conflict of interest: None

Purpose: The aim of this study was to identify risk factors for non-responder of treatment by denosumab (DMAb) for osteoporosis. Subject and Methods: Site specific (lumbar, total hip, neck and trochanter) bone mineral densities (BMDs) from 49 osteoporotic subjects including 27 rheumatoid arthritis (RA) patients for one year were available. We evaluated the effects of age, body mass index (BMI), use of prednisone (PSL), previous treatment for osteoporosis, BMD at baseline, bone metabolic markers (BAP, uNTX), serum Ca and P levels and previous vertebral fracture for no response to DMAb (patients did not reach the 2% increase in lumbar or the 4% increase in hip BMD). Results: Dose of PSL was significantly high in non-responder at non-RA trochanter and RA lumbar BMD (p=0.043, 0.011). BAP was higher in non-responder at RA lumbar BMD (p=0.021). Urinary NTX was significantly low in non-responder at RA lumbar and trochanter BMD (p=0.02, 0.005). Multivariate regression analysis including age, BMI, dose of PSL, BMD at baseline, BAP, uNTX, Ca and P level as confounders revealed that dose of PSL was the significant risk factors for no-response in RA patients at lumbar BMD (p=0.006). Conclusion: The use of PSL acted against DMAb treatment.

W67-4

Efficacy of denosumab in steroid-induced osteoporosis against insufficient effect by bisphosphonate

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Conflict of interest: Yes

<Objectives> Although it's reccomended by bisphosphonate against treatment of steroid-induced osteoporosis, there is insufficient case treated by bisphosphonate. We administered denosumab to patients with steroid-induced osteoporosis against insufficient effect by bisphosphonate, and the efficacy of denosumab were prospectively investigated. <Materials and Methods> We enrolled 30 patients of steroid-induced osteoporosis against insufficient effect by bisphosphonate; female 29, male 1, mean

age was 68.4years old. Patients were 13 of rheumatoid arthritis, 6 of sysytemic erytematosus, 3 of dermatomyositis, 8 of others. Mean dose of prednisolone was7.01mg. Previous treatments were 12 of risedronate, 10 of minodronate, 8 of alendronate. The changes in bone mineral density (BMD) and bone turnover markers were investigated at 24 and 52 weeks. <Rsults> BMD of the frontal lumbar spine and right femur significantly increased after treated to 52 weeks, but lateral lumber spine and left femur do not significant. The values of TRACP-5b and BAP significantly decreased after treated to 52 weeks. There were no patients with a incident fracture and adverse events. <Conclusions> Denosumab was effective by steroid-induced osteoporosis against insufficient effect by bisphosphonate.

W67-5

The efficacy of 2-years denosumab treatment for glucocorticoid-induced osteoporosis (GIO)

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Conflict of interest: None

[Purpose] Osteoporosis is one of important adverse effects in the glucocorticoids treatment for the patients with rheumatoid arthritis (RA) and connective tissue diseases (CTD). Although the efficacy of denosmab for primary osteoporosis has been well-established, the efficacy for GIO remains unclear. This study aimed to clarify the therapeutic effects of denosumab for GIO. [Methods] We evaluated bone mineral density (BMD) and serum markers of bone metabolism of patients who had been treated with over 5mg of predonisolone for RA and CTD, and denosumab for GIO, for two years in Kobe University Hospital. [Results] Number of the patients were 53 (male: 4 cases, female; 49 cases), and their characteristics at the beginning of denosumab treatment were as below; age: 64.19±12.0 years old, dose of prednisolon: 10.59±9.97mg/day, lumber BMD: 0.768±0.112g/cm^3, lumber T-score: -2.28±1.01, hip BMD: 0.540±0.085g/cm^3, hip T-score: -2.28±0.76. Lumber and hip T-scores were significantly increased with 2-years denosumab treatment. In addition, the serum markers of bone metabolism, both absorption and formation, were significantly suppressed with denosumab. [Conclusion] Denosumab can suppress bone metabolic turnover, and increase lumber and hip T-scores of GIO patients.

W67-6

The predictors for 24 months efficacy of denosumab, an anti-RANKL antibody, on osteoporosis in patients with rheumatoid arthritis from multicenter study (TBCR-BONE)

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Conflict of interest: Yes

[Objectives] To investugate predictors of 24 months efficacy of denosumab (DMB) on opteoporosis in RA (RA-OP). [Methods] 59 female RA-OP were included. BMD of lumbar spine (LSBMD) and total hip (THBMD) and bone turnover markers (BTMs) were measured at every 6 month. Spearman's rank correlation coefficient was calculated between %increase of BMD at 24 months and various data (baseline characteristics, parameters of RA disease activity and BTMs. Time averaged data (ta-data) which was averaged data at every 6 month was utilized for analysis. [Results] Mean age 59 yo. Mean RA duration 16y. Concomitant PSL 33.9%. 26% had the past history of fracture. %increase of LSBMD at every 6 month was significantly increased (4.7-6.7-7.7-8.3). %increase of THBMD was also significantly increased (2.9-3.3-4.9-4.9). Parameters correlated with %increase of LSBMD at 24 months were %increase of LSBMD at 6 months, baseline P1NP and ta-%decrease of TRACP-5b. Parameters correlated with %increase of THBMD at 24 months were %increase of LSBMD at 6 months, %increase of THBMD at 6 months, ta-%decrease of P1NP, baseline TRACP-5b and ta-%decrease of TRACP-5b. [Conclusion] Early response of BMD, baseline values of BTMs and response of BTMs were suggested to be the predictors of the efficacy of DMB in RA-OP.

W68-1

Cytomegalovirus infections after treatments for rheumatic diseases

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Conflict of interest: None

[Objective] To reveal risk factors of cytomegalovirus (CMV) infections. [Methods] We examined rheumatic diseases patinets with positive CMV antigenemia from 2012 until 2016. The age, primary diseases, PSL doses, immunosupressive periods before CMV infections were examined. [Result] Among the patients, 82 had positive CMV antigenemia. The average age was 67.3 and 52 were female. AAV (33), SLE (22), PM/DM (8), AOSD (5), GCA/PMR (5), and RA (3) were found. All the patients were treated with steroids and 45 (55%) received additional immunosupressive therapies. We treated 55 patients, while 24 were spontaneously resolved. Three died after primary disease. Of treated 55 patients, 13 needed retreatments because of CMV reactivations, 32 were no reactivation, and 10 were excluded because of death and transfer. CMV enterogastritis (9) and CMV associated-hemophagocytosis (2) were found. In the treatment group, the average age was higher than in the non-treatment group (69.7±1.7 vs 60.6±4.1: *p=0.020*) and the average PSL dose was higher (51.7±2.2 vs 43.5±2.6 mg/day: *p=0.031*). There were no significant differences in age, PSL dose, and period until CMV reactivation between relapse and non-relapse group. [Conclusion] Age and high dose PSL can be risk factors in CMV infections.

W68-2

Clinical features of cytomegalovirus (CMV)-antigen-positive patients with connective tissue disease (CTD) receiving immunosuppressive therapy

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Conflict of interest: None

Objectives: Our purposes were to investigate clinical features of CMV reactivation in patients with CTD. **Methods:** We retrospectively analyzed clinical features of CTD cases who initiated or intensified immunosuppressive therapy with CMV pp65 antigen tested from January 2008 until October 2016. **Results:** 121 cases were enrolled. The median age was 67 (IQR 54-76) and 74 patients were female (61%). The initial prednisolone (PSL) dose was 0.94 mg/kg (IQR 0.66-1.08), steroid pulse therapy was performed in 44 cases (36%) and immunosuppressive agents were concomitantly used in 52 cases (43%). 43 patients (35%) were positive for CMV antigen test. Significant risk factors for CMV reactivation included initial high-dose PSL (mg/kg) (1.01 vs 0.81, p=0.001), steroid pulse therapy (OR 3.12, 95%CI 1.43-6.81), concomitant immunosuppressive agents (OR 2.62, 95%CI 1.22-5.64), 4-week-after lymphocyte count (/μL) (653 vs 1083, p<0.001), platelet count (×10^4/μL) (12.5 vs 16.6, p=0.001), albumin (g/dL) (2.8 vs 3.3, p<0.001) and comorbid fungal infection (OR 3.01, 95%CI 1.10-8.19). The median period of CMV reactivation after starting immunosuppressive therapy was 30-day (IQR 26-43). **Conclusions:** These findings could serve as risk factors of CMV reactivation in immunosuppressive patients with CTD.

W68-3

The Usefulness of Cytomegalovirus Infection Management Strategy based on The Guideline of Hematopoietic Cell Transplantation 2011 in Patients with Connective Tissue Disease 2nd Report

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Conflict of interest: None

[Objectives] There is no official guideline for managing cytomegalovirus (CMV) infection in the patients with connective tissue diseases (CTD) undergoing immunosuppressive therapy. CMV infection management according to the guideline of hematopoietic cell transplantation (HCT) 2011 was performed in CTD patients and its usefulness was evaluated. [Methods] In 89 CTD patients receiving ≥20 mg/day of prednisolone, we managed CMV infection according to the guideline. [Results] 63 events of the positive CMV pp65 antigen occurred in the 89 patients. According to the guideline, an antiviral drug was administered in 35 events (treatment group). The patients did not get treatment in the remaining 28 events (observation group). Three of treated-patients died because of interstitial pneumonia, renal failure, or Pneumocystis pneumonia. Persistent major organ involvement due to CMV infection did not occur in both groups. The risk factors for CMV infection were older age, steroid pulse therapy, and diabetes mellitus. The risk factors for CMV disease were steroid pulse therapy and CMV test positivity in the initial phase of steroid therapy. [Conclusion] This study demonstrates the usefulness of CMV infection management according to the HCT guideline for CTD patients under immunosuppressive therapy.

W68-4

The Possibility of Latent Epstein-Barr Virus (EBV) Infection Needs to be Considered when Treating Connective Tissue Diseases

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Conflict of interest: None

Background: As Epstein-Barr Virus (EBV) is associated with pathogenic conditions such as methotrexate-induced lymphoproliferative diseases and hemophagocytic syndrome, we proactively examine EBV antibody and DNA presence in the blood of patients with suspected viral infection at our department. **Purpose**: The aim of this study is to analyze the correlation between EBV infection and clinical background. **Methods**: We retrospectively investigated 162 cases that had undergone EBV-DNA quantification using real-time PCR from 2013 through 2015. **Results**: EBV-DNA were detected in blood from 55 out of 162 patients (≥ 20 copies/10^6 cells). There was no significant correlation between positivity of anti-VCA-IgM antibodies or anti-EA antibodies and detection of EBV-DNA (OR: 2.33, 95% CI: 0.67–8.15). However, a significant correlation was observed between the prior use of immunosuppressive therapy and EBV-DNA-positivity (OR: 2.95, 95% CI: 1.43–6.12), while there was an even stronger correlation between the use of glucocorticoids alone and other immunosuppressants (OR: 3.78, 95% CI: 1.53–9.31). **Conclusions**: As these results indicate that a significant number of patients with connective tissue diseases are EBV-DNA-positive, this possibility must be kept in mind on prescribing immunosuppressants.

W68-5

The screening and the monitoring of the hepatitis B virus infection in the patients of rheumatoid arthritis in our hospital

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Conflict of interest: None

[Object] Hepatitis B virus (HBV) reactivation became the problem treated in immunosuppressive therapy (IST) for the rheumatoid arthritis (RA). We investigated the situation of the HBV infection for patients with RA. Methods: We examined HBs antigen (HBs-Ag), HBs antibody (HBs-Ab), HBc antibody (HBc-Ab), quantity of HBV-DNA about 825 patients with DMARDs in our hospital for 2009-16. [Results] HBs-Ag was measured in 1,147 cases. The positive were 22, the negative were 1,125 cases. One strange case was present in positive from negative. HBs-Ab and HBc-Ab were measured in 726 cases. The negative were 544, and the positive of HBs-Ab or HBc-Ab were 182 cases. 2 cases were turned into negative from positive. HBV-DNA was measured in 164 cases. Detected HBV-DNA was 15 cases. 5 cases were biological preparation and 14 patients treated MTX. All the cases were treated with hepatologist, and 11 patients 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, but enough attention is necessary for the HBs-Ab /HBc-Ab to have possibilities to turn into negative from positive. In the case that HBV reactivated, we can continue IST by treating with hepatologist without hepatitis developing.

W68-6

Immunogenicity of the Qudrivarent Influenza HA Vaccine for Patients with Rheumatic Diseases

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Conflict of interest: None

It is generally accepted the influenza vaccine is effective even for immunosuppressed patients. However, it was reported that trivalent vaccine was insufficient for influenza B. Now quadrivalent vaccine (QV) containing two strains of B has been utilized since 2015. We examined the immunogenicity of the QV for rheumatic disease patients. Objective and Method: 143 rheumatoid arthritis, and 8 other rheumatic diseases patients were enrolled. HI titers of QV vaccinated patients were evaluated at the time of vaccination (S0), three ± 1 week post vaccination (S1), and end of flu season (S2), respectively. Results: The seroconversion ratio (SCR) for each vaccine strain at S1 and S2 were: AH1 (35%, 29%), AH3 (56%, 51%), BY (29%, 29%), and BV (31%, 23%), respectively. While the protection ratio (SPR) were (83%, 77%), (73%, 69%), (73%, 69%) and (71%, 66%), respectively. Conclusion: Concerning QV, SCR was not so high, but SPR was sufficient for not only influenza A, but also for B.

W69-1

Three cases of CADM complicated with pneumomediastinum

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Conflict of interest: None

【Case 1】A 41-year-old male with skin lesion, and interstitial pneumonia, and anti-MDA-5 antibody positive, was diagnosed with CADM. Despite combined modality therapy, interstitial pneumonia was aggravated. Bronchial mucosa was showed in the wall of the trachea by bronchoscopy. 2 months from diagnosis, pneumomediastinum (PM)was developed. The patient died 3 months after diagnosis. 【Case 2】A 59-year-old male with skin lesion, and interstitial pneumonia, and anti-MDA-5 antibody positive, was diagnosed with CADM. According to combined modality therapy, interstitial pneumonia was improved. One month from diagnosis, PM was developed, but improved one month later, and he was

discharged from the hospital.【Case3】A 46-year-old male with skin lesion, and interstitial pneumonia, and anti-MDA-5 antibody positive, was diagnosed with CADM. According to combined modality therapy, interstitial pneumonia was improved. 2 months from diagnosis, PM was developed, but improved one month later, and he was discharged from the hospital.【Clinical meaning】PM was often complicated with fatal CADM. Bronchial mucosa was detected before PM, so this report is very suggestive. This report provides a potential importance of assessment of the PM risk with bronchoscopy.

W69-2

Two cases of rapid progressive interstitial lung disease with clinically amyopathic dermatomyositis discussed about pulmonary pathology

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Conflict of interest: None

【Case 1】A 57-year-old female was diagnosed with rheumatoid arthritis (RA) in X-7 year. In X year, she came to our hospital with ulcerated erythema on the right index finger. We diagnosed as RA with vasculitis because of vasculitis of ocular fundus and interstitial pneumonia (IP). Although treated with prednisolone (PSL) and tacrolimus (Tac), her IP was progressive. Video-assisted lung biopsy revealed fibrotic nonspecific IP (NSIP). Gottron papule lead us to diagnose her as overlap syndrome of RA and clinically amyopathic dermatomyositis (CADM), because she had no manifestation of muscle. Cyclophosphamide (CY) and plasma exchange improved her IP effectively.【case 2】A 73-year-old female had erythema on the forehead in January of X year. She came to our hospital suffering from erythema spreading her left upper eyelid in March. She was diagnosed as CADM with Heliotrope rash and ILD in July. As her lung didn't improve even after administration of PSL and Tac for two weeks, CY was added. Nevertheless, she died after second CY, because of rapid progression of IP. Autopsy findings showed coexistence of diffuse alveolar damage and NSIP.【clinical significance】We experienced two rare cases of CADM discussed pathologically. Both cases proved the positivity of anti -MDA antibody later.

W69-3

Effect of combination therapy with tofacitinib on amti-MDA5 positive interstitial lung disease in dermatomyositis

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Conflict of interest: None

Purpose: Anti-MDA5 Ab positive ILD in DM is a serious complication that determines the prognosis of the patients, Against the ILD, a combination therapy including high dose glucocorticoid, calcinulin inhibitors and intravenous cyclophosphamide, the triple therapy, is widely used and improved the prognosis of the patients. However, there are patients with poor prognosis who fail to respond to the therapy. Therefore, a new therapy has been required Here, we report two cases in which tofacitinib (TOF) saved the patients with anti-MDA5 Ab positive ILD who failed to respond to the triple therapy. **Cases:** Through analysis of anti-MDA5 Ab ILD cases, we identified risk factors as follows; 1) serum ferritin levels >1000, 2) increase in serum ferritin levels during treatment, 3) number of lung fields affected by GGO>4, and 4) worsening/ emerging GGO. The cases were 64 year old woman with ADM and 43 year old man with DM. These patients met all 4 poor prognostic factors and their respiratory condition was worsened despite of the triple therapy. Then, TOF was added to the triple therapy, which improve their symptoms and GGO and decreased the ferritin levels. **Conclusion:** The combination therapy, including TOF is suggested to be an effective treatment for refractory anti-MDA5 Ab positive ILD.

W69-4

The efficacy of add-on methotrexate on four cases with inflammatory myopathy and interstitial lung disease treating with both glucocorticoids and calcineurin inhibitors

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Conflict of interest: None

[Objective] We studied the efficacy of triple therapy (glucocorticoids (PSL), calcineurin inhibitors (CNi) and methotrexate (MTX)). [Methods] We extracted cases where were given triple therapy from our medical records, and examined these cases retrospectively. [Results] Two men (case 1, 2), 2 women (case 3, 4). These patients showed mean age 56.8 year-old, mean PSL dose 11.3 mg/day, CNi dose (CyA 170 mg/day in case 1, mean Tac 3.3 mg/day in case 2-4), mean MTX dose 11.5 mg/week. Clinical course after initiating MTX: [Case1] Erythema of his hand disappeared, but KL-6 did not change. [case2] His muscle strength improved, and KL-6 declined, but CK stopped to 300 U/L. [case3] Her muscle pain disappeared, and CRP was normalized. KL-6 decreased to 400 U/ml [case4] KL-6 dropped from 600 to less than 500 U/ml. In all case, respiratory function test did not change remarkably and chest CT images did not get worse. [Discussions] It is thought that the combination of MTX is hesitated about by concern of the MTX-induced Interstitial pneumonia. The report about the triple therapy with PSL, CNi and MTX for myositis was only two cases as far as searched in Pubmed. Safety about this therapy did not have the problem in our report, but will be the concern that we should investigate in future.

W69-5

Severe Cardiac Involvement in Polymyositis and Dermatomyositis: 2 Cases

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Conflict of interest: None

【Background】Although cardiac involvement with polymyositis (PM) and dermatomyositis (DM) are severe pathological condition, there are only a few reports and attentions. We report this two cases with our considerations of literatures.【Case1】A 42-year old woman. Serum skeletal muscle enzyme elevation and ventricular premature contraction existed. She was diagnosed with PM and myocarditis, and treated with prednisolone 1mg/kg. Afterward, she was attacked by ventricular tachycardia and became cardiopulmonary arrest. She was treated with antiarrhythmic drug and intravenous immunoglobulin (IVIg) and escaped death.【Case2】A 48-year old woman. Serum skeletal muscle enzyme elevation, heliotrope eruption and gottron papule were existed. She was diagnosed with DM and interstitial pneumonia. she was treated with steroid pulse therapy, tacrolimus and IVIg. Afterward, she was suddenly became bradycardia and then became cardiopulmonary arrest. Despite intensive care she died.【Consideration】There are various clinical features of cardiac involvement with PM/DM. Along with advances in cardiac MRI, asymptomatic lesion can be detected. It revealed that cardiac involvement was latently progressed. To detect them at an early stage are important and to establish effective treatment is urgent.

W69-6

A case of anti-TIF-1γ (transcription intermediary factor 1γ) antibody positive refractory dermatomyositis associated with dysphasia for which single-course intravenous immunoglobulin therapy is effective

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Conflict of interest: None

A 62-year-old woman presented to our hospital with 2-month history of skin rash of upper chest and knuckles and proximal muscle weakness. On admission, we diagnosed as dermatomyositis because of the typical symptoms and elevated level of serum creatine kinase (CK). Skin biopsy, electromyogram and muscle biopsy confirmed it. After administration of prednisolone (PSL) 65mg/day and azathioprine, skin rash, CK level and muscle weakness were improving. But progressive dysphagia preceded by elevated level of serum ferritin was refractory to intravenous steroid pulse with 1 g of methylprednisolone. Further investigation revealed anti-TIF-1γ antibody was positive but screening tests for cancer ware negative. Single course of high-dose intravenous immunoglobulin (IVIG) ameliorated dysphagia and lowered ferritin level, which enabled PSL dose-reduction. Skin rash of upper limbs relapsed with increasing level of serum ferritin, when the dose of PSL was reduced to 9mg/day, and we needed to increase it to 30mg/day. This case of DM associated with dysphagia without interstitial pneumonia responded very well to only one course of IVIG and serum ferritin level was associated with disease activity. We report this case with some literature review.

W70-1

Clinical significance of Rheumatoid Factor in patients with ANCA associated vasculitis

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Conflict of interest: None

[Object] Some patients with ANCA associated vasculitis (AAV) have a presence of rheumatoid factor (RF). This study was made to clarify relations between RF and clinical features in patients with AAV. [Methods] Medical records from January 2006 to December 2015 were obtained from patients with AAV in whom RF was measured. Ten patients with eosinophilic granulomatosis polyangitis (EGPA), fourteen patients with granulomatosis polyangitis (GPA), sixteen patients with microscopic polyangitis (MPA) and seven patients with unclassifiable vasculitis (UV) were enrolled. [Results] The presence of RF in EGPA, GPA, MPA, and UV were 80%, 50%, 56% and 71%, respectively. The mean value of Birmingham vasculitis activity score (BVAS) was 16.3 in EGPA, 7.4 in GPA, 18.5 in MPA and 13.4 in UV. The titer of RF had a significant correlation with BVAS (r=0.495) and CRP (r=0.409) in all of the AAV patients. The frequency of the development of end stage renal disease, commencement of dialysis therapy, usage of ventilator and mortality was higher in RF-positive AAV patients than in RF-negative those. [Conclusions] In AAV, RF had a significant correlation with disease activity. In addition, this study suggested that the presence of RF could be a poor prognostic factor in patients with AAV.

W70-2

Clinical characteristics of 47 patients with necrotizing arteritis of medium and small arteries

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Conflict of interest: None

[Object] Polyarteritis nodosa (PAN) is a necrotizing arteritis of medium and small arteries and contains systemic and cutaneous type. The aim of this study is to evaluate characteristics of patients with necrotizing arteritis of medium and small arteries. [Methods] 47 patients with necrotizing arteritis of medium and small arteries were enrolled to this study. Clinical symptoms, laboratory findings, treatments, and the rate of relapse or death were evaluated. [Results] 35 patients presented cutaneous type (eruptions only, 14; ulcer or necrosis, 8; mononeuritis, 9; both, 4), and 12 patients manifested systemic vasculitis. Systemic PAN patients tended to be older, and have higher inflammatory markers, and renal damage. Liver dysfunction was seen in 89% of patients with systemic PAN. The relapse/mortality rate was 90% in ulcer or necrosis group. 58% of patients with systemic PAN possessd MPO-ANCA, suggesting the high frequency of MPO-ANCA in medium and small arteritis in Japan. [Conclusions] 25% of patients showed systemic vasculitis. Older age, presence of MPO-ANCA, higher inflammatory markers, and renal or hepatic dysfunctions were indicators for systemic involvement. Patients with ulcer or necrosis relapsed frequently, indicating unmet needs to establish optimal treatments.

W70-3

Clinical and pathogenic association between ANCA-associated vasculitis (AAV) and nontuberculous mycobacteriosis (NTM)

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Conflict of interest: None

[Background] ANCA-associated vasculitis (AAV) patients are at risk of infection with the use of immunosuppressive therapy, but infection itself can cause AAV. However, reports of an association between AAV and nontuberculous mycobacteriosis (NTM) are limited. [Case 1] A 70-year-old woman was diagnosed as AAV based on the presence of otitis media with a granulomatous lesion and a high titer of MPO-ANCA in X-4 year. It was found that she also suffered from NTM. Antibiotic therapy was started to treat the progression of lung lesions in X-3 year. Treatment for NTM led to amelioration of the MPO-ANCA titer. NTM subsequently flared, leading to an increase in the MPO-ANCA titer in X year. She was treated with antibiotics again, resulting in a decrease in the MPO-ANCA titer. [Case 2] A 62-year-old woman was found to have NTM in X-4 year. In addition to progression of the respiratory symptom, renal disturbances and a high titer of MPO-ANCA appeared in X year. She was treated with PSL because she suffered from crescentic glomerulonephritis. Although her kidney function and ANCA titer improved, the lung nodules of NTM worsened. [Discussion] It is possible that NTM is related to the etiology of AAV. We present two interesting AAV cases with NTM, and include a review of the literature.

W70-4

Two cases of infectious endocarditis (IE) with rapid progressive glomerulonephritis (RPGN) needed to distinguish angiitis

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Conflict of interest: None

【Introduction】We experienced two cases of IE developing RPGN which showed crescentic glomerulonephritis and several autoantibodies-positive confused with angiitis.【Cases】Case 1 is 69 year old man. He had developed fever, decreased renal function, increased proteinuria, and PR3-ANCA positive. Renal biopsy revealed crescentic glomerulonephritis. He was diagnosed IE because of the positive blood cultures and vegetation of the aortic valve. IE was improved after the aortic valve replacement surgery. At the same time, nephritis and the titer of PR3-ANCA were also improved. Case2 is 46 year old man. He had developed fever and arthritis and diagnosed Sjogren's syndrome. He was prescribed with prednisolone for ankle pain. After that, the renal function got worse and he visited our hospital. Deterioration of proteinuria and hematuria, lowering complement, increased immune complex were seen. Renal biopsy showed crescentic glomerulonephritis. He was diagnosed IE because of the positive blood cultures and vegetation of the mitral valve. IE was improved after the mitral valve replacement surgery. Nephritis and the several laboratory findings were also improved.【Conclusion】Caution is required to differentiate IE from autoimmune disease because opposite treatment is needed.

W70-5

The utility and safety of the parietal branch temporal artery biopsy in the diagnosis of giant cell arteritis

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Conflict of interest: None

[Objective] The temporal artery biopsy (TAB) remains the principal method of diagnosing giant cell arteritis (GCA). Reported TAB positivity rates vary, ranging from 4 to 25 percent. In previous prospective studies, postoperative complications occurred in 3 to 16 percent of TAB cases. The difference in TAB positivity rates and complication rates among temporal artery branches is unknown. [Methods] The subjects were GCA-suspected patients who underwent TAB at Tokyo Metropolitan Tama Medical Center between April 1st 2001 and September 30th 2016. The data were collected retrospectively through review of the medical records. [Results] During the study period, 180 temporal artery branches were biopsied in 102 patients. Out of these, 124 parietal branch were biopsied in 73 patients. The biopsy positivity rate for all of the biopsy and for parietal branch biopsy alone was 26.7% and 28.2%, respectively. There was no postoperative neurological complication, bleeding, or infectious complication resulting from the biopsy. [Conclusions] The positivity rate for parietal branch biopsy was similar to that seen in previous studies, in most of which the frontal branch was biopsied. No postoperative neurological complications occurred.

W70-6

The discordance rate of temporal artery biopsies in Japanese patients with giant cell arteritis

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Conflict of interest: None

[Objective] The term ‘discordance’ describes one unilateral positive biopsy combined with one contralateral negative biopsy. The temporal artery biopsy (TAB) is the golden standard of diagnosing giant cell arteritis (GCA). Some non-Japanese studies investigating the discordance rate (DR), reported a range of 5 to 20%, suggesting that the bilateral biopsy may increase diagnostic yield. The differences in DR between each branch of the temporal artery remain unknown. We investigated the DR in temporal artery branches among Japanese GCA patients. [Methods] The subjects were GCA patients who underwent a bilateral biopsy at Tokyo Metropolitan Tama Medical Center between April 1st 2001 and September 30th 2016. The data were collected retrospectively through the medical records. [Results] During the study period, 28 GCA patients with bilateral TAB were seen. Of these, 18 had a bilateral positive biopsy, 5 had a unilateral positive biopsy, and 5 had a bilateral negative biopsy. The DR for all TABs, parietal branch biopsies, and TABs not including the parietal branch was 21.7%(5/23), 23.5%(4/17) and 16.7%(1/6), respectively. [Conclusion] The DR was similar among temporal artery branches. The bilateral biopsy saved approximately 10% of cases from false negative in Japanese GCA patients.

W71-1

A rare complication of ruptured renal interlobular arterial aneurysms in a patient with granulomatosis with polyangitis (GPA)

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Conflict of interest: None

A 77-year-old woman presented with otitis media, fever and dyspnea. On admission, her temperature was 37.8 degree. Urinalysis showed proteinuria (0.64g/24 h) without hematuria. Leukocyte was 14500/mL, serum creatinine level, 0.76mg/dL, CRP level, 18.7 mg/dL and PR3-ANCA > 350 U/mL. Chest CT revealed multiple coin lesions in bilateral lung. After admission, serum creatinine level was elevated (1.8mg/dL), therefore, a renal biopsy was performed at the right kidney. On the next day, she suddenly suffered from left abdominal pain and hypotension. 3D-CT revealed extravasation of contrast media around left kidney. Multiple aneurysms were also detected in bilateral kidneys, liver and spleen. Left renal artery angiography revealed the many aneurysms at interlobular arteries with ruptured aneurysms. Transcatheter arterial embolization for aneurisms in left kidney was performed and she was getting better. A renal biopsy showed necrotizing vasculitis in capillaries and venules, but not necrotizing glomerular lesions. From these findings, she was diagnosed with GPA. Arterial aneurysms are quite unusual of GPA. In the literature 28 cases of GPA complicated by arterial aneurysms are documented. Arterial aneurysms should be kept in mind in treating GPA patients.

W71-2

Case of right common iliac artery aneurysm rupture into the inferior vena cava during treatment of microscopic polyangiitis

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Conflict of interest: None

[Case] A 72-year old man was treated and followed up for angina pectoris, arteriosclerosis obliterans, abdominal aortic aneurysm, and right common iliac artery aneurysm at another hospital. The patient had been treated for lupus nephritis since 2001. In April 2016, he was diagnosed with microscopic polyangiitis (MPA). The symptoms improved with PSL (1 mg/kg). In June, when he developed back pain and nausea. His blood pressure subsequently decreased. Contrast-enhanced CT revealed enlargement of the right common iliac artery aneurysm, which had penetrated the inferior vena cava to form a fistula. Endovascular repair was impossible because of a history of stent placement. Surgery was considered futile; he therefore received palliative care and died in 2 days. [Discussion] Causes of aneurysm formation include inflammatory cell infiltration into the vascular wall; thinning, rupture, and disappearance of the extracellular matrix, with involvement of matrix metalloproteinases, have been noted. MPA is a small-vessel vasculitis and not thought to form aortic aneurysms directly; however, some studies report that an aortic aneurysm can be caused by inflammation of minute blood vessels around the aorta. We report the association between aortic aneurysm and small-vessel vasculitis.

W71-3

An autopsy case of MPO-ANCA positive polyarteritis nodosa with acute kidney injury

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Conflict of interest: None

A-78-year-old woman was admitted to nearby hospital on May 16, 2016 because of left middle cerebral artery embolism. She was treated with intravenous tissue-type plasminogen activator. On admission, she had a fever and her C-reactive protein was high. Her urinalysis revealed proteinuria and hematuria. She was treated with several antibiotics. But she had persistent fever and her renal function was rapidly declined. Because MPO-ANCA was positive, she was transferred to our hospital on June 14. Her renal function had severely deteriorated (Cr 6.0mg/dL, BUN 93.6mg/dL). She was diagnosed microscopic polyangitis (MPA) and rapidly progressive glomerulonephritis (RPGN). Because her general

condition was bad, renal biopsy and hemodialysis were not performed. Steroid therapy was not effective, she died on June 23. An autopsy revealed vasculitis of medium and small blood vessels of the kidney, cerebral artery and GI tract. She was finally diagnosed with polyarteritis nodosa (PAN). The diagnosis of PAN was sometimes difficult. This case was very instructive on diagnosing acute kidney injury with MPO-ANCA.

W71-4

Arthritis as the initial episode of polyarteritis nodosa : 2 case reports

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Conflict of interest: None

【Case1】A 51-year-old female, who had 7 months episode of arthritis on right knee joint, was diagnosed as polyarteritis nodosa (PAN). She received synovectomy because of arthritis getting worse. The pathological finding of synovium indicated fibrinoid necrotizing arteritis in small to medium-sized arteries. No positivity for rheumatoid factor (RF) and ANCA was detected, whereas increase of CRP was shown. Co-administration of predonisolone (PSL) and methotrexate (MTX) was effective for achieving remission.【Case2】A 60-year-old female had refractory arthritis on bilateral ankles, which was resistant to low dose PSL and MTX, as well as showing high level of CRP.RF and ANCA were negative. She had erythema and fasciitis on her lower legs, from which biopsies were performed, 13 months later. The pathological findings demonstrated inflammatory cells infiltration and fibrinoid necrosis with narrowing vessels in small to medium-size arteries, resulting in the diagnosis of PAN. Remission was achieved by increasing PSL together with azathioprine.【Conclusion】It may be difficult to make early diagnosis of PAN in the case of arthritis without other manifestations associated with PAN. It was valuable to determine the diagnosis of PAN by the pathological findings in the present cases.

W71-5

Usefulness of ultrasound evaluation of disease activity in large vessel vasculitis; two case reports

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Conflict of interest: None

Objectives. This study aims to evaluate the usefulness of ultrasound (US) examination of main arteries in patients with large vessel vasculitis (LVV). Methods. Patients with LVV were prospectively enrolled from April to October 2016 at the University of Yamanashi Hospital. US examinations were performed before and 4 weeks after the treatment. The following arterial regions were evaluated; carotid, vertebral, brachiocephalic, subclavian, axillary, celiac, superior mesenteric, iliac artery, and abdominal aorta. Results. Two patients were enrolled. The first patient was a 31-year-old male with Takayasu arteritis (TAK). The second one was a 73-year-old female with giant cell arteritis (GCA). An increase in wall thickness in brachiocephalic and left subclavian arteries were found in TAK patient and an increase in wall thickness in carotid and subclavian arteries were demonstrated in GCA. Both patients were treated with prednisolone 40mg/day. Wall thickness was significantly improved in both patients following the 4-week treatment period. Conclusions. US is a useful tool for the diagnosis and the therapeutic evaluation of affected arteries in LVV. We think that combination of US and other modalities such as CT or MRI is more appropriate and useful to examine arteries in LVV.

W71-6

Two cases of adult-onset Kawasaki disease

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Conflict of interest: None

Adult-onset Kawasaki disease (AOKD) is very rare although KD most commonly develops in children. We described two cases of AOKD. Case1; A 32-year-old woman was admitted to our hospital suffering from high fever (38˚C) lasting for five days, polymorphic erythema of the trunk and legs, indurative edema of the palms, desquamation around the finger tips, strawberry tongue, and cervical lymphadenopathy. We diagnosed her with AOKD and treated with intravenous immunoglobulin (IVIG) 80mg/day and high-dose aspirin 1500mg/day. She became afebrile on the next day and other clinical symptoms were steadily improved. The Coronary computed tomography revealed no aneurysms at 2 weeks follow-up. Case2;The A 45-year-old woman presented with high fever (40˚C), polymorphic erythema of the trunk, bilateral non-exudative conjunctival injection, indurative edema of the palms, desquamation around the finger tips, strawberry tongue, and cervical lymphadenopathy. We diagnosed her with AOKD although she had fever only for 3 days. Since administration of high-dose aspirin 1500mg/day alone rapidly ameliorated her fever on the next day, we did not add IVIG to her. Other clinical symptoms were also improved. The echocardiography revealed no coronary aneurysms at follow-up.

W72-1

Chronic inflammation may affect the irreversible organ damage in SLE patients with long-term treatment

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Conflict of interest: None

Background: There are few reports that elucidated role of aging for the development of irreversible organ damage in patients with systemic lupus erythematosus (SLE). **Method:** SLE patients at our hospital and Showa University Hospital were enrolled. The patients were divided into following groups by chronological order of disease onset: group 1, before 1995; group 2, from 1996 to 2009; group 3, after 2010. We explored the factors which promote chronic damage using SLICC/ACR damage index (SDI). **Result:** Of 245 enrolled patients, average SDI were 1.93 in group 1, 1.24 in group 2, and 0.53 in group 3, respectively. Ocular and renal involvements exhibited positive correlation with disease duration in all groups (p=0.0007). Other criteria of SDI were not associated with disease duration. In all groups, the patients with high SDI were older than those with low SDI at the time of disease onset. In addition, the patients with high SDI in group 1 and group 2 exhibited higher levels of CRP (group 1: 0.75±1.71 vs 0.16±0.20, p=0.0195; group 2: 0.59±0.74 vs 0.18±0.30, p=0.0006) and C4 (group 1: 21.4±8.6 vs 16.1±7.0, p=0.0044; group 2: 18.0±8.5 vs 14.1±6.0, p=0.0194). **Conclusion:** Not only aging but chronic inflammation may affect the chronic damage in SLE patients with long-term treatment.

W72-2

Attainment of steroid free remission in Systemic Lupus Erytematosus

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Conflict of interest: None

Objectives: To determine the frequency of steroid free remission and to define disease characteristics of lupus patients achieving steroid-free remission. Methods: We retrospectively reviewed clinical charts of 200 consecutive patients (age 46±13.6 y.o., female 94.5%, disease duration 16.4±11.5 years) who met 1997 ACR SLE Classification Criteria followed in our university hospital. Steroid free remission was defined as a 3-month consecutive period of no disease activity without corticosteroid treatment. Corticosteroid use, SLEDAI-2K and clinical characteristics were examined. Results: Frequency of current corticosteroid users of all the SLE patients was 80%, and that of life time users was 99.8%. Thirty–five patients (18.5%) achieved steroid free remission. There were no differences in onset of age, disease duration, co-administration of immunosuppressants between two groups. Patients in steroid free remission were older (p=0.006), without butterfly rash (p=0.04), nephritis (p=0.03) and positive anti-DNA Ab (p=0.01). Conclusion: Steroid-free remission might be a realistic goal in some patients with lupus.

W72-3

Results of Safety and Efficacy of Belimumab 10mg/kg in the Japanese SLE patients: Results of the Japanese population from the BEL113750 Pivotal Phase III, Randomized, Placebo-controlled Study of Belimumab in Patients with Systemic Lupus Erythematosus

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Conflict of interest: Yes

Background: BEL113750 assessed the efficacy and safety of belimumab when added to standard of care therapy compared to placebo over 52 weeks in SLE patients located in NE Asia. **Methods:** 707 SLE subjects (Japan cohort: 60) were randomized to treatment in a 2:1 ratio [belimumab (B) group: 471, placebo (P) group: 236], whose age ≥18 yrs with a SELENA SLEDAI score of ≥8, were to be dosed every 28 days through W48, with a final evaluation at W52. The primary endpoint was the SLE responder index (SRI) response rate at W52. **Results:** The SRI response rate at W52 was significantly higher for B group [242/446 (54.3%)] compared with P group [87/217 (40.1%)] [OR: 2.03 (95%CI: 1.43-2.88), p<0.0001]. That results in the Japan cohort was higher for B group [18/39 (46.2%)] compared with P group [5/20 (25.0%)] and that was directionally consistent with the Overall. The safety profile of belimumab was generally favorable and similar to that of placebo. The safety data in the Japan cohort were generally consistent with those in the Overall. **Conclusions:** The efficacy and safety results in this study were similar to that of in previous belimumab IV/SC P3 studies; no new safety issues are identified. The results of Japan cohort in this study were similar to the results of overall. GSK funded this study.

W72-4

Association between alcohol, smoking, and disease activity of systematic lupus erythematosus:cross sectional study

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Conflict of interest: None

【Object】It is unknown how alcohol and smoking work to its disease activity. To evaluate the association between alcohol, smoking and disease activity of SLE.【Method】238 SLE patients who satisfied ACR criteria were targeted. They were registered in databases currently being constructed at Okayama University Hospital and Showa University Hospital. The research design was cross-sectional study. Patients divided into 4 groups;group1:smoking (-)alcohol (-), group2:smoking (-)alcohol (+), group3:smoking (+)alcohol (-), group4:smoking (+)alcohol (+). The Main outcome was SLEDAI. Confounding factors were sex, age, present corticosteroid dosage and present immunosuppressant use.【Results】Mean age was 46.2±15.3 years old. 91% was female. Mean corticosteroids dosage was 6.7±5.9mg. Immunosuppressant use was 61.3%. SLEDAI was 3.9 ± 5.1. Group1 was 186/238. Group 2 was 16/238. Group 3 was 26/238. Group4 was 10/238. No significant difference was observed between the 4 groups in One-way ANOVA (p=0.253) and no significant difference was observed in multiple regression analysis【Conclusion】It is unable to validate the association between alcohol, smoking and disease activity of SLE.

W72-5

The prevalence and the risk factor of hypertension and dyslipidemia in systematic lupus erythematosus patients

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Conflict of interest: None

【Object】There were few reports about the risk factors of hypertension (HT) and dyslipidemia (DL). The purpose of this study is to describe a prevalence of HT and DL and to evaluate the risk factor of HT and DL.【Methods】238 SLE patients who satisfied ACR criteria were targeted. They were registered in databases currently being constructed at Showa University Hospital and Okayama University Hospital. The definition of HT and DL was a use of anti-HT drug and anti-DL drug. We performed descriptive statistics and binomial logistic regression analysis to evaluate the risk factors of HT and DL.【Results】Mean age was 46.2±15.3 years old. 91% was female. Mean corticosteroids dosage was 6.7±5.9mg. Mean SLEDAI and SLICCDI was 4.98±5.2, 1.26±1.7. A prevalence of HT and DL was 71/244 (29.1%), 54/244 (22.1%). On binominal logistic regression analysis to evaluate the risk of HT, BMI, drinking status, past maximum corticosteroid dose and lupus nephritis were the independent factors. On binominal logistic regression analysis to evaluate the risk of DL, age was the independent factor.【Conclusion】Present PSL dose and SLICC-DI might not be associated with HT and DL.

W72-6

Healthcare resource utilization and cost in Japanese patients with systemic lupus erythematosus from claims database

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Conflict of interest: Yes

Objective: This study assessed the economic burden of Japanese systemic lupus erythematosus (SLE) patients. **Methods:** This was a retrospective study (No. HO-15-16208) using the Japan Medical Data Center claims database. SLE patients aged 15 to 65 years were identified between April 2010 and March 2012 and followed up for three years from the first visit during the period. SLE severity and flare episode were defined by proxy algorithms. All-cause healthcare resource utilization (HRU) and direct medical cost were calculated over the study period, and productivity loss of full-time workers was estimated by considering facility visit and stay as absenteeism. **Results:** Among 295 SLE patients, mean direct medical cost for 3 years was 2,913,509JPY per patient and increased with SLE severity (p<0.001). The major component was medications (42.5%). The mean direct medical cost per flare episode and productivity loss per patient were estimated 157,581JPY and 214,536JPY, respectively. Mean number of outpatient visits was 64.9 times. Number and duration of inpatient were 116 (39.3%) and 19.9 days per event. **Conclusion:** This study demonstrated high levels of HRU and direct medical cost associating with severity in Japanese SLE patients. A major cost driver was medications.

W73-1

SPIRIT-P1, a phase 3 study of ixekizumab (IXE): 52-week efficacy and safety results in patients with active psoriatic arthritis (PsA)

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Conflict of interest: Yes

Objectives: To evaluate efficacy and safety of IXE over 52 weeks in patients with active PsA. **Methods:** Biologic DMARD-naive active PsA patients (N=417, 12 Japanese) were randomized 1:1:1:1 to placebo, adalimumab, or IXE 80 mg once every 4 weeks (Q4W) or 2 weeks (Q2W) including a 160 mg starting dose in the Double-Blind Treatment Period (DBTP: Weeks 0 to 24). Of these, 381 patients (11 Japanese) completed DBTP and entered the Extension Period (EP: Weeks 24 to 52) where they continued on or were assigned to 80 mg IXEQ4W or IXEQ2W. **Results:** A total 304 patients (8 Japanese) completed EP. At Week 52 for the IXEQ4W/IXEQ4W and IXEQ2W/IXEQ2W groups who were treated with IXE for 52 weeks, the response rates for ACR20/50/70 were 69.1/54.6/39.2% and 68.8/53.1/39.6%, PASI 75/90/100 were 78.8/66.7/56.1% and 81.8/78.2/67.3%. Adverse events (AEs) frequency in EP was consistent with that in DBTP; the majority were mild or moderate in severity. In EP, serious AEs occurred in 4 patients treated with IXE for 52 weeks, and no deaths occurred. **Conclusion:** At Week 52, IXE showed clinically significant improvements in joint and skin symptoms of PsA. The safety profile of IXE observed in EP was consistent with that in DBTP and other phase 3 studies of IXE in patients with plaque psoriasis.

W73-2

Efficacy and safety of tofacitinib for rheumatoid arthritis refractory to methotrexate and/or biological agents

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Conflict of interest: None

[Objective] Tofacitinib (TOF) is a novel, oral Janus kinase (JAK) inhibitor that was approved for the treatment of rheumatoid arthritis (RA) in Japan in 2013; however, its impact on patient outcomes in real-world practice is unclear. This study was performed to evaluate the efficacy and safety of TOF in routine care settings. **[Methods]** A total of 116 RA patients who had an inadequate response to MTX and/or biologic agents were enrolled in this study. Efficacy of TOF (5 mg B.I.D) were examined at weeks 4, 12, and 24. Therapeutic responses were expressed as response rates by ACR ≥ 20% improvement criteria (ACR20), EULAR response criteria (good or moderate response), and CDAI decreases ≥ 6.5. Adverse events were also recorded. **[Results]** ACR response rates at weeks 4 and 24 were 60% and 73.2%, respectively. At week 24, 52.2% and 31.5% of patients showed the good and moderate EULAR response, respectively. A rate of patients with CDAI decreases ≥ 6.5 at week 24 was 87.9%. Herpes Zoster (4 cases), pneumonia (3 cases), and lymphopenia (2 cases) were most often seen during the 24 weeks of follow-up. Two patients died of pneumonia or sepsis. **[Conclusion]** TOF appears to have an important role in the treatment of intractable RA through improvement in patient outcomes and safety profiles.

W73-3

Evaluation of baricitinib (Bari) in patients with active rheumatoid arthritis (RA) who have had an inadequate response to background Methotrexate (MTX) therapy: Results in patient-reported outcomes (PROs) and work productivity from a phase 3 study (RA-BEA

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Conflict of interest: Yes

Objectives: To evaluate the effect of Bari on PROs and work productivity in patients with active RA who have had an inadequate response to MTX therapy. **Methods:** 1305 patients (Japan: 249) with active RA despite stable background MTX were randomized to Bari 4 mg QD, adalimumab (ADA) 40 mg biweekly, or placebo (PBO), and received study drug. Study measurements included duration of morning joint stiffness (MJS), worst tiredness, and worst joint pain in subset of the total study population and Work Productivity and Activity Impairment (WPAI)-RA in all patients. **Results:** Median change from baseline (minutes) in the duration of MJS at Week 12 was -30.0 in Bari group, -13.0 in ADA group, and -2.0 in PBO group. Least squares mean changes from baseline in worst tiredness, worst joint pain at Week 12 were -2.7, -3.2 in Bari group, -2.3, -2.7 in ADA group, and -1.7, -1.9 in PBO group, respectively. Compared to PBO, Bari showed statistically significant improvement in these measurements at Week 12 ($p<0.001$). Bari also showed statistically significant improvements in all 4 scores of the WPAI-RA against PBO ($p<0.05$). **Conclusion:** In patients with active RA despite background MTX, Bari improved PROs and work productivity compared to PBO.

W73-4

Efficacy and Safety of Switching from Adalimumab (ADA) to Baricitinib (Bari): Phase 3 Data in Patients (pts) with Rheumatoid Arthritis (RA)

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Conflict of interest: Yes

Object: To evaluate efficacy and safety of switching from ADA to Bari in pts with RA. **Methods:** 1305 pts (249 Japanese [JP]) were randomized to placebo, Bari or ADA, and received study drug. At Week (wk) 52, pts could enter long-term extension (LTE) study, where all pts received Bari. No ADA washout period was applied for switch from ADA to Bari. NRI were used for missing value imputation for ACR responses. **Results:** 186 pts (35 JP) switched from ADA to Bari in the LTE and included in efficacy analysis. At wk 52, 85/64/40% achieved ACR20/50/70, mean CDAI, SDAI, and HAQ-DI were 8.9, 9.6, and 0.8, respectively. 12 wks post-switch, 91/67/44% achieved ACR20/50/70, mean CDAI, SDAI, and HAQ-DI were 6.9, 7.4, and 0.7, respectively. Exposure-adjusted incidence rates for treatment-emergent adverse events (AEs), Serious AEs, AEs leading to study drug discontinuation, and serious infections for 238 pts (46 JP) switched from ADA to Bari and included in safety analysis were 132.9, 9.1, 5.5, and 1.8/100 patient-years of exposure, respectively. There was no notable difference between JP and overall. **Conclusions:** Switching from ADA to Bari was associated with improvements in disease control through 12 wks post-switch, without evidence of worsening and any safety concerns, including in the JP.

W73-5

Evaluation of baricitinib (Bari) in DMARD-naïve patients with early rheumatoid arthritis (RA): Results in patient-reported outcomes (PROs) and work productivity from a phase 3 study (RA-BEGIN)

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Conflict of interest: None

Objectives: To evaluate the effect of Bari on PROs and work pro-

ductivity in DMARD-naïve patients with early RA. **Methods:** 584 patients (including 104 Japanese patients) with no or limited exposure to DMARDs were randomized to methotrexate (MTX), Bari 4 mg QD or Bari 4 mg+MTX and received study drug. Study measurements included duration of morning joint stiffness (MJS), worst tiredness, worst joint pain, and Work Productivity and Activity Impairment (WPAI)-RA. **Results:** Median change from baseline (minutes) in the duration of MJS at Week 12 was -30.0 in MTX group, -50.0 in Bari group, and -60.0 in Bari+MTX group. Least squares mean changes from baseline in worst tiredness, worst joint pain at Week 12 were -1.9, -2.7 in MTX group, -2.7, -3.6 in Bari group, and -2.8, -3.8 in Bari+MTX group, respectively. Compared to MTX, Bari and Bari+MTX showed statistically significant improvement in these measurements at Week 12 ($p<0.05$). Statistically significant improvements were also seen at Week 24 in both Bari groups compared to MTX group for all 4 scores of the WPAI-RA ($p<0.05$). **Conclusion:** In DMARD-naïve patients with early RA, Bari used alone or in combination with MTX improved PROs and work productivity compared to MTX.

W73-6

Response to Baricitinib (Bari) at Week (wk) 4 Predicts Response at wk 12 and 24 in Patients (pts) with Rheumatoid Arthritis (RA): Results from 2 Phase 3 Studies (RA-BEAM and RA-BEGIN)

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Conflict of interest: Yes

Object: To determine if, in Bari-treated pts with RA, early changes in disease activity predicted later achievement of low disease activity (LDA)/remission. **Methods:** 1305 pts (249 Japanese [JP]) with inadequate response to methotrexate (MTX) were randomized to placebo, Bari or adalimumab, and received study drug in RA-BEAM. 584 pts (104 JP) mostly untreated with DMARDs were randomized to MTX, Bari or Bari + MTX, and received study drug in RA-BEGIN. Early responder and nonresponder were predefined as CDAI improvement ≥6 and <6, respectively, at wk 4. Improvement was used to predict LDA/remission defined by DAS28-ESR at wk 12/24. **Results:** LDA/remission rates in the early responder vs early nonresponder with Bari-treated pts at wk 12/24 were as follows: RA-BEAM LDA 27.8% vs 3.2%(wk 12), 37.4% vs 11.5%(wk 24); remission 12.5% vs 0%(wk 12), 21.2% vs 4.9%(wk 24); RA-BEGIN LDA 26.4% vs 0%(wk 12), 42.7% vs 16.7%(wk 24); remission 16.3% vs 0%(wk 12), 25.8% vs 8.3%(wk 24). Negative predictive values (NPV) for LDA at wk 12/24 associated with early nonresponder exceeded 80%; NPV for remission exceeded 90%; NPV for LDA/remission with early nonresponder in the JP exceeded 80%. **Conclusions:** Early nonresponders were unlikely to achieve LDA/remission at wk 12/24, including in the JP.

W74-1

Clinical characteristics in late-onset spondyloarthritis

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Conflict of interest: None

[Object] To evaluate the clinical characteristics in late-onset spondyloarthritis (LOSpA). [**Methods]** Eighty-seven patients diagnosed with SpA at our center were enrolled. The clinical characteristics of patients with onset at age < 50 years (young-onset SpA; YOSpA, n=30) and those with onset at age > 50 years old (LOSpA, n=57) were compared. [**Results**] The median onset age of YOSpA was 38 years, and that of LOSpA was 66 years. In comparing the two groups, more YOSpA than LOSpA fulfilled the ASAS Axial SpA criteria (33%; $p<0.01$). On the other hand, more LOSpA fulfilled the peripheral SpA criteria (96%; $p<0.05$). In clinical symptoms, there was no difference in the frequency of inflammatory back pain, arthritis of the lower limbs and tenderness of enthesis, but the frequency of dactylitis was higher in LOSpA (46%; $p <0.01$). In laboratory findings, the frequency of HLA-B27+ was higher in YOSpA (30%; $p<0.001$). Among LOSpA patients, 39% had been diagnosed with another rheumatic disease such as polymyalgia rheumatica (PMR), seronegative RA or RS3PE syndrome at the time of the first visit. [**Conclusion]** The clinical characteristics of LOSpA are a higher frequency of dactylitis and a lower frequency of HLA-B27+. It is important to differentiate the diagnosis from PMR, RA and RS3PE syndrome.

W74-2

Frequency and HLA phenotype of reactive arthritis, uveitis, and conjunctivitis in Japanese patients with bladder cancer following intravesical BCG therapy: a 20-year, two-center retrospective study

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Conflict of interest: None

Background: Intravesical instillation of BCG (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. **Objective:** To evaluate the frequencies and HLA phenotype of ReA and other adverse events in Japanese patients with bladder cancer following iBCG therapy. **Methods:** The clinical findings of Japanese patients who received iBCG (n = 555) for bladder cancer from 1997 to 2016 were retrospectively assessed. We also looked at HLA phenotypes of patients with ReA. **Results:** 91 (16.4%), 121 (21.8%), and 196 (35.3%) of all enrolled 555 patients presented with fever, haematuria, and dysuria, respectively. ReA, uveitis and conjunctivitis were revealed in 11/555 (2.0%), 4/555 (0.7%) and 33/555 (5.9%), respectively. Notably, HLA-B27, -B35, -B39 and -B51 positivity was more frequent in ReA patients (9.1%, 36.3%, 36.3% and 63.6%, respectively) than in healthy subjects without ReA (0.3%, 8.3%, 4.0% and 9.1%, respectively). **Conclusions:** The 2.0% ReA frequency in iBCG treated Japanese patients exceeds that in Western countries. HLA phenotype, especially HLA-B51 and -B39 alleles in addition to -B27, may be a risk factor in iBCG-induced ReA in Japanese patients.

W74-3

Investigation of Health Related Quality of Life Burden in Spondyloarthritis: effects of failure of advanced therapy and fatigue

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Conflict of interest: Yes

To evaluate the burden of illness as measured by Health Related Quality of Life (HRQoL) in patients (pts) with Ankylosing Spondylitis (AS) and Psoriatic Arthritis (PsA) pts worldwide. The Adelphi Survey collected a real world sample from physicians and their AS and PsA pts in 18 countries. Advanced Therapy (AT) failure was defined as worsening or remaining severe of disease severity after ≥3 months, physician dissatisfaction with control or perceived disease activity as 'unstable' or 'deteriorating' or did not consider treatment a success when asked in the survey. Severe fatigue was defined as BASDAI-Fatigue >5 and SF-36 Vitality Domain <45 for AS and PsA pts respectively. HRQoL was measured by EQ-5D, SF-36 PCS, SF-36 MCS. 1379 pts with AS (including 26 in Japan) and 1827 pts with PsA (including 160 in Japan) were analyzed. AS and PsA pts failing AT had significantly worse HRQoL than those not failing across all the HRQoL parameter analyzed (all $p<0.0001$). Further pts who had 'severe fatigue' also had significantly

worse HRQoL than those with non-severe fatigue across all the HRQoL domains analyzed (all p<0.0001). Suboptimal treatment is associated with significant burden of illness including lower HRQoL in AS and PsA pts; addressing the issue could have significant benefits for pts.

W74-4

Diagnosis of spondyloarthritis in patients with uveitis: a retrospective case series of five patients

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Conflict of interest: None

Object: To investigate the prevalence and characteristics of patients with spondyloarthritis (SpA) happen to be diagnosed due to concomitant uveitis. Methods: A retrospective search was performed using medical records to extract patients with uveitis who had been investigated for underlying causes or background systemic diseases at our institution. Clinical characteristics of those with SpA diagnosed during the evaluation were determined. Results: Total of 67 patients with uveitis were evaluated and five patients were diagnosed as SpA. Preceding joint symptom was present in one out of five patients in the peripheral joints and three patients had previous inflammatory back pain, whereas peripheral joint symptom revealed in two patients after the onset of uveitis. HLA-B27 was positive in two patients and the presence of sacroiliitis was confirmed by imaging either x-ray or MRI in four patients. Conclusion: There should be certain proportion of concomitant SpA in Japanese patients with uveitis.

W74-5

Clinical condition and treatment of the SAPHO syndrome (Ver.2)

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Conflict of interest: None

【Introduction】The synovitis-acne-pustulosis-hyperostosis-oeteitis (SAPHO) syndrome has been known for a few decades though relevant treatment remains uncertain. We report clinical evaluation of disease activity and new approach to decrease disease activity of SAPHO syndrome.【Methods】99 patients with SAPHO syndrome treated by us for January 2014 to October 2016 were analyzed. We cited clinical information from the medical records. To treat the SAPHO syndrome, combinations of prednisolone, DMARDs and immunosuppressants were provided. To evaluate the impact of these drugs, we applied modified FAS31 and PPPASI.【Results】There were 14 men and 85 women. The mean age at diagnosis was 50 years old. X-ray showed fused vertebral in 16 cases. MRI showed osteitis in every case. 34 cases had pustulosis at the first visit to our clinic and 11 cases developed pustulosis. CRP and serum copper increased in 23% and 48% of patients respectively. After treatment FAS31 decreased and cutaneous disorders improved in 68% of patients though 6 cases developed mild adverse event.【Conclusion】SAPHO syndrome develops fused vertebral over time. Combinations of prednisolone, DMARDs, and immunosuppressants were potential way for SAPHO syndrome patients with FAS31 and PPPASI for assessment.

W74-6

Ultrasound features of finger symptoms in undifferentiated Spondyloarthritis at disease onset

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Conflict of interest: None

[Background] While axial Spondyloarthritis (SpA) is rare in Japan, HLA-B27 negative undifferentiated SpA (uSpA) is thought to be relatively common. Because uSpA patients don't always fulfill the ASAS criteria at disease onset, early diagnosis is often difficult, especially when finger swelling is the only symptom. It might result in delay of treatment. [Methods] To clarify clinical and ultrasound (US) features of finger symptoms in uSpA, we reviewed medical records of uSpA patients in our hospital who underwent US examination at the onset. [Result] In two patients who presented dactylitis on physical examination (PE), US revealed finger flexer tenosynovitis (FFT). In six patients who presented PIP/MCP joint swelling on PE, US revealed finger collateral ligament inflammation (CLI). Only two patients showed large tendon enthesitis at the onset. Patients with CLI were aged over 50 and older than those with FFT. Most of them were treated with SASP, followed by MTX. TNF inhibitors were used in two. Although treatment response was generally good in both groups, range of motion of finger tended to remain impaired in the patients with CLI. [Conclusions] It may be important to use US appropriately to diagnose uSpA early enough to be treated without sequela in fingers.

W75-1

Difference of clinical characteristics between patients in cancer-associated myositis with and those without anti-TIF1-γ antibody

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Conflict of interest: None

Objective: To clarify difference of clinical characteristics in cancer-associated myositis (CAM) between patients with and without anti-TIF1-γ. **Methods:** Twenty-three patients with CAM were enrolled at this study. Myositis-specific autoantibodies (MSAs) were measured in all of them. We retrospectively compiled data such as content of treatment and clinical outcome. **Results:** Breast, gastric, ovarian, colorectal and lung cancer were detected in 6, 5, 2, 2 and 2 patients, respectively. Anti-TIF1-γ, anti-ARS, anti-NXP-2, anti-SRP antibodies were found in 11, 3, 2 and 1, respectively. Male (p=0.41), skin rash (p=0.21) and no-complication of interstitial lung disease (p=0.01) were much more found in the subset with anti-TIF1-γ than in the other subset. In only three patients, anti-tumor therapy alone ameliorated skin rash or myositis. Progressive disease of cancer was much more found in the subset with anti-TIF1-γ(45%vs25%, p=0.40). Half of patients in each subset were alive for more than 5 years. Muscle weakness or skin rash at the latest visit was found more frequently in patients of the subset with anti-TIF1-γ than in those of the other subset (82%vs33%, p=0.04). **Conclusion:** CAM with anti-TIF1-γ could be more refractory for myositis or dermatitis than CAM without anti-TIF1-γ.

W75-2

Study of association between anti-MDA5 antibody titer and cytokine concentration in disease activity in anti-MDA5 antibody-positive dermatomyositis (DM)

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Conflict of interest: None

【OBJECTIVE】We measured the anti-MDA5 antibody titer and cytokine concentration in patients with anti-MDA5 antibody positive DM treated at our hospital and related to disease activity.【METHODS】We compared anti-MDA5 antibody titers, IL-18, and neopterin concentrations in 13 patients with anti-MDA5 antibody-positive DM who underwent treatment for the first time between 2009 and 2016, At the end of

the IVCY treatment, and the results were examined retrospectively.【RESULTS】The anti-MDA5 antibody titer before treatment was 169.8 ± 24.3 (mean ± standard deviation: INDEX ≦ 32), which was high in all cases, and in all patients with stable disease activity after treatment. IL-18 and neopterin concentrations were also high before treatment, but decreased after treatment.【CONCLUSION】In this study, the anti-MDA5 antibody titer after treatment was significantly lowered, and the antibody titer was lowered to normal value after 1 year in patients with stable disease. And the anti-MDA5 antibody titer correlated with the disease activity. It was suggested that the cytokine concentration also reflects disease activity and that activation of the macrophage system is associated with this disease state.

W75-3

Analysis of the clinical course of anti-MDA-5 (melanoma differentiation-associated gene 5) antibody-positive dermatomyositis in patients with interstitial lung disease during the acute and chronic phase

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Conflict of interest: None

Objective: Anti-MDA-5 antibody-positive dermatomyositis (DM) in patients with rapidly progressive interstitial lung disease (RP-ILD) is known to have a poor prognosis. The aim of this study is to analyze the clinical features of anti-MDA-5 antibody positive DM in patients with ILD in the acute and chronic phases. Methods: A total of 11 patients diagnosed as having anti-MDA-5 antibody-positive DM with ILD from 2008 to 2015 were analyzed, retrospectively. Three of the 11 DM patients had clinically amyopathic DM (CADM). Results: Titers for anti-MDA-5 antibody were significantly elevated for the 5 fatal cases compared with the 6 survivors. Five patients died within 90 days after the initial diagnosis. Median survival for these five patients was 28 days (range: 17 - 83 days). Among the 6 survivors, improvement of more than 10% in forced vital capacity (FVC) was observed for 4 patients, whereas exacerbation of respiratory function of more than 10% FVC was detected in only 1 patient in the chronic phase. Conclusion: A higher titer for anti-MDA-5 antibody was an indicator of a poor prognosis for DM in patients with ILD. In the chronic phase of anti-MDA-5 antibody-positive DM patients with ILD, pulmonary function test results were well maintained and had a good clinical course.

W75-4

Influence of residential environment on the onset of polymyositis/dermatomyositis with interstitial lung disease

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Conflict of interest: None

[Objective] To investigate the influence of residential environment on the onset of polymyositis (PM) and dermatomyositis (DM) with interstitial lung disease (ILD) in terms of myositis-specific antibodies. [Methods] From a 44-center cohort of PM/DM with ILD, 483 patients with postal code information were extracted. The cohort consisted of patients with adult onset PM/DM (including clinically amyopathic DM and probable cases) with ILD confirmed by CT. Anti-MDA5 antibody was detected by ELISA, and anti-ARS antibody (Jo-1, PL-7, PL-12, EJ, OJ, and KS) was detected by RNA-immunoprecipitation. Calculated from area of Japan and number of postal codes, the waterfront was defined as area within 1.75 km from water on the Google map. [Results] Anti-MDA5 and anti-ARS antibodies were detected in 202 and 165, respectively. Since one had both antibodies, 117 were regarded as the anti-MDA5/ARS-negative group. The proportion of patients who resided in waterfront was significantly higher in anti-MDA5-positive group than in the other two groups (70% vs 55%/55%; $p<0.01$). The difference was significant only if compared about freshwater (65% vs 50%/50%; $p<0.01$), not from sea. [Conclusion] Anti-MDA5 antibody-positive PM/DM with ILD clustered around waterfront, especially around freshwater.

W75-5

Analysis of immune cell subsets in peripheral blood mononuclear cells (PBMCs) from patients with idiopathic inflammatory myopathy (IIM)

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Conflict of interest: Yes

Background: The pathophysiology of polymyositis (PM) and dermatomyositis (DM) is still unknown, although the type 1 IFN pathway and STAT4 polymorphisms have been suggested to be related to its etiology. We are trying to elucidate the mechanism by FACS analysis and sorting 20 immune cell subsets followed by transcriptome analysis. **Methods**: 20 idiopathic inflammatory myopathy (IIM) patients (Mean age: 55±12) and 32 healthy controls (HC) (Mean age: 51±14) were picked up. The details of 20 IIM cases are as follows: 7 PM, 12 DM and 1 necrotizing myopathy. 9 have anti-ARS antibody and 3 have anti-MDA5 antibody. 14 have interstitial pneumonia (IP). 14 cases are in remission. Each immune cell subset in PBMCs was identified by FACS and sorted for NGS analysis. **Results**: In IIM compared with HC, Th17 cell ($p<0.0001$), plasmablast ($p<0.0001$), and CD16-negative monocyte ($p<0.0001$) increased, while unswitched memory B cell ($p<0.001$), Tfh cell ($p<0.0001$) and Treg cell ($p<0.01$) decreased. Interestingly, in exacerbation phase, unswitched memory B cell significantly decreased. **Conclusion**: More cases recruitment is needed for the analysis of IIM subsets like antibody/IP profile. The transcriptome analysis of each PBMC subsets would be beneficial for the elucidation of IIM pathophysiology.

W75-6

Programmed death ligand 1, immunoinhibitory protein, is induced on myotubes by interferon gamma

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Conflict of interest: None

Objective: C protein–induced myositis (CIM) is a mouse model of polymyositis. Since IFNγ-/- mice developed severer myositis via IL-17A-independent pathway, IFNγ should have a suppressive role in CIM. IFNγ acts on various cells as an immune stimulatory or inhibitory cytokine. In mononuclear cells and some tumor cells, IFNγ induces the expression of PD-L1, which inhibits the local immune reaction. Since PD-L1 is expressed on myofibers in muscle tissues from patients with myositis, impaired induction of PD-L1 in muscles may lead to the exacerbation of CIM in IFNγ-/- mice. However, the effect of IFNγ on the protein expression of PD-L1 in myotubes remains unclear. The aim of the present study is to study the effect of IFNγ on the PD-L1 expression in myotubes (C2C12 cells). Methods: The protein expression of PD-L1 in C2C12 cells treated with or without IFNγ was examined. Results: IFNγ enhanced the protein expression of PD-L1 in C2C12 cells. Conclusion: Since IFNγ en-

hanced the protein expression of PD-L1 in C2C12 cells, PD-L1 in muscles may suppress the development of CIM.

W76-1

Interim Safety Report from Post-marketing Surveillance of Tofacitinib 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 evaluate the safety of tofacitinib in Japanese patients (pts) with RA using interim post-marketing surveillance (PMS) data. **Methods:** A 6-month interim analysis of safety data from an ongoing 3-year PMS study was conducted (Aug 4, 2016 data-cut). Adverse events (AEs) were coded using MedDRA/J. **Results:** 2102 tofacitinib-treated pts were enrolled (901.8 pt-yrs of exposure); of these, 511 pts (24.3%) discontinued treatment, mainly due to AEs (n=208; 9.9%) or lack of effectiveness (n=194; 9.2%). 1591 (75.7%) completed the 6-month observation period. At least one AE was observed in 727 pts (34.6%), the most frequent of which was herpes zoster (HZ) (n=72; 3.4%). Serious AEs occurred in 171 pts (8.1%); the most frequent were pneumonia (n=15; 0.7%), interstitial lung disease (n=14; 0.7%), and HZ (n=12; 0.6%). Infections (n=273; 13.0%) were serious in 77 pts (3.7%). Eleven pts (0.5%) each reported malignancy, including diffuse large B-cell lymphoma (n=2; 0.1%) and ovarian cancer (n=2; 0.1%). **Conclusion:** Review of AEs during the initial 6-month treatment period from PMS reports in Japanese pts did not reveal any new or unexpected safety signals compared with the tofacitinib RA clinical program.

W76-2

Clinical and Radiographic Efficacy and Safety of Tofacitinib in Combination with Methotrexate in Japanese Patients with Rheumatoid Arthritis: 12-month Analyses from a 24-month Phase 3 Study

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Conflict of interest: Yes

Objectives: Tofacitinib is an oral JAK inhibitor for the treatment of rheumatoid arthritis (RA). To report 12-month (mo) tofacitinib efficacy and safety vs placebo (PBO) in Japanese patients (pts) with RA and methotrexate (MTX) inadequate response in global Phase 3 study ORAL Scan. **Methods:** Pts on stable-dose MTX were randomized 4:4:1:1 to tofacitinib 5 or 10 mg BID or one of two PBO sequences advancing to tofacitinib 5 or 10 mg BID at Mo 3 (if non-responsive) or Mo 6. **Results:** 118 Japanese pts were treated and groups had similar BL characteristics. At Mo 6, pts on tofacitinib had significantly higher ACR20 response rates, lower mean increases from BL in modified Total Sharp Score (mTSS) and higher non-progressor (change from BL ≤0.5 mTSS) rates vs PBO. Pts on tofacitinib had greater HAQ-DI improvements from BL at Mo 3 vs PBO. Pts on tofacitinib 10 mg BID had numerically higher DAS28-4 (ESR) <2.6 rates vs 5 mg BID or PBO at Mo 6. Improvements were sustained over 12 mo. Adverse event (AE), serious AE and serious infection rates were similar among groups over 12 mo; infections were the most common AEs. **Conclusion:** Tofacitinib improved symptoms and reduced structural damage progression vs PBO in Japanese pts over 12 mo. Safety signals were consistent with previous Japanese studies.

W76-3

Safety and Efficacy of Tofacitinib in Combination with Methotrexate in Japanese Patients with Rheumatoid Arthritis: Results from a 24-month Phase 3 Study

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Conflict of interest: Yes

Objectives: Tofacitinib is an oral JAK inhibitor for the treatment of rheumatoid arthritis (RA). We report 24-month (mo) tofacitinib efficacy and safety vs placebo (PBO) in Japanese patients (pts) with RA and methotrexate (MTX) inadequate response in global Phase 3 study ORAL Scan. **Methods:** Pts on stable-dose MTX were randomized 4:4:1:1 to tofacitinib 5 or 10 mg BID or one of two PBO sequences advancing to tofacitinib 5 or 10 mg BID at Mo 3 (if non-responsive) or Mo 6. **Results:** For tofacitinib 5 and 10 mg BID pts, ACR20/50/70 response rates, DAS28 <2.6 and ≤3.2 rates, and improvements from baseline in DAS28-4 (ESR) and HAQ-DI seen through 12 mo were maintained over 24 mo. Mo 6–24, adverse event (AE), serious AE (SAE) and discontinuation (DC) due to AE rates, were 85.1%, 14.9% and 10.6% for tofacitinib 5 mg BID, and 80.9%, 10.6% and 14.9% for tofacitinib 10 mg BID. AEs and SAEs occurred in 83.3% and 8.3% of PBO to 5 mg BID and 50.0% and 0.0% of PBO to 10 mg BID pts, Mo 6–24; no PBO to tofacitinib pts DC due to AEs. PBO to 5 mg BID pts had a lower incidence of laboratory abnormalities (27%) vs other groups (55–63%), Mo 6–24. **Conclusion:** Tofacitinib maintained symptom improvement through Mo 24 for Japanese pts. Safety signals were consistent with previous Japanese tofacitinib studies.

W76-4

Early clinical response predicts low disease activity at one year in rheumatoid arthritis patients on treatment with tofacitinib in clinical practice

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Conflict of interest: None

OBJECTIVES:To determine which baseline variables are responsible and whether the low disase activity (LDA) in Disease activity Score (DAS) 28ESR at three months predicts for a preferable DAS outcome at one year in patients with active rheumatoid arthritis (RA) treated with tofacitinive (TOF), a JAK inhibiter. METHODS:Fortytwo RA patients who had treated with tofacitnib were enrolled in this study. The variables at baseline and at three months that were predictive of LDA according to the DAS at one year were assessed by logistic regression analysis. RESULTS:Thirteen patients achieved LDA at one year. The average of DAS of them and the other patients were 4.91 and 5.28 respectively ($p=0.23$), but at three months were decreased to 2.87 and 4.34 respectively ($p<0.05$). Most patinets (12 out of 13, 92%) whose DAS at three months showed LDA continued to LDA at one year. Logistic regression analysis revealed that only LDA at three months as determined by the DAS was predictive of LDA at one year as determined by the DAS (odds ratio 40.0, $p<0.001$). CONCLUSIONS:A preferable clinical outcome as estimated by the DAS at one year in active RA patients treated with TOF is predicted by the DAS at three months.

W76-5

Tofacitinib, an Oral Janus Kinase Inhibitor: Analysis of Serious Infections in Japanese Patients Across the Rheumatoid Arthritis Clinical Program

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Conflict of interest: Yes

Objectives: Tofacitinib is an oral JAK inhibitor for the treatment of RA. Here, we describe the risk of serious infection events (SIE) in Japanese patients (pts) in the tofacitinib RA clinical program. **Methods:** Data were pooled from Japanese pts in tofacitinib Phase (P)2, P3 and an open-label, long-term extension (LTE) study (A3921041 [NCT00661661]). Pts received tofacitinib 1, 3, 5, 10 or 15 mg BID (P2) or tofacitinib 5 or 10 mg BID (P3/LTE) as monotherapy or with csDMARDs. SIE were coded using MedDRA Preferred Terms. Exposure-adjusted incidence rates (IR; pts with events per 100 pt-years) with 95% confidence intervals (CI) were calculated. **Results:** 556 pts received tofacitinib (total exposure:1704.8 pt-years); 57 pts had 63 SIE. The most common were herpes zoster (n=19), pneumonia (n=8), pyelonephritis (n=5), cellulitis (n=4), gastroenteritis (n=3), *Pneumocystis jirovecii* pneumonia (n=3), pneumonia haemophilus (n=2) and urinary tract infection (n=2). One pt had pulmonary TB. Overall IR (95% CI) for SIE was 3.4 (2.6, 4.4) and was stable over >4.5 years. **Conclusion:** The overall SIE IR in Japanese pts was similar to the global RA tofacitinib population and to the SIE IR seen in Japanese pts treated with bDMARDs. Further monitoring in clinical practice is needed to evaluate SIE risk.

W76-6

Efficacy and Safety of Tofacitinib in Japanese Patients with Rheumatoid Arthritis Stratified by Background Methotrexate Dose Group

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Conflict of interest: Yes

Objectives: To investigate the effect of methotrexate (MTX) dose on tofacitinib efficacy and safety in Japanese RA patients (pts) **Methods:** Data were pooled from a 3-month (mo) Phase 2 (A3921039) and a 24-mo Phase 3 (ORAL Scan) randomized controlled trial. Pts received tofacitinib 1 or 3 mg BID (low-dose; LD), 5 or 10 mg BID with either LD (>0–≤8 mg/week [wk]) or high-dose (HD; >8 mg/wk) MTX. Efficacy endpoints at Mo 3: ACR20/50/70 rates, mean changes from baseline (CFB) in DAS28-4 (ESR) and HAQ-DI. Safety was assessed at Mo 3. **Results:** 202 pts received tofacitinib LD (n=55), 5 mg (n=74) and 10 mg (n=73); 122 received LD MTX and 80 HD MTX. Independent of tofacitinib dose, ACR rates were similar with LD or HD MTX. Mean CFB in DAS28-4 (ESR) for tofacitinib LD, 5 mg and 10 mg were -2.07, -2.55 and -2.89 with LD MTX; -2.10, -2.16 and -2.29 with HD MTX; mean CFB in HAQ-DI were -0.29, -0.53 and -0.71 with LD MTX; -0.54, -0.45 and -0.54 with HD MTX. Fewer tofacitinib LD and 5 mg pts had AEs with LD (50% and 57%) vs HD (67% and 64%) MTX; 74% and 68% of tofacitinib 10 mg pts had AEs with LD and HD MTX. **Conclusion:** Efficacy appeared similar in Japanese RA pts given tofacitinib with LD or HD MTX. AEs were numerically lower when pts received tofacitinib LD or 5 mg BID with LD MTX vs with HD MTX.

W77-1

A Randomized, Double-Blind, Parallel-Group, Phase III Study of Shortening the Dosing Interval of Subcutaneous Tocilizumab Monotherapy in Japanese RA Patients with an Inadequate Response to Subcutaneous Tocilizumab Every Other Week: SHINOBI study

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Conflict of interest: Yes

Objective: To investigate the efficacy and safety of weekly subcutaneous tocilizumab (TCZ-SC QW) monotherapy in Japanese RA patients (pts) with inadequate response (IR) to TCZ-SC every other week (Q2W). **Methods**: Pts with IR to TCZ-SC Q2W were randomly assigned to TCZ-SC QW or TCZ-SC Q2W in 12-week double-blind (DB) period. In open-label period, all pts received TCZ-SC QW until Week 52. The primary endpoint was a change in DAS28-ESR (ΔDAS28-ESR) at Week 12 using analysis of covariance, adjusted by DAS28-ESR at randomization. **Result**: TCZ-SC QW and TCZ-SC Q2W were administered to 21 pts each. TCZ-SC QW was superior to TCZ-SC Q2W for adjusted mean of ΔDAS28-ESR at Week 12 (-2.10 vs. -0.89; the difference: -1.21 [95% CI: -2.13 to -0.30, P=0.0108]). In open-label period, the improvement in DAS28-ESR was observed in TCZ-SC Q2W group and continued in TCZ-SC QW group. In the DB period, adverse events (AE) were reported in 71.4% and 66.7% of pts in TCZ-SC QW and TCZ-SC Q2W group and serious AEs were reported in 1 pt in each group. There was no increase in the incidence of AEs in open-label period. **Conclusion**: The efficacy and safety of TCZ-SC QW was demonstrated in RA pts with IR to TCZ-SC Q2W. Shortening TCZ-SC dosing interval up to QW might be a considerable treatment option for RA.

W77-2

Use experience of Bio-switch treatment of RA patients in our Hospital

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Conflict of interest: Yes

Object: This study aimed to evaluate the effectiveness of Biologics in patients in daily clinical practice. Method:Data were collected retrospectively in 508 RA patients.508 cases were started in our Hospital by March, 2014 from 2003. Result:1) 75% RA patients were started by TNFi.2) There were many switches between the TNFi at first. But the starts from non-TNFi gradually increased. Now the use of the non-TNFi exceeds TNF i recently. 3) The case that continued the first Bio was 31% of the whole. The patients of the remission and discontinuation was 7% of the whole. 4) The about half of the case that started TNFi were choosed anotherTNFi to the second Bio. 5) The most of cases that started non-TNFi were choosed non-TNFi by the second Bio.6) The duration of mean Bio use of the first swich case was approximately two years and three months. The duration of the second and thired Bio use gradially became short. Conclusion: The achievement of the RA treatment target with the first Bio is extremely important.

W77-3

Discontinuation of Certorizumab Pegol (CZP) in patients with rheumatoid arthritis

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Conflict of interest: None

Certorizumab Pegol (CZP) is a unique protein which lacks immunoglobulin Fc region, and has polyethylene glycol. We examined disease

activity score 28 CRP and duration of biologics free or JAK antagonists free (BIO/JAK free) period of 40 cases who has been stopped CZP administration after J-RAPID and HIKARI trial was completed. Patients characteristics are, 34 wemen and 6 men, 57.6±10.2 years of age, body weight 56.7±9.9kg, time after diagnosis 49.4±48.7 months, Steinbrocker Stage I/II/III/IV 0/11/14/15 cases, and class 1/2/3/4 is 7/25/8/0 cases respectively. Duration of CZP administration is 29.6±12.7 months until the end of the study. 18 cases (45%) were BIO/JAK free one year after the discontinuation of CZP, 13 cases (32.5%) were BIO/JAK free two years after the discontinuation of CZP. Conclusion: 18 (45%) cases were able to discontinue CZP for one year.

W77-4

Efficacy of Switching between etanercept, tocilizumab, and abatacept in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To examine what parameter of rheumatoid arthritis (RA) patients is useful to anticipate achieving remission in the patients treated with etanercept (ETN)-tocilizumab (TCZ), ETN-abatacept (ABT) switch. [Methods] We examined RA patients treated with ETN switching to TCZ (group ET) or ABT (group EA) and switching from TCZ (group TE) or ABT (group AE). We examined following parameters at start of biologics, switching, and the last observation; age, RA duration, swollen/tender joint counts, swollen parts, VAS, CRP, ESR, DAS28. We evaluated the rate of clinical remission (SJC ≤1, TJC ≤1, patients VAS≤10mm, CRP≤1 mg/L) in each group at the last observation. [Results] The rate of clinical remission were 36% (8/22) in group ET, 0% (0/9) in group EA, 25% (1/4) in group TE and 0% (0/3) in group AE. In ET group, RA duration of the patients in clinical remission was significant shorter than those not in remission. [Conclusions] Early treatment of biologics might lead to achievement of clinical remission.

W77-5

Efficacy, safety and drug retention rates of tocilizumab in biologically naive and switched patients with rheumatoid arthritis

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Conflict of interest: None

【Objective】To compare the efficacy and safety of TCZ between naive and switched patients with RA.【Methods】We retrospectively evaluate the efficacy, safety, and retention rates of TCZ by classifying 91 patients with RA into two groups of 27 naive and 64 switchers.【Results】Characteristics of patients;naive/switch:onset age (mean) 56/46 years old, age at initiation 64/56 years old, duration of disease 8/11 years, DAS28-ESR4 5.39/ 5.38, HAQ 1.01 /1.24, MTX 3.3/ 6.3 mg/ week, PSL 3.1/3.0 mg/ day. Older age at onset, at initiation and lower MTX were significant in naive compared with switchers. The difference of disease activity and physical dysfunction was not significant between the groups. Improvement of DAS28-ESR and HAQ were maintained in both groups for one year. TCZ continued in 17 naive (63%) and 36 switchers (56%). Retention rates were not significantly different between two groups. The reasons terminated TCZ; naive / switch: adverse events 6 (22%) /14 (22%) cases, lack of efficacy 0/10 cases, remission 1/0 cases. Lack of efficacy increased in switched group.【Conclusions】Efficacy, safety and drug retention rates of TCZ in the switched case were not inferior to naive patients with RA, suggesting the usefulness of TCZ in patients who previously used ≧1 other biologics.

W77-6

Maintenance Treatment using Abatacept with Dose Reduction after Achievement of Low Disease Activity/Remission in Patients with Rheumatoid Arthritis (MATADOR) - A prospective, multicenter single arm clinical trial in

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Conflict of interest: Yes

Objectives: To evaluate the feasibility of maintenance therapy with reduced dose of monthly ivabatacept (ABT). Patients and Methods: RA patients treated with ABT were enrolled during the period between March 2013 and March 2015. Inclusion criteria were 1) age at 20 years or older, 2) under treatment with iv ABT monthly at approved doses, 3) DAS28-CRP lower than 2.7 at least for 6 months, 4) agreed to join this trial with written informed consent, 5) body weight under 125kg. Maintenance with iv ABT at a dose of 250 mg/body/month (MATADOR protocol) was introduced. The primary end point was the proportion of the patients continued with MATADOR protocol at week 48. Results: Fifty-three patients were enrolled and followed for 1-year. MATADOR protocol was continued for 1-year in 81% of the patients. Higher anti-CCP antibody titre above median (>87.5 U/mL) was significantly correlated with discontinuation of MATADOR protocol (HR 4.88 95% CI [1.18-16.7]). Mean DAS28-CRP and remission rate was 1.56 and 88% when ABT reduced and 1.80 and 81% at 1-year, respectively. Structural remission was achieved in 34 out of 42 evaluated patients. Conclusion: Dose reduction of intravenous ABT is a possible choice for maintenance therapy in RA patients after achievement of remission/LDA.

W78-1

Comparison between patients in good progress and not so, by starting Abatacept at our hospital

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Conflict of interest: None

Purpose: To compare the difference between patients in good progress and bad progress by starting Abatacept (ABT). Subject: RA patients who started ABT at our hospital and was able to follow up for a year, whether ABT was continued or not. We identified 23 cases, that was able to continue ABT for a year and the annual DAS28-CRP measure was either in remission or in low disease activity, as in good progress. Rest of the 13cases were identified as in bad progress, 10cases showing DAS28-CRP measure moderate or high, 3cases needed change in medication. We compared all 10 criteria; tender joint count, swelling joint count, CRP, ESR, MMP-3, patient VAS, docotor VAS, DAS28-CRP, DAS28-ESR and modified HAQ (mHAQ) score, at start, 3month, 6month, a year among the two groups. Results: There was no significant difference in all criteria before starting ABT. Good progress group showed better results in joint count, DAS28-CRP, DAS28-ESR at 3month. On addition, CRP, patient

VAS, doctor VAS, mHAQ became better at one year. Discussion: Starting ABT, good progress group showed significantly better results in joint count, DAS28-CRP, DAS28-ESR at an early stage. CRP, patient VAS, mHAQ got better at one year. Criteria that improve at an early stage may be used as a prognostic factor.

W78-2

Tips on selection of biologics for patients with rheumatoid arthritis based on treatment patterns

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Conflict of interest: None

Objective:Participants were RA patients treated with one of three biologics having different mechanisms of action who achieved therapy targets with long-term treatment efficacy. Patients' background characteristics and long-term treatment patterns were evaluated. **Methods**: Between November 2004 and October 2016, 338 RA patients were treated with etanercept (ETN), tocilizumab (TCZ), and abatacept (ABT). These patients were divided into the continuation group and the discontinuation group. Finally, relative dose intensity (RDI) was calculated. **Results**: The 3-year continuation rates of therapy with ETN, TCZ, and ABT were 54.2%, 23.8%, and 35.8%, respectively. The proportion of patients treated with ETN plus concomitant MTX was significantly higher in the continuation group than in the discontinuation group. Mean RDI values (95% CI) over a 3-year period were as follows: 0.95 (0.83-1.06) for 25 mg/week ETN therapy; 0.78 (0.66-0.89) for 50 mg/week ETN therapy; 0.84 (0.76-0.89) for TCZ therapy; and 0.87 (0.79-0.95) for ABT therapy. **Conclusion**: Treatment with ETN plus concomitant MTX showed high continuation rates, and long-term achievement of therapy targets was maintained at a lower dosage (and thus, lower costs). It is beneficial to choose this method over non-TNF inhibitors.

W78-3

Analysis of persistency rate of golimumab in patient with rheumatoid arthritis

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Conflict of interest: Yes

[Purpose] We report the persistency rate of five years with golimumab in RA and analyzed the clinical factor related with persistency rate. [Methods] 149 cases with golimumab, 124 femail, 25 male, mean age of 62.7 years, mean disease duration of 13.2 years, 100g golimumab 30.9% was analyzed by Kaplan-Meier methd and Cox hazard regression analysis. [Results] The 5 years persistency rate of golimumab was 79%, naïve 85%, switch 77%, 50mg 82.3%, 100mg 65.4%. Age, disease duration, golimumab dose, naïve were not related to the persistency rate of golimumab. [Conclusion] 5 years persistency rate of golimumab was 79% which was not related to age. Therefore elderly RA could be continued to use golimumab for long period with efficacy.

W78-4

Efficacy of biologics treatment in RA patients without MTX −Data from Kansai consortium for well-being of rheumatic disease patients (ANSWER Cohort)−

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Conflict of interest: None

【Objective】To evaluate the efficacy of biologics treatments in RA patients without MTX in ANSWER cohort【Method】In ANSWER cohort, we retrospectively analyzed RA patients who had been started biologics treatment without MTX between May 2009 and December 2015.【Result】Total 110 patients (ABT n=31, TCZ n=31, and TNFi: ETN 16, ADA 6, GLM 16, CZP 10) were enrolled. In the baseline characteristics, bio naïve or csDMARDs combination rate was significantly high in ABT group. Each disease activity measured DAS28, SDAI, and CDAI, was moderate and no significant differences among 3 groups. Although, at 12 month, all biologics treatments reduced disease activity, no differences of efficacy measured by DAS28-CRP, DAS28-ESR, SDAI, and CDAI among all groups. Remission rates were ABT 16%, TCZ 16%, TNFi 39%. Persistence rates at 12 month were ABT 87%, TCZ 80%, TNFi 79%.【Conclusion】The efficacy of biologics therapy without MTX for RA may be equivalent if we choose any drug in consideration of a patient background.

W78-5

A Study of Retention and Switching Rates of 1st Line Biologics for Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] This study aimed to analyze the effective usage retention rate of TNF inhibitors and non-TNF inhibitors in rheumatoid arthritis (RA) patients. **[Patients]** Three hundred twenty nine patients who had been treated for more than 5 years since the first introduction of biologics were included in this study. These patients were divided into TNF inhibitor and non-TNF inhibitor groups to investigate the number of patients who progressed to 2nd or 3rd line therapy by 5 years after introduction. **[Results]** TNF inhibitors and non-TNF inhibitors were used as 1st line therapy in 278 and 51 patients respectively. In the TNF inhibitor group, 94 of 278 patients (33.8%) progressed to 2nd line therapy. Thirty-four of these patients were switched to TNF inhibitors and 60 to non-TNF inhibitors. Conversely, 6 of 51 patients in the non-TNF inhibitor group (11.8%) advanced to 2nd line therapy, with 2 switching to TNF inhibitors and 4 to non-TNF inhibitors. Additionally, 25 and 3 patients advanced to 3rd line therapy in the TNF inhibitor and non-TNF inhibitor groups respectively. **[Conclusion]** It appears that non-TNF inhibitors are not inferior to TNF inhibitors as 1st line therapy biologics in terms of retention rate and number of switches to TNF inhibitors.

W78-6

The persistence rate of 2nd and more biologic agents

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Conflict of interest: None

Objective: To compare drug persistence rates of biologic agents after inadequate response to other biologic agents. Methods: All patients treated with biologic therapy for RA at Kitasato University Medical Center were analyzed. They treated with an alternative therapy after a prior inadequate response to anti tumor necrosis factor agent (TNF-i) and/or non-TNF biologic agent (Non-T), The drug retention rates were compared using Log-rank test. Results: 103 treatment courses after TNF-i and/or Non-T failure were available for analysis. 59 were only used TNF-i be-

fore switching to new biologic agent, 14were only used Non-T, and 30 were used both TNF-i and Non-T. The persistence rate of Non-T after inadequate response to TNF-i of Non-T was higher than TNF-i, although it did not reach the statistical significance. On the other hand, the persistence rate of Non-T after both TNF-i and Non-T was significantly higher than TNF-i (p=0.0074). Conclusion: After inadequate response to both TNF and non-TNF biologic agents, patients on a Non-T agent have significantly higher drug persistence rates.

W79-1

Clinical Significance of Serum Amyloid Protein A in Rheumatoid Arthritis Assessment of clinical remission and prediction of structural remission

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Conflict of interest: None

Objective: We investigated the association with remission, how the inflammatory marker is related to estimation of clinical remission and prediction of structural remission. Methods: Patients with active RA in our hospital were treated for several years from 2012 to 2016. CRP and SAA were measured over time, and the joint Xp of 2016 was compared with the Xp of treatment Start. We investigated CRP, SAA at Boolean remission. We investigated the association of CRP, SAA and SAA / CRP (μg / ml / mg / dl) at the start of treatment with an progression in bone erosion and narrowing of joint space. Results: 50 cases. Average age 62 years old, 7 years of disease durations, male / female ratio 3: 7, all cases had positive for rheumatic reaction. At clinical remission, CPR showed all cases negative, but SAA was positive in 3 cases. CRP, SAA and progressions of bone destructions was no relevance, but SAA / CRP> 100 was significantly more progressive. Conclusion: SAA positives are present at the time of clinical remission, because SAA is considered to be highly sensitive to inflammation. It was suggested that the inflammatory cytokine pattern promoting bone destruction amplifies SAA more than CRP. It was suggested that SAA / CRP> 100 is predictive for difficult structural remission.

W79-2

Factors that influence on pain improvement after bDMARD or tsDMARD thrown

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Conflict of interest: None

[Objective] Factors that influence on pain improvement after bDMARD or tsDMARD (BIO) is thrown was investigated and evaluated with our clinical cases. [Methods] 191 patients who have been thrown BIO were enrolled. Patient's pain degree measured with visual analogue scale (PS-VAS) were measured just before and one month after thrown. Relationships between improvement of PS-VAS and numerous factors were evaluated statistically with multiple linear regression analysis (MLR). Statistical significance was set within 5%. [Results] With single mode, sex, each of factors that were measured at start as below, age, history of RA, number of BIO of which already thrown, Sharp/van der Heijde Score, HAQ-DI, patient's global assessment (PGA), evaluator's global assessment (EGA), swollen joint count (SJC), DAS28-ESR, CRP, MMP-3, MTX dosage, tacrolimus thrown, glucocorticoid thrown, had demonstrated significant regression with PS-VAS improvement. However, factor that has shown significant regression with PS-VAS for multiple mode MLR was only PGA. No BIO agent have demonstrated significant regression. [Conclusions] It is suggested that PGA degree have mostly influenced on PS-VAS improvement after BIO in a short term. Kind of BIO agent does not matter.

W79-3

Efficacy, immediate effectivity and safety of Abatacept in combination with Tacrolimus in patients with rheumatoid arthritis

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Conflict of interest: None

【Objective and methods】Efficacy and safety of Abatacept (ABT) in combination with Tacrolimus (Tac) in patients with rheumatoid arthritis (RA) are still largely unknown. We evaluated the efficacy, immediate effectivity and prevalence of infectious diseases in RA patients who were treated with ABT at our hospital by comparing the Tac combination group (7 cases), Methotrexate (MTX) combination group (36 cases) and monotherapy group (26 cases).【Results】The baseline disease activity of the 3 groups were comparable 4.34/4.61/4.66 (DAS28-ESR). A good EULAR response was achieved in 57.1%/11.1%/7.4% at 4 weeks, 57.1%/44.5%/38.5% at 24 weeks. When high disease activity patients were assessed, it was achieved in 100%/0%/12.5% at 4 weeks, 100%/41.7%/37.5% at 24 weeks. The Tac combination group showed greater improvement and also showed immediate improvement of RA. The prevalence of infectious diseases per month in each group was 3.88%/4.40%/2.42%, of severe infection requiring hospitalization was 0.86%/0.31%/0.61%.【Conclusions】The treatment of RA with a combination of ABT and Tac is more effective than that with ABT and MTX or with ABT alone. We have also shown that the combination of ABT and Tac suppressed disease activity more rapidly comparing to ABT and MTX or ABT alone.

W79-4

Use of a 8-week observational period for predicting remission and low disease activity at 52 weeks in RA patients treated with certolizumab pegol ~A MULTICENTER STUDY~

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Conflict of interest: None

[Objectives] This study aimed to provide clinical evidence of an adequate observational period for predicting remission and low disease activity achievement at 52 weeks in RA patients treated with Certolizumab pegol (CZP). [Methods] Participants were all patients registered in a Japanese multicentre registry who were treated with CZP and had at least 52 weeks of follow-up (n = 98). [Results] The mean age was 59.5±14.7 years; the disease duration was 9.4±8.8 years; the patients of receiving MTX was 73 cases (74%) and the patients of previous bDMARDs was 57 cases (61%) Clinical findings related to RA were as follows: tender and swollen joint count, 5.2±4.7 and 5.0±4.0; patient's and physician's global assessment of disease activity, 48.9±27.4 and 42.3±23.3mm; CRP 1.9±2.2 mg/dL; ESR 47.4±34.0 mm/h and DAS-ESR 4.84±1.36. Areas under the receiver operating characteristic curves for the DAS28-ESR and SDAI at each time point for remision achievement at 52 weeks were each 0.578 and 0.702 at baseline, 0.755 and 0.822 at 4 weeks, 0.821 and 0.856 at 8 weeks, and 0.820 and 0.809 at 12 weeks. [Conclusion] This study suggested that eight weeks is an adequate observational period to judge the long-term clinical efficacy of CZP.

W79-5

The effect of the use of glucocorticoids on health assessment questionnaire in patients with rheumatoid arthritis in clinical remission – Data from Kansai consortium for well-being of rheumatic disease patients (ANSWER Cohort)-

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Conflict of interest: None

【Objective】To investigate the effect of the use of glucocorticoids (GCs) in patients with rheumatoid arthritis (RA) who had maintained clinical remission on damage-related health assessment questionnaire (DAM-HAQ). 【Methods】Among 2,649 patients with RA who achieved DAS-ESR<2.6 after 2013 in the ANSWER Cohort, 1,171 patients who had maintained DAS-ESR<2.6 were eligible. We calculated odds ratio (adjOR) (95% confidence interval) of the use and dose of GCs adjusted for 12 covariates in multiple logistic regression model. 【Results】Characteristics of patients were as follows (median (IQR), proportion). The age was 61 (48-68) years, female was 70.6%, disease duration was 4.5 (1.7-10.7) years, RF-positive was 64.4%, ACPA-positive was 70%, DAS-ESR was 2.0 (1.6-2.6), HAQ-DI score was 0.125 (0-0.5). Of the 1,171 patients, 158 patients had been treated with oral GCs, and median dose of GCs was 4.5 (2.5-5.5) mg/day. Two hundred eighty-seven (24.5%) patients' yearly change of HAQ-DI score incresed. The adjOR of the use of GCs was 2.01 (1.07-3.76). Whereas the adjOR of the daily dose of GCs <5mg was 1.61 (0.73-3.56), that of GCs≧5mg was 2.65 (1.11-6.34). 【Conclusions】The use of GCs in the patients with sustained remission was the risk factor of progression of DAM-HAQ dose-dependently.

W79-6

Utility of Gray scale ultrasound joint assessment in the prediction of the assessment of therapeutic response in the biological therapy in patients with RA

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Conflict of interest: None

[Objectives] The aims of this study were to assess the value of the US as a screening tool to predict therapeutic response in RA patients. [Methods] A total of 86 consecutive RA patients who were classified by the rheumatologists as being in remission were studied. Disease activity was assessed by DAS28 -CRP and SDAI. US examination for joint effusion and synovial hypertrophy (SH) was carried out by grey-scale imaging, and synovial vascularization was assessed by power Doppler (PD) of 48 joint regions (28 joints). [Results] Remission was available for 44 patients (51.2%) at 54 week. The cut-off values in the remission at 54 week for baseline SHI and DSI significant variable calculated from the ROC curves were: SHI ≦ 34 and DSI ≦ 7. The cut-off values of SHI and DSI showed the highest sensitivity and specificity for remission at 54 week (SHI; 86.3% and 71.5%, DSI; 77.2% and 48.8%). Based on these cut-off values, all variables were dichotomized and a logistic regression was performed. The odds ratio was: 6.7 [1.9–27.4] for SHI ≦ 34. [Conclusions] US assessment would be highly useful predictor in achieving the clinical remission.

W80-1

Cost and effectiveness analysis of DMARDs therapy (annual report from Ninja 2015)-the cost of biologics stopped to increase?-

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Conflict of interest: None

[Objectives] To evaluate the balance between the clinical effects of recent anti-rheumatic treatment and its cost [Method] The Data from RA patients registered in the large cohort database *(NinJa)* in 2002-2015 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 490,000 yen / patient in 2015, less than 10,000 yen higher than the cost in 2014. The rate of the cost of biologics was 75.8% and decreased slightly. Usage rates of ABT and TCZ, whose prices are cheaper than other biologics, increased constantly. [Conclusion] NHI price revision leaded to the stop of increase of the DMARDs' cost in 2012 and 2014. The increase of the biologics cost was not so much in spite of no price revision in 2015. Therefore, this tendency may continue hereafter. This tendency was thought to be caused by the increase of the usage of cheaper biologics and the decrease of the dosage of biologics.

W80-2

Effect of patient education on self-injection of biologic agents in rheumatoid arthritis

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Conflict of interest: None

[Objectives] The present study was undertaken to investigate the effect of patient education on self-injection of biologic agents in rheumatoid arthritis. [Methods] This study included 70 RA patients with self-injection of biologic agents who answered the questionnaires about self-management of biologic agents both in May 2015 and February 2016. The patients with mis-recognition were educated after first questionnaire. [Results] Recognition was improved for discarding method, recap, withdrawal in having a cold and perioperative withdrawal, but not improved for hand washing before self-injection. The patients with mis-recognition for discarding method and hand washing in both questionnaires were significantly younger than without mis-recognition. As the patients with mis-recognition for withdrawal in having a cold and perioperative withdrawal in both questionnaires, the proportion of men was significantly higher than without mis-recognition. [Conclusions] Patient education after questionnaire has efficacy for discarding method, recap, withdrawal in having a cold and perioperative withdrawal. Younger and male patients have a tendency to have mis-recognition even after patient education.

W80-3

The present situation of transition to our department from Tokyo Metropolitan Children's Medical Center

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Conflict of interest: None

【Objective】It has been said lately that patients with children's clonic disease should continue to be treated by transiting to clinical department for adult. However, this is the repot about patients who were referred to our department from Tokyo Metropolitan Children's Medical Center (TMCMC). 【Method】We studied patients' diseases and hospital situa-

tions from March 2010. The total number of patients who were referred was 22.【Result】12 of 22 were patients who had ever been treated before at TMCMC. They all were SLE patients. The onset age was 12.6 yeas old on an average (8-15). The average age was 21.1 years old when they were referred. They continue to attend our department, no one drops out so far.【Discussion】Their transitions were done by a usual letter of reference without any special programs, but there still are a lot of patients with connective tissue diseases who are beyond 16 year-old. TMCMC might choose patients who had few problems about transition. We are working on transitional medicine for children's clonic diseases, and have to find any problems more.【Conclusion】Their transition is so far successful.

W80-4

Actual condition survey about medication adherence in patients with rheumatoid arthritis

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Conflict of interest: None

[OBJECTIVE] The proportion of elderly patients with rheumatoid arthritis (RA) becomes higher. Also residual medication has become important issue. It will be necessary for keeping medical care safety that we provide the nursing to allow for age of the patients. We investigate the characteristics of the patient's behavior for medical care. [METHODS] We examined 341 patients with RA by questionnaires about the influence of age. Research contents are as follows: 1) Residual medication (MTX, csDMARD and self-injection biologics), 2) Explanation of infection 3) Understanding for specific infections 4) Knowledge of side effects 5) Motivation to understand side effects. We classified A:22-49, B:50-69, C:70-88 according to age. [RESULTS] 1) MTX was not related to age. csDMARDs, biologics were related to increased age. 2) A92.7%, B82%, C65.3% recognize explanation. 3) The highest answer was respiratory diseases. 4) A70%, B68.1%, C47.7% understood. 5) A94.9%, B96.9%, C96.6 had motivation. [CONCLUSION] Elderly patients tend to comply with prescription drugs compared to young patients, but the elderly patients have little knowledge of side effects. However, they have motivation to gain their knowledge, so we believe that active intervention will be beneficial effect on medical care.

W80-5

Clinical features of idiopathic multicentric Castleman disease in Japan

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Conflict of interest: None

【Aims】Idiopathic multicentric Castleman disease (iMCD) is a unique lymphoproliferative disorder exhibiting various symptoms due to excessive IL-6 production. No large-scale epidemiological investigation has been conducted yet, thus we should clarify its clinical features and optimal treatments.【Method】We selected and analyzed 149 cases of defined iMCD from 201 cases of a retrospective MCD registry in Japan.【Results】The median age at diagnosis was 49 years (84 male, 65 female). Nine cases were hyaline-vascular type, 59 plasma cell type, 44 mixed type, and 37 unclassifiable by histopathology. Major symptoms were fever (57%), anemia (Hb<12 g/dL, 81.2%), thrombocytosis (>45x10^4, 8%), thrombocytopenia (<10 x 10^4, 42.9%), anasarca (43.6%), renal dysfunction (30.8%), lung disease (13.4%), and skin leasions (12%). Serum IL-6 level in most cases was elevated (median 25.3 pg/mL). One hundred twenty-five cases were treated with glucocorticoids, 70 with tocilizumab, and 15 with cyclosporin A; 10 were observed without treatment. Sixteen cases died; the most common cause was infection (13 cases).【Conclusion】Despite various limitations of a retrospective investigation, this study provides valuable information concerning the clinical features and treatments of iMCD in Japan.

W80-6

Therapeutic response and prognosis of PMR (polymyalgia rheumatica)

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Conflict of interest: None

[Object] The PSL get consensus as a therapeutic drug with PMR treatment. However, we experienced we could not reduce the quantity of the PSL. There is the report that the weight loss effect of the steroid is provided by adding an antiIL-6 therapeutic drug together when we experienced treatment difficulty. We conducted a comparison study with PMR patients to clarify the actual condition of PSL mono-therapy and MTX combination therapy. **[Methods]**We examined 38 cases who treated by us until 2016 from 2009, and compared with PSL mono-therapy group P (GP) and Add-on MTX therapy group M (GM). **[Results]**The mean onset age was 73.3years. All patients started treatment with PSL therapy. For PSL resistance, 7 cases added MTX therapy among them. In the final observation, we could reduce PSL dosage to 2.9mg in GP. On the other hand, in GM, we could reduce them to 3.2mg. In the period to arrive at the weight loss target, we examined the mean period required for the reduce from 10mg to 5 mg and from 5mg to 2.5mg. In GP, the period was 8.7months, 7.5months, respectively. And in GM, it was 4.9 months, 7.0 months, respectively. **[Conclusions]**We suggest that we could reduce PSL for treatment and shorten the period of the reduce steroid by adding MTX therapy in the case of steroid resistance in PMR.

W81-1

Influence of visceral fat on atherosclerosis in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] It was previously reported that RA patients have altered body composition (reduced muscle mass and increased fat mass). We hypothesized that some RA patients may have increased visceral fat without obesity. We also examined the influence of visceral fat on atherosclerosis. [Methods] We recruited 142 patients with RA from the KURAMA cohort. Age 63.2±12.2 years, male14%. Visceral fat area (VFA) and common carotid artery intima media thickness (IMT) were examined by dual bioelectrical impedance analysis and ultrasonography, respectively. Multiple liner regression analysis was performed to assess IMT as dependent variable, and body composition index, traditional risk factors of cardiovascular diseases and RA related factors as independent variables. [Results] 21 (14.8%) subjects had VFA≥100cm^2, 4 (2.8% of the whole) subjects had both BMI<25 and VFA≥100 cm^2. Age, visceral fat/subcutaneous fat ratio (V/S ratio), muscle mass percentage, SBP, LDLchol and eGFR were correlated with IMT. In multiple regression analysis, age (β,0.41; p=0.0008) and V/S ratio (β,0.29; p=0.028) remained as the independent factor significantly associated with IMT. [Conclusion]

Increased visceral fat may accelerate atherosclerosis in RA patients.

W81-2

Adult Human Parvovirus Infection in Our Hospital

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Conflict of interest: None

Purpose: Human parvovirus B19 (HPVB19) infection is the cause of erythema infectiosum in children. HPVB19 infection often cause acute arthritis without erythema in adult. This infection is an important disease to differentiate connective tissue disease (CTD). We examined the characteristics of adult HPVB19 infection. **Method:** We examined suspect cases of HPVB19 infection in our hospital from Mar to July 2016. We compared characteristics of 15 positive (+) and 10 negative (-) HPVB19 IgM cases. **Result:** HPVB19 IgM (+); Mean age: 42.4, M1, F14, Clinical findings: musculoskeletal (MS) symptom: 13, skin rush: 6, fever: 5, children contact: yes: 12, unknown: 3. Lab data: pancytopenia: 4, normal CRP: 11, low complement: 5, ANA (+): 3, CTD complication: 2. HPVB19 IgM (-); Mean age49, M3, F7, MS: 3, skin: 3, fever: 4, children contact: unknown: 9, yes1. Lab data: pancytopenia: 0, normal CRP: 4, low complement: 2, ANA (+): 3, CTD: 3. **Conclusion:** HPVB19 infection often take atypical clinical course in adult. So, it is important to be confirmed by serological test to differentiate other CTD etc. PVB19 IgM is allowed to be measured only in pregnant period in Japanese national health insurance program. We hope to be able to check it for differentiation between HPVB19 infection and CTD etc.

W81-3

Anxiety factors by different age, sex and disease duration among patients with RA

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Conflict of interest: None

INTRODUCTION Our hospital was a secondary level, general hospital. We treated mainly usual orthopedics disease and trauma patients. To take more time to support RA patients, we had established an outpatients service for RA patients since 2014. OBJECTIVE We aimed to clarify the anxiety factors among RA patients and the satisfaction for nursing supports. METHODS Study duration was from June to August 2016. We performed questionnaire survey on the office visit. The questionnaire included age, sex, disease duration and open ended question about anxiety and satisfaction. We analyzed description data with a text-mining. RESULTS Fifty four patients were evaluated. The forties connected with “kind”, “doctor” and “nurse”. The fifties whose disease duration within a year connected with “the biological drugs”. The sixties and seventies connected with “anxiety”. CONCLUSION We started the biological drugs to the fifties smoothly because of their economic stability after child raising. The female sixties and seventies felt anxiety of maintaining their current life. The eighties might be the generation to need more nursing supports. The establishment of the outpatients service for RA patients made us support the patients with enough time and meet the needs of the patients.

W81-4

Two cases with SAPHO syndrome which presented femoral lesion

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Conflict of interest: None

SAPHO syndrome is the disease which includes arthro-osteitis with or without skin lesion and chronic recurrent multifocal osteomyelitis. Although common sites of this disorder are sternum, clavicle and spine, we report two patients with SAPHO syndrome which presented femur lesion. The first case is a 46 years old man with the right femoral pain. Because the pain persisted for a month, MRI was performed. MRI showed osteomyelitis and he came to receive further examination. We performed bone biopsy. The pathological examination showed the invasion of the neutrophil and osteoclasts. There was no malignancy and no bacterial culture. He was diagnosed SAPHO synd. and has been now treated with SASP and MTX. The second case is a 35-year-old man who had history of pustulosis palmaris and plantaris (PPP). He suffered from the right femoral pain and was diagnosed SAPHO. The pain remitted by NSAIDs, but the pain got worsen half a year later., he came to receive further treatment. MRI showed myelitis and thickening of the cortical bone These results did not contradict the diagnosis of SAPHO synd and he has been treated by SASP, MTX and Bisphosphonate. In SAPHO syn, femoral lesion is rare. This disease should be considered when there is osteomyelitis or hyperplasia of the cortical bone in femur.

W81-5

A case of achilles tendinopathy probably caused by atorvastatin

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Conflict of interest: None

【Case】A 76 year-old woman visited our hospital, complaining morning stiffness for a year and bilateral heel pain by 20 minute-walk for a month. She had been taking atorvastatin, candesartan cilexetil, amlodipine, limaprost alfadex, minodronic acid hydrate and sennoside. Atorvastatin has been taken daily for about 8 years. Laboratory studies showed CRP 0.16mg/dl, ESR 17mm/hr and ANA x320 (Ho and Spe) without other autoantibodies. X-ray revealed coincidental osteoarthritis of both hands only. A musculoskeletal ultrasonography showed not enthesitis of the heels but bilateral achilles tendinopathy. As atorvastatin might be a causative agent (Chazerain P et al. Joint Bone Spine. 2001;68:430-433.), only atorvastatin was stopped, resulting disappearance of her heel pain within 2 weeks. Because her LDL cholesterol level was elevated, pitavastatin instead of atorvastatin was started 7 months after her first visit. Re-examination of ultrasonography after 8 months revealed low grade inflammation in only right achilles tendon. She was well when she visited our hospital after 10 months.【Discussion】Atorvastatin might be the cause of achilles tendinopathy because her heel pain disappeared only by cessation of it. We must bear in mind that atorvastatin has a potency to cause achilles tendinopathy.

W81-6

Two cases of arthralgia following CELESTAMINE withdrawal

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Conflict of interest: None

Case1: A 56-year-old women had complained polyarthralgia for two months. CRP, RF, ACPA and ANA were negative. MRI showed no sign of synovitis and bone edema. Her sympton gradually disappeared and it took six months until she had no arhtralgia. She admitted that she had taken CELESTAMINE for four years and cease taking it right before she developed arthralgia. Case2: A 52-year-old women had complained polyarthralgia for six months. There is no sign of arthritis, but it became clear by an interview that she took CELESTAMINE for over five years and it was changed before she developed symptoms. Laboratory test were within normal range except for cortisol (3.76μg/dl) and ACTH (35.3pg/ml). She was diagnosed with adrenal insufficiency (steroid withdrawal syndrome). Prednisolone was started and her symptoms improved. CELESTAMINE (Betamethasone */d*-Chlorpheniramine Maleate) is used for skin symptom and allergic rhinitis, but patients end even medical personnel as well may not recognized it contains steroid component. In case of difficulty in diagnosis with arthralgia, accurate medical history including CELESTAMINE is important to find out adrenal insufficiency.

W82-1

Functional and quantitative changes of CCR6+ type3 innate lymphoid cells in murine collagen-induced arthritis

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Conflict of interest: None

«Background»Innate lymphoid cells (ILCs) are a group of lymphocytes that lack antigen-specific receptors. ILCs are classified into three subsets, ILCs 1, 2, and 3, based on their patterns of cytokine production. ILC3s produce cytokines such as IL-17, IL-22, and TNF-α, which play critical roles in inflammatory arthritis. In this study, we tried to evaluate the ILCs in various tissues isolated from collagen induced arthritis (CIA) model mice, in order to clarify the role of ILCs in the development of rheumatoid arthritis (RA). «Method»We isolated lymphocytes from bone marrow, spleen, peripheral blood, local lymph nodes and joints in normal and CIA model mice. ILC subsets were determined by flow cytometry. Gene expression patterns of the transcription factors (TFs) and cytokines were measured by quantitative real time PCR. Finally, we compared the absolute cell number, the polarization and gene expressions patterns of TFs and cytokines of each ILC subsets in normal and CIA model mice. «Result»The gene expression levels of TFs and cytokines in CCR6+ILCs were elevated after the induction of arthritis, in addition to the skew toward CCR6$^+$ILC3s in joints. «Conclusion» CCR6+ILC3 may play some roles in pathogenesis of RA through its production of cytokines.

W82-2

Effects of interleukin-2/anti-interleukin-2 monoclonal antibody immune complex to regulatory T cells on collagen-induced arthritis

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Conflict of interest: None

Objectives: To clarify the function of IL-2IC to regulatory T (Treg) cells in autoimmune arthritis, we examined the effects of IL-2IC administration during the course of collagen-induces arthritis (CIA) model and analyzed Treg cells. Methods: CIA model was performed with the compound in DBA/1 mice. Mouse paws were scored for arthritis using a macroscopic scoring system. CD4$^+$CD25$^+$ Treg cells were analyzed for suppressive activity against proliferation of effector CD4$^+$ T cells. Intracellular cytokines such as IL-10, IL-17 and IFN-g were analyzed spleen and lymph node cells using flow cytometry by intracellular staining. Results: To define the effect of IL-2IC of disease induction, we administered IL-2IC, observed a significant decrease in both the incidence and severity of arthritis. The expression of inflammatory cells in arthritis was reduced by IL-2IC. Injection of IL-2IC effectively elicited expansion of Tregs and induced the IL-10 expression of Tregs in spleen and lymph node cells. The IFN-g and IL-17 expression of CD4$^+$ T cells in spleen were decreased by injection of IL-2IC. Conclusions: These observations indicate that IL-2IC increase the number of Tregs. Furthermore, IL-2IC activate suppressibility of Tregs and suppress the IFN-g and IL-17 expression of CD4$^+$ cells.

W82-3

Lupus-prone SLAM haplotype exerts monocytosis and develops specific phenotype of autoimmune disease introduced by *Yaa* mutation

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Conflict of interest: None

[Object] We previously obtained a 129-derive FcγRIIB-deficient C57BL/6 (B6) mice, which spontaneously developed rheumatoid arthritis (RA). The introduction of the *Yaa* mutation, which shows dupulication of *Tlr7* gene, to the FcγRIIB-deficient B6 (B6.FcγRIIB-/-.*Yaa*) mice developed lupus like nephritis but not RA. By extensively backcrossing 129-based FcγRIIB-deficient mice to B6 mice, we established wildtype FcγRIIB and 129-derive autoimmune-prone SLAM haplotype (*Slam*^{129}). We examined the phenotype of *Slam*^{129} mice, and also *Slam*^{129}. *Yaa* mice by introducing *Yaa* mutation to these mice. [Methods] We analyzed peripheral blood monocytes and also serum autoantibodies as well as immunohistopathological findings of kidneys and lungs. [Results] *Slam*^{129} mice showed monocytosis but they did not show any pathogenic autoantibodies. While *Slam*^{129}. *Yaa* mice showed significant increase the serum levels of anti-RNP antibodies and anti-Sm antibodies without elevation of anti-dsDNA antibodies. They developed nephritis but the pathological score was significantly lower than B6.FcγRIIB-/-.*Yaa* mice. [Conclusion] Autoimmune-prone SLAM haplotype plays a role for monocytosis and *Slam*^{129}.*Yaa* mice developed specific lupus phenotype with elevation of anti-RNP and anti-Sm autoantibodies.

W82-4

Essential role of Egr2/Egr3 in CD4$^+$CD25$^-$LAG3$^+$ regulatory T cell-mediated regulation of humoral immune responses

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Conflict of interest: None

[Objective] Early growth response gene-2 (Egr2) is required for T cell anergy induction and CD4$^+$CD25$^-$LAG3$^+$ regulatory T cell (LAG3$^+$ Treg) characteristically express Egr2. Intriguingly, Egr2 is a susceptibility gene in SLE, and T- and B-cell specific Egr2/Egr3 double knockout (Egr2/3DKO) mice develop more severe lupus-like autoimmune symptoms than Egr2 conditional knockout (Egr2CKO) mice using a CD2-Cre driver. These studies suggest a tight connection between Egr2/3 and development of SLE. In this study, we examined the role of Egr2 and Egr3 in LAG3$^+$ Treg-mediated regulation of humoral immune responses. [Methods] We generated T- cell specific Egr2CKO (Egr2$^{fl/fl}$CD4-Cre$^+$) and Egr2/3DKO mice (Egr2$^{fl/fl}$Egr3$^{fl/fl}$CD4-Cre$^+$), and analyzed phenotypes. We also addressed the function of Treg from these mice. [Results] Egr2/3DKO mice developed early onset lupus-like syndromes compared to Egr2CKO mice, associated with excessive germinal center reactions due to defective TGF-b3 production from Egr2-expressing LAG3$^+$ Treg. Ltbp3 expression maintained by Egr2/3 was required for effective TGF-b3 secretion. [Conclusions] Our findings suggest that Egr2/3 have important roles in regulating TGF-b3 production from Treg for the maintenance of self tolerance and prevention of autoimmune disease.

W82-5

Cell type-specific analysis of the effect of inhibitory IgG Fc receptor IIb deficiency on *Yaa*-induced murine lupus

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Conflict of interest: None

[Object] B6.FcγRIIb$^{-/-}$.*Yaa* mice develop lethal lupus nephritis. This study was performed to define the cell type specific role of FcγRIIb in the disease. [Methods] B cell (CD19^{Cre}.*Yaa*), myeloid cell (C/EBPα^{Cre}.*Yaa*), and dendritic cells (DC) (CD11c^{Cre}.*Yaa*) specific FcγRIIb-deficient B6.*Yaa* mouse strains were established, and the disease severity was compared with B6.FcγRIIb$^{-/-}$.*Yaa* mice. [Results] CD19^{Cre}.*Yaa* mice developed milder lupus nephritis compared to B6.FcγRIIb$^{-/-}$.*Yaa* mice, indicating that FcγRIIb deficiency on only B cells is not sufficient for the development of severe disease. C/EBPα^{Cre}.*Yaa* mice developed similar mild disease as CD19^{Cre}.*Yaa* mice whereas CD11c^{Cre}.*Yaa* stayed disease free. B cell activation in C/EBPα^{Cre}.*Yaa* mice was well correlated with increased frequency of activated Gr-1^{-} monocytes. Transcriptome analysis revealed that BSF-3, IL-10, IL-1β were up-regulated in Gr-1^{-} monocytes. [Conclusions] FcγRIIb on B cells and monocytes controls B cell activation and autoimmune responses via different but synergistic pathways in *Yaa*-associated lupus nephritis.

W82-6

In vivo role of neutrophil extracellular traps (NETs) in the autoimmune mouse model and inhibition of NETs as a potential therapy target

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Conflict of interest: None

Backgrounds: Neutrophil extracellular traps (NETs) is associated in many autoimmune diseases, but their roles in vivo are not revealed sufficiently. In a lymphopenia-induced proliferation (LIP)-induced systemic autoimmune model, microbiota mediate the LIP-induced Tfh generation and the autoimmune diseases. Then we investigated the involvement of NETs in this model. **Methods**: CD4^{+}CD25^{-} T cells were isolated from spleens from wild type mice and were transferred to nude mice. Before the adoptive transfer, the NETs inhibitors were administered intraperitoneally to the recipient mice. Splenocytes from the recipient mice were analyzed. Detection of antinuclear and anti-parietal antibody and the histological assessment were carried out. **Results**: The NETs inhibitors decreased the generation of Tfh cells and autoantibody production, and ameliorated gastritis and colitis in LIP model. Inflammations in salivary gland, ovary, and thyroid, which are isolated from the bacteria, were not affected. **Discussion**: Involvement of NETs in the recognition of microbiota in the induction of Tfh cells and autoantibodies in the LIP models were indicated. NETs are also shown to be directly involved in the pathogenesis of gastritis and colitis. Inhibition of NETs could be a potential therapeutic approach.

W83-1

The 8-joint ultrasonography assessment is useful for monitoring therapeutic response in rheumatoid arthritis

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Conflict of interest: None

[Object] To investigate the utility of the 8-joint ultrasonography (US) assessment in monitoring response to treatment for RA. [Methods] Power Doppler (PD) US was performed in 24 joints (all PIP, MCP, bilateral wrist and knee joints) as comprehensive evaluation in 24 RA patients treated with certolizumab pegol or tofacitinib. Before and after treatment, PD signals were scored semiquantitatively in each joint. Total PD score-24 and total PD score-8 were calculated by summing up PD scores of the 24 joints and the selected 8 joints (bilateral second and third MCP, wrist, and knee joints), respectively. [Results] Change of total PD score-8 by treatment exhibited strong correlations with the changes of disease activity indices, SDAI ($r_s = 0.86$, $p < 0.0001$) and DAS28-CRP ($r_s = 0.86$, $p < 0.0001$). The correlation coefficients were comparable with those for total PD score-24. Although the change of total PD score-8 correlated with the changes of swollen joint count, tender joint count, CRP and ESR, there were no significant correlations between the changes of total PD score-8 and the changes of patient's global assessment and evaluator's global assessment. [Conclusions] The 8-joint US assessment can be a useful method for monitoring response to treatment in RA patients.

W83-2

Importance of ultrasonography of metatarsophalangeal joint in diagnosis of rheumatoid arthritis

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Conflict of interest: None

[Objectives] Although ultrasonography (US) of joints (jts) is important in diagnosis of RA, it is difficult to examine all jts. It has been basic set of US to examine PIP, MP, wrist and metatarsophalangeal (MTP) in our institute. We retrospectively investigated our data to evaluate importance of US of MTP. [Methods] 337 cases in whom US was performed for diagnosis were included. 134 cases were diagnosed as RA. Detection rates of grey scale score (GS), pulse Doppler score (PD) were investigated. The results in RA group were compared with that in cases who were not diagnosed as specific disease (undiagnostic group). [Results] 422/1340 jts (31.5%) were evaluated as grade 1 (G1) and over in GS of MTP in RA group. 137/1340 jts (10.2%) were evaluated as G1 and over in PD of MTP in RA group. In contrast, 125/760 jts (16.4%) were evaluated as G1 and over in GS of MTP in undiagnostic group. 10/760 jts (1.3%) were evaluated as G1 and over in PD of MTP in undiagnostic group. 14 cases in 134 cases (10.4%) had positive in both GS and PD with negative GS and PD in PIP, MP and wrist. [Conclusions] Some patients were evaluated as negative in US of joints if only finger and wrist were examined. MTP should be examined in addition to fingers and wrist if time and stuff are enough to perform.

W83-3

Active synovitis with oteitis progressed to residualsynovitis leading to disease flare in rheumatoidarthritis (2nd report)

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Conflict of interest: None

Objective: To study pathology of ultrasound detected residualsynovitis in rheumatoid arthritis (RA) with clinical improvementstate. Methods: Sequential observation for finger joints by ultrasound andMRI were performed. Joints with positive synovial vascularity detectedby ultrasound at baseline were judged as active synovitis. Joints withpositive synovial vascularity (>semi-quantitative score grade2) at the24th week were judged as residual synovitis (R-synovitis). Joints with osteitis at baseline werejudged by MRI. Patients who need therapeutic intenfication were diagnosed as disease flare. Results: 16 of 21 patients who achieved clinical improvement werestudied. Totally 320 finger joints were analyzed. 116 joints hadactive synovitis at baseline and 47 joints had residual synovitis atthe 24th week. Active syonovitis with osteitis weresignificantly in accordance with residual synovitis (P<0.0001). Five of the 9 patients with R-ynovitis showed disease flare. None of the 7 patients without R-synovitis showed disease flare (P=0.034). Conclusion: Active synovitis with osteitis progressed to residual synovitis. Residual synovitis might have relation with flare in RA.

W83-4

Semi-quantitative evaluation of extra-synovial soft tissue inflammation in the shoulders of patients with polymyalgia rheumatica and elderly-onset rheumatoid arthritis by power Doppler ultrasound

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Conflict of interest: None

[Objectives] To develop a scoring system for evaluating the extra-synovial soft tissue inflammation of the shoulders in patients with polymyalgia rheumatica (PMR) and elderly-onset rheumatoid arthritis (EORA) with PMR-like onset using ultrasound (US). **[Methods]** We analyzed stored power Doppler (PD) images obtained by the pretreatment examination of 15 PMR patients and 15 EORA patients with PMR-like onset. Scoring system for evaluating the severity of PD signals adjacent to the anterior aspect of the subscapularis tendon was designed. **[Results]** A semi-quantitative four-point scale scoring for the hyperemia on the subscapularis tendon (HSScTS) was proposed as follows in brief: 0 = absent or minimal flow, 1 = single vessel dots or short linear-shape signals, 2 = long linear-shape signals or short zone-shape signals, or 3 = long zone-shape signals. The intra- and inter-observer kappa statistic for HSScTS was 0.852 and 0.745, respectively. HSScTS was well correlated with the quantitative evaluation of PD-positive pixels. Bilateral HSScTS positively correlated with CRP but not with MMP-3. **[Conclusions]** We proposed a reliable scoring system using US for the evaluation of extra-synovial soft tissue inflammation of the shoulders in patients with both PMR and EORA with PMR-like onset.

W83-5

Comparison of shoulder bursitis in localization and severity between polymyalgia rheumatica and elderly-onset rheumatoid arthritis with polymyalgic-onset

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Conflict of interest: None

[Objectives] To investigate the differences in shoulder synovial lesions between polymyalgia rheumatica (PMR) and elderly-onset rheumatoid arthritis with PMR-like onset (pm-EORA) using ultrasound (US). **[Methods]** We analyzed stored US images obtained by the pretreatment examination of 15 PMR patients and 15 EORA patients with PMR-like onset. A four-point semi-quantitative evaluation of both grey-scale (GS) and power Doppler (PD) was done for biceps tendon sheath (LHB), glenohumeral joint (GHJ) and subacromial/subdertoid/subcoracoid bursa (SAB/SDB/SCB). **[Results]** Intra- and inter-observer concordance was better in bursitis than in LHB or GHJ. Pm-EORA group tended to be high in severity of each synovial pathologyies. Significant difference was observed in the GS grade of bursitis and PD grade of bursitis. Analyzing separately three types of bursitis revealed that GS grade of SAB was significantly higher in pm-EORA group than in PMR group. **[Conclusions]** Although previous reports have suggested that shoulder bursitis is the hallmark of PMR, our data revealed that the proliferative bursitis, especially in SAB, is more severe in the EORA patients with PMR-like onset.

W83-6

New Image Analysis of Bone Erosion for Patients with Rheumatoid Arthritis: a Study by HR-pQCT

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Conflict of interest: None

[Object] HR-pQCT is a high resolution CT dedicated to human extremities with a voxel size of 0.06mm. It was developed in Switzerland in 2004, and installed only in Nagasaki University in Japan. The purpose of this study is to develop the method to quantify erosions of RA by HR-pQCT. [Methods] Five patients with RA (71±10 years, all female) participated in this study. The second and third MCP joints was scanned by HR-pQCT (XtremeCT II, Scanco Medical, Switzerland) at the voxel size of 61 μm. Erosions were detected and their volume was measured at 4 regions: metacarpal bone and proximal phalanx side of the second and third MCP joints. Using a dedicated software (TRI/3D-BON, Ratoc System Engineering, Tokyo), concave regions on the bone surface around the MCP joints were extracted semiautomatically, and their volume was measured. [Results] In a total of 20 regions (5 patients, 4 regions), 11 erosions were detected by HR-pQCT (9 erosions: metacarpal, 2 erosions: phalanx side). The volume of erosions was average 3.51mm^3, minimum 0.53mm^3, and maximum 14.4mm^3. [Conclusions] We developed the method to quantify the volume of erosions semiautomatically at MCP joints of RA patients. It is possible to be applied for the analysis of the drug efficacy in the future.

W84-1

The assessment of median nerve stiffness measured by elastosonography in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] The aim of this study was to compare the elasticity of the median nerve between patients with rheumatoid arthritis (RA) and controls by quantitative elastosonography. [Methods] Four hundred two hands in 201 patients with RA and 222 hands in controls were included. All participants were examined both wrists. The inlet of the carpal tunnel at the scaphoid-pisiform level and the proximal portion of the car tunnel inlet were scanned in a transverse plane. The cross-sectional area (CSA) and the elasticity of the median nerve were evaluated. [Results] The CSA of the median nerve at the level of inlet of the carpal tunnel and proximal portion of the carpal tunnel inlet were not significantly different in both groups. Strain ratio in the patients with RA were significantly higher than those in the controls (2.66 vs 2.20; p=0.003 in right hand, 2.59 vs 2.13; p=0.002 in left hand) at the inlet of the carpal tunnel level. However, strain ratio at the proximal portion of the carpal tunnel inlet level was not significantly different in both groups. [Conclusions] The median nerve stiffness measured by elastosonography in patients with RA was higher than controls. This results suggest that inflammation of flexor tendon and wrist joint may generate fibrotic change for median nerve.

W84-2

Ultrasound (MSKUS) findings of feeding vessels (FV) and bone surface irregularity (BSI) in wrist joints (WJ) of healthy volunteers (HV)

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Conflict of interest: None

Object: To clarify the distribution (DIS) of FV and BSI in WJ of HV **Methods:** The dorsal side of WJ was scanned with 2D-probe in HV. The DIS and symmetry (S) of FV in the capsule and the extensor (E.) tendon sheath (TS), and the evaluation of BSI at Lunate (Lu) were validated. **Results:** The DIS and S of FV in HV (n=30) were near-Trapezoid (Rt100%, Lt100%, S100%), E.digitorum TS (Rt86.7%, Lt66.7%, S43.3%), E.digiti minimi TS (Rt30%, Lt30%, S10%), near-Capitate (Rt23.3%, Lt30%, S10%), near-TFCC (Rt16.7%, Lt30%, S6.7%), distal radial side of radiocarpal joint (Rt20%, Lt23.3%, S0%), distal end of Ulna (Rt10%, Lt16.7%, S0%), dorsal side of Lu (Rt6.7%, Lt0%, S0%), and palmar side of E.digitorum TS (Rt0%, Lt3.3%, S0%). FV from vascular channels

were depicted at Lu (Rt53.3%, Lt46.7%, S43.3%), Radius (Rt20.0%, Lt16.7%, S3.3%), Triquetrum (Rt10%, Lt16.7%, S0%) and Capitate (Rt6.7%, Lt10%, S0%). The frequency of BSI at Lu in HV (n=47) and transverse diameter (TD) (Mean±S.D.) of those were Rt longitudinal plane (LP)57.4%(TD1.26±0.33mm), Rt transverse plane (TP)51.1%(TD1.20±0.31mm), Lt LP 68.1%(TD1.06±0.28mm), and Lt TP42.6%(TD1.29±0.31mm). Symmetrical evaluation of those was 53.2%. **Conclusions:**MSKUS evaluation in WJ revealed various FV and BSI of Lu. It's crucial to distinguish normal pattern from pathological one in MSKUS examination.

W84-3

Assessment of large joint damage in no radiographic progression joints according to Larsen grade in patients with rheumatoid arthritis

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Conflict of interest: None

Objective:To assess large joint damage in rheumatoid arthritis (RA) which is not detected by Larsen grade. Methods:Twenty seven RA patients (6 men and 21 women) were enrolled, and radiographs of the 10 large joints (shoulder, elbow, hip, knee and ankle) per patient were obtained at baseline and 3 years. Large joints with no radiographic progression of joint destruction according to Larsen grade were evaluated by ARASHI score. Clinical parameters and the disease activity were evaluated at baseline, 6 months, 1,2 and 3 years. Results:Among the 206 joints with no radiographic change based on Larsen grade, radiographic progression was detected in 77 joints by the ARASHI score. The DAS28-CRP and Larsen grade at baseline were significantly higher in the radiograpphic progression group (p= 0.04, p=0.02). Furthermore, TNF blocking therapy was performed more frequently in the radiographic progression group (p= 0.015). A logistic regression analysis revealed the Larsen grade at baseline was the most associated factor with radiographic progression of joint destruction at 3 years. Conclusion:The ARASHI score may allow more detailed assessment of large joints than the Larsen method in RA. Radiographic progression of join damage may progress in large joints with high Larsen grade at baseline.

W84-4

Relationship between treatment response to rheumatoid arthritis and periodontitis using FDG-PET/CT

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Conflict of interest: None

Objectives: The aim of this study was to evaluate the relationship between treatment response to rheumatoid arthritis (RA) and periodontitis using [18F] fluorodeoxyglucose–positron emission tomography (FDG-PET). Methods: Sixty RA patients (male14, female46) treated with biological therapies were assessed. FDG-PET was performed at baseline and six months after the initiation of biological therapy. The maximal standardized uptake value (SUVmax) was used as a representative value for the assessment of the FDG uptake in periodontal tissue (upper posterior gingival tissue). We also evaluated DAS28-CRP and clinical parameters. Paired t test and Spearman's rank correlation test were applied to assess the correlation between the periodontal SUVmax and the clinical parameters. Results: There was no significant change in periodontal SUVmax before and after treatment. But, there were significantly negative correlations between periodontal SUVmax at baseline and ΔDAS28-CRP (r=-0.369, p=0.004). Conclusion: Periodontitis might decrease the response to the biological therapies in RA patients.

W84-5

Deep learning based automatic bone erosion classification on conventional radiography in rheumatoid arthritis and the effect of grouping of training data set

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Conflict of interest: None

[Object] Recent developments in machine learning yielded deep neural network (deep learning) which resulted in highly successful applications in many pattern recognition tasks. We attempted deep neural network as erosion classification in radiography rheumatoid arthritis patients. Previous our research revealed that the performance of classification fluctuates with training data set, especially grouping of the joints. The aim of this study was to compare the effects of grouping of joints. [Methods] One hundred wrist and finger radiographs with rheumatoid arthritis patients were used as training data sets. The radiocarpal joints, proximal interphalangeal (PIP) joints, metacarpophalangeal (MCP) joints were assessed for bone erosion, and erosion score was used as label data. We constructed deep neural network using Convolutional Neural Network (CNN) in matlab programming environment. This system was trained firstly mixed joint group and secondly separate joint group. We investigated the correct answer rate of these group. [Results] Correct answer rate of mixed joint group, radiocarpal joints group, PIP joints group, MCP joints group were 54±8%, 67±7%, 71±6%, and 59±6%. [Conclusions] The decrease in the type of joint led to the improvement of the correct answer rate.

W84-6

The Analysis of Usability of PET-CT in Vasculitis

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Conflict of interest: None

Background/Purpose: To investigate the usability of PET-CT for diagnosis and monitoring of vasculitis. **Methods:** We retrospectively analyzed the usability of PET-CT for diagnosis and monitoring of vasculitis by investigating the data of patients followed from 2007 to 2016 at Yokohama City University. **Results:** PET-CT was performed in 16 patients for making diagnosis. The mean age was 55 ± 16 years, and 11 (69%) were female. Patients who had a fever were 7 (44%), and CRP was 1.28 mg/dl [IQR 0.17-7.13]. Nine (56%) were diagnosed with vasculitis and all of them were large vessel vasculitis. There was no correlation between SUVmax and serum CRP level (r = -0.03, p = 0.91), and reaching a diagnosis was not related to fever or serum CRP level (p = 0.38, p =0.49). Oral prednisolone therapy was initiated in 8 patients, and symptoms and SUVmax were improved in all patients. Only one patient showed relapse with symptoms and elevation of SUVmax. Although the symptoms and SUVmax improved by increasing the dose of oral prednisolone, the serum CRP level was not associated with these improvement. **Conclusion:** We showed that PET-CT was useful for patients who had suspected of vasculitis in not only diagnosis but disease activity monitoring.

W85-1

Ultrasound-detected monosodium urate crystal deposition in the feet of patients with gout

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Conflict of interest: None

[Object] To determine the prevalence of monosodium urate (MSU) crystal deposition detected by ultrasound (US) in the feet of patients with gout. [Methods] Patients were included retrospectively in this study who had US scanning of the feet to evaluate MSU crystal deposition from September, 2013 to October, 2015. The prevalence of MSU crystal deposition and the association with clinical history were analyzed respectively in three divided area of the feet; metatarsophalangeal (MTP) joints, midfoot and hindfoot. [Results] Total of 67 patients (125 feet) were evaluated. The first MTP joint was the most commonly involved, followed by the Achilles tendons, other MTP joints, tibiotalar joints, flexor tendons, peroneal tendons and the deltoid ligaments. Presence of MSU crystal deposition was significantly associated with previous history of gouty arthritis and with current acute attack in last one year in each joint area, and the total number of the joints, tendons and ligaments with MSU crystal deposition was larger than those with clinical involvement in last one year in all joint area except hindfoot. [Conclusions] US evaluation detects MSU crystal deposition in the feet, in which a trend of the presence and clinical association were to be recognized.

W85-2

Ultrasonographic evaluation with two paramators in major salivary glands of Sjogren's syndrome

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Conflict of interest: None

[Objective] To evaluate two ultrasonographic (US) parameters of parotid and submandibular salivary glands associate with Sjogren's syndrome (SS). And reveal the relationship between salivary flow (Saxon test) and those scoring systems. [Methods] In 45 patients with suspected SS, US of both parotid (PG) and submandibular salivary glands (SG) and Saxon test were performed. Two US parameters were assessed: hyperechogenic bands (HB) and hypoechoic areas (HA). The imaging features were graded into five (G0-G4), and the grading scores of the PG and SG were summed. [Results] In 45 patients, the average Salivary flow of Saxon test were 1.56±1.6g. Total HB and HA scores of 4 salivary glands had statistically significant negative correlation with Saxon test (r=-0.7431). And there were statistically significant positive correlation between total SG scores and PG scores (r=0.8982), same as between total HB scores and HA scores (r=0.8759). In the low salivary flow group (≦2.0g of Saxon test), there were no significant difference between total HB scores and HA scores. But in the high salivary flow group (>2.0g), there were significant difference. [Conclusions] We can predict the clinical damage of the salivary glands using the two paramators of ultrasonography easily.

W85-3

Joint Ultrasnographic Findings Including Synovial Brightness are Reflecting the Changes of Local Pathophisiology in Rheumatoid Arthritis

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Conflict of interest: None

[Object] To determine whether synovitis defined by ultrasonography (US) reflect local joint pathophysiology. [Methods] Forty-four RA patients were enrolled.19 were untreated and 25 were treated. Knee US examination and synovial fluid (SF) aspiration were performed. The levels of 9 SF inflammatory proties were measured. US images were assessed by semi-quantitative scoring and quantitative measurement for hypertrophy (GSquant), vascularity (PDquant) and brightness. US guided synovial biopsy was also performed In 2 of treated patients. [Results] The mean DAS28 of all RA patients were 5.9. Quantitative US measures were substantially correlated with corresponding US scoring. ($p<0.05$) GSquant and PDquant were significantly associated with many SF inflammatory proteins in untreated group. In treated group, not only PDquant was significantly associated with SF IL-6 and VEGF but also synovial brightness was inversely associeted with those proteins. The histopathology of synovium with high-brightness revealed greater fibrotic lesion, less vascularity and cell invasion compared to that with low-brightness. [Conclusion] Joint US findings including synovial brightness are reflecting the changes of local pathophisiology in rheumatoid arthritis

W85-4

The measurement of MCP joint space distance by using super resolution image and curve fitting methods for rheumatoid arthritis

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Conflict of interest: None

[Objectives] To evaluate the correlation between joint space distance (JSD) of MCP joints with super-resolution image (SRI) using the curve fitting method and other clinical findings (physical findings, ultrasound findings). [Methods] We investigated the JSD of MCP joints at baseline and last observation (mean observation period 2.13 years), physical findings (tenderness, swelling) and ultrasound findings (power Doppler (PD), gray scale (GS)) in sixteen rheumatoid arthritis patients. [Results] The mean age of patients was 48.7 years old. The mean disease duration was 3.6 years. The mean of JSD with index finger, middle finger, ring finger and little finger (estimated as 0 in Sharp score) was 0.884, 0.795, 0.783 and 0.728, respectively. In GS>2 group and GS <= 1 group, the mean of the change of JSD was 0.022 and 0.005 ($p=0.097$), respectively. In PD>2 group and PD<= 1 group, the mean of the change of JSD was 0.024 and 0.006 ($p=0.014$). In the presence or absence of physical findings, there was no statistical difference about the change of JSD. [Conclusion] In JSD of the MCP joint which was not found of the joint destruction, the difference in value was confirmed in a 2-5 finger. We confirmed that joint space narrowing with the measurement of SRI for an average of two years in PD>2.

W85-5

Changes of synovial vascularity in finger and wrist joints on joint power Doppler ultrasonography in rheumatoid arthritis

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Conflict of interest: None

[Objectives] We evaluated the changes of synovial vascularity in finger and wrist joints on joint power Doppler ultrasonography (PDUS) in rheumatoid arthritis (RA). [Methods] We performed PDUS in finger and wrist joints on 1819 patients, and 164 patients had the PDUS for the first time between Jan. 2014 and Dec. 2014. We evaluated the improvement rate, speed and remission rate using the changes of PDUS grade (PD-Gd) and PDUS vascularity (PD-Vs) by box method in 67 RA patients among 74 patients with positive PD-Gd and PD-Vs in finger and wrist joints. [Results] The improvement rate of PD-Gd is 78.69% in finger, 66.57% in wrist, and the improvement rate of PD-Vs is 78.69% in finger, 66.57% in wrist, but both rates of finger are not significantly higher than them of wrist. The improvement speed and remission rate of wrist tend to be higher than them of finger, but there is no significant difference. Finger

and wrist are favorite sites for synovitis in RA, and some patients often have treatment-resistant synovitis in wrist consists of multiple joints. Synovitis in wrist is not significantly difficult to improve than that of finger in this study. We should try to get a complete remission to calm down synovitis patiently in both wrist and finger joints.

W85-6

Factors related to atherosclerosis in Japanese patients with rheumatoid arthritis -Investigation of KURAMA cohort-

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Conflict of interest: None

[Puropose] Cerebral and cardiovascular disorders are common in patients with rheumatoid arthritis (RA). Although there are some reports from abroad suggesting that thickening of carotid arteries (CAs) of RA patients correlated with disease activity, there has been no survey of CAs in Japanese RA patients. In this study, we aimed to reveal the factors related to atherosclerosis in Japanese RA patients. [Methods] We measured the intima-media thickness (IMT) and plaques of 216 RA patients who were registered in KURAMA cohort with ultrasonography of CAs. We defined that patients with IMT>1.0cm or plaques≧1.1cm have atherosclerosis and investigated the factors related to atherosclerosis with multivariate analysis. [Results] 47% of patients had atherosclerosis. The risk factors were gender (p=0.012), age (p=0.009) and mean CRP (p=0.014). The mean IMT was correlated with hypertension (p=0.014) and eversmoking (p=0.002), and max IMT was correlated with hypertension (p<0.001), hypertriglyceridemia (p=0.002) and CDAI (p=0.033). The plaque scores were correlated with age (p=0.012) and anti-CCP antibody (p=0.011). [Conclusion] These results suggest that atherosclerosis of Japanese patients with RA is affected by not only classical risk factors of atherosclerosis but also the activity of RA.

W86-1

Inhibition of IL-23 ameliorated murine model of polymyositis

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Conflict of interest: None

Objectives We established C protein-induced myositis (CIM), a murine model of polymyositis, to investigate the pathogenesis of idiopathic inflammatory myopathies (IIM). Although we reported the involvement of IL-1 and IL-6 in the pathogenesis of CIM, more disease-specific therapeutic targets for IIM were desired. As increased serum concentrations of IL-23 in IIM have been reported, we studied the role of IL-23 in CIM. **Methods** Serum concentrations of IL-23 in CIM mice were measured. Muscle specimens from CIM mice were examined for IL-23 expression immunohistochemically. CIM was induced in IL-23-null mice. Anti-IL-23R antibodies (Abs) were applied to CIM mice. Lymph node cells from CIM mice were adoptively transferred into naïve mice. **Results** Serum concentrations of IL-23 were higher in CIM mice than controls. CD68+ cells infiltrating into the lesions of CIM expressed IL-23. IL-23-null mice were resistant to CIM. The anti-IL-23R Abs ameliorated CIM therapeutically. The severity of transferred myositis in IL-23-null recipients was comparable to that in wild type ones. **Conclusion** IL-23 was produced locally at the lesions of CIM. The pathogenesis of CIM depends on IL-23 that contributes to induction of autoreactive T cells. IL-23 could be a promising target for IIM.

W86-2

Cytokine networks in polymyositis/dermatomyositis with interstitial lung disease

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Conflict of interest: None

[Objectives] The aim of this study is to identify the utility of multiple cytokines measurement in polymyositis (PM)/dermatomyositis (DM) with interstitial lung disease (ILD). [Methods] 40patients with PM/DM-ILD, in either rapid progressive ILD (RPILD) or chronic ILD were enrolled from Nagasaki University Hospital. Serum levels of 42 cytokines were measured by multi-suspension cytokine array. Serum levels of Anti-MDA-5 antibody and ferritin were measured by enzyme linked immunosorbent assay. We tried identify a set of specific biomarker by using multivariate classification algorithms for distinguishing patients with RPILD. To identify specific molecular networks, we performed a cluster analysis of each specific biomarker. [Results] Twenty-four out of 42 cytokines, anti-MDA5 antibody and ferritin were available for further analyses. Serum levels of 3 cytokines (IL-6, IL-15 and VCAM-1), anti-MDA-5 antibody and ferritin were significantly elevated from RPILD than chronic ILD. We found that anti-MDA-5 antibody and IL-15 were the best combination to distinguish RPILD from chronic ILD (sensitivity: 83.3%, specificity: 86.4%, accuracy: 85%). [Conclusions] Our data suggest the combinational biomarkers is a useful tool to diagnose more severe PM/DM-ILD.

W86-3

Chemokine profiles of interstitial pneumonia in patients with dermatomyositis: a case control study

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Conflict of interest: None

(Objectives) Chemokines play an important role in the pathophysiology of DM-IP. However, the relation between chemokines and the disease activity or prognosis of DM-IP has not been elucidated. We evaluated the serum CCL2, CCL17, CXCL9, CXCL10, and CXCL11 before and after treatment and examined the relation between chemokines and the disease activity or prognosis of DM-IP. (Methods) We examined 30 patients admitted to Osaka Medical College Hospital from October 2011 to March 2015 and compared these chemokines between the survival and death groups. (Results)Initial CCL2 level was higher in the death group. To determine the cut-off points effective as poor prognostic factors of DM-IP, ROC curve analysis was carried out on initial CCL2 level. The value that maximized the area under the ROC curve was 894 pg/mL (sensitivity: 100%, specificity: 70.8%). CCL2, CXCL9, CXCL10, and CXCL11 levels were lower at 2 and 4 weeks after treatment initiation than before treatment. CCL2, CXCL10, and CXCL11 levels at 2 and 4 weeks after treatment initiation were higher in the death group. (Discussion) Serum levels of chemokines such as CCL2, CXCL10, and CXCL11 may be possible biomarkers of disease activity and prognosis in DM-IP patients, and CCL2 level may be useful when deciding initial treatment.

W86-4

Serum conventional biomarkers are useful for stratification of prognosis in polymyositis/dermatomyositis with interstitial lung disease

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Conflict of interest: None

[Object] The aim of this study is to investigate stratification of prognosis in polymyositis (PM)/dermatomyositis (DM) with interstitial lung disease (ILD) [Methods] From a multicenter cohort of PM/DM-ILD including 44 institutions, 497 patients with PM/DM-ILD were enrolled. Anti-MDA-5 antibody and anti-ARS antibody was detected by enzyme linked immunosorbent assay and immunoprecipitation, respectively. We investigated risk factors for prognosis using serum biomarkers including CRP, ferritin, KL-6 and SP-D. [Results] The mortality rate was higher in the subset with CRP≥1 mg/dl or ferritin≥500 ng/ml in patients with anti-MDA-5 (n=206) or those with anti-ARS (n=159). In patients without anti-MDA-5 or anti-ARS, the mortality rate was higher in the subset with KL-6≥1000 mg/dl or SP-D≥100 ng/ml. The multivariate analysis revealed that a presence of anti-MDA-5 (odds ratio [OR] 7.9), CRP≥1 mg/dl (OR 3.9) and KL-6≥1000 mg/dl (OR 2.8) were risk factors for poor prognosis. The mortality rate was less than 5%, 10%, 35% and 60% in patients without any risk factors, with any one, with any two and with all of the three, respectively. [Conclusions] The combined evaluation of autoantibodies and serum biomarkers is a significant clinical tool to stratify prognosis of PM/DM-ILD.

W86-5

Initial Predictors of Short-term Poor Survival Rates in Patients with Polymyositis/ Dermatomyositis-associated Interstitial Lung Disease

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Conflict of interest: None

[Objectives] To examine initial predictors of poor survival in patients with PM/DM-associated ILD. **[Methods]** This study used a database of a multicenter retrospective cohort. Clinical data were retrospectively collected and anti-MDA5 and anti- ARS were examined. Cumulative survival rates were calculated using the Kaplan-Meier method and the Breslow test and was applied to select possible explanation variables for multivariate analysis. The prediction model for poor survival was estimated using the multivariate Cox proportional hazards model with stepwise selection. **[Results]** This study enrolled 497 patients, including 76 with PM, 158 with classic DM, 263 with CADM. By univariate analysis, age at onset (>60 years), male, CADM, fever, Raynaud phenomenon, absence of muscle weakness, skin ulceration, CRP (>1 mg/dL), CK (<750 IU/L), aldolase (<17.5 IU/L), SP-D (<100 ng/mL), ferritin (>500 ng/mL), random GGA pattern on CT, SpO_2 (<95%), positive anti-MDA5, and negative anti-ARS were identified as initial parameters associated with mortality. By testing various combinations of parameters selected, we propose a model consisting of independent predictors of poor survival rates. **[Conclusions]** We have successfully identified prediction model of mortality in patients with PM/DM-associated ILD.

W86-6

Effects and safeties of high trough tacrolimus in acute/subacute interstitial pneumonia with dermatomyositis during short/middle term

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Conflict of interest: None

【Objective 】We examined the efficacy and safety of high trough tacrolimus (TAC) for acute/subacute interstitial pneumonia in dermatomyositis (DM-A/SIP) during short/middle term.【Method】Eleven patients with DM-A/SIP treated with TAC were enrolled in this study. We initiated TAC and maintained the trough level 15~20 ng/ml during the first 3months, 10-15 ng/mL during the second 3 months, and thereafter 5-10ng/mL. We assessed laboratory findings and respiratory function test results before and 24, 48 weeks after TAC initiation.【Results】The median age was 66 (38-79) years and 10 were female. Seven patients (64%) were clinically ADM (CADM), 6 (55%) were anti-ARS antibody (ab) positive, 2 (18%) were anti-MDA-5 ab positive. During 48 weeks follow-up period, 10 patients survived, and 1 patient died for viral encephalitis suspection even though IP was improved. The respiratory symptom improved in 8 patients, and CK, aldorase, CRP, KL-6, %FVC, CT score significantly decreased. The serum creatinine (Cr) elevated significantly in the first 6 months, but it was able to continue TAC in all the survivors by tapering without elevating Cr afterwards.【Conclusions】High trough TAC may be effective for DM-A/SIP, but complicating infections should be mentioned.

W87-1

Associations of clinical features with fetal outcomes in pregnancies of mothers with connective tissue diseases

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Conflict of interest: None

<Objectives> To clarify association of clinical features with fetal outcomes of pregnancies in mothers with connective tissue diseases (CTDs). <Methods> We examined 1) background, 2) autoantibodies (Ab), 3) flares of CTDs, 4) therapy, and 5) fetal outcomes, in 90 pregnancies (66 mothers) with CTDs at our hospital from Jan 2006 to Sep 2016, retrospectively. <Results> 1) Mean age of mothers was 32±5 years old. Underlying CTDs were SLE (N=41), MCTD (N=10), RA (N=15), SS (N=10), and others (N=14). 2) Anti-SS-A Ab was detected in 60%(47/78 cases), LAC was in 12%(8/65), and anti-CLb2GP1 Ab was in 20%(13/65). 3) Flares of CTDs occurred in 20 cases (22%). 4) Corticosteroid (CS) was administered in 73 cases, immunosuppressant in 4. 5) Among 85 pregnancies other than 5 early abortions (<12W), perinatal complications occurred in 33 cases (1 neonatal death, 25 low-birthweight, 21 light for date, 3 malformation, and 9 others, with overlap), while other 52 cases were normal. In univariate analysis, MCTD (OR13.7), high CS (OR1.1), flares of CTDs (OR4.2), and LAC (OR10.6) significantly correlated with complications, while only LAC was identified as an independent predictor in multivariate analysis (OR11.0). <Conclusion> LAC might relate to perinatal complications in mothers with CTDs

W87-2

Analysis of risk factor for perinatal complications in 136 pregnancies complicated with connective tissue disease

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Conflict of interest: None

[Objective] We examine the issue of pregnancy and delivery complicated with connective tissue diseases (CTD) by the analysis of the cases in our institution. [Method] We investigated the risk factors of abortion, preterm birth, LFD (light for dates) and perinatal complication from exacerbation of underlying disease, anti SS-A antibody, antiphospholipid antibody and dose of corticosteroid in 136 cases in our institution. [Result] In 22 among all cases underlying diseases were exacerbated, and they needed to increase doses of corticosteroid or pulse therapies. Disease activities were more exacerbated in PM/DM, MCTD and SLE. Preterm births and LFD were closely related to disease exacerbation and dose of corticosteroid, pulse therapy, and these were extracted as risk factors. However, there was no significant difference in threatened premature delivery and premature rapture of membrane. In SLE, preterm birth was associated with low complement and high titer of anti-double stranded DNA antibody. In RA, preterm birth, LFD and perinatal complication were not influenced by biologics before pregnancy. [Conclusion] In pregnancy complicated with CTD, we need to control the disease activity strictly, however, we should consider the increase or pulse therapy of corticosteroid carefully.

W87-3

Clinical features and prognostic factors in thrombotic microangiopathy associated with connective tissue diseases

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Conflict of interest: None

To clarify the clinical features of thrombotic microangiopathy (TMA) in patients with connective tissue diseases (CTD). <METHODS> Twelve cases diagnosed with CTD-TMA in University of Tsukuba hospital between 1995 and 2016 were included in this study. We retrospectively evaluated 1) characteristics, 2) treatment, 3) outcome, and 4)clinical manifestations between the cases survived and fatal. <RESULTS> 1) TMA developed in 4 cases of systemic sclerosis (SSc), 3 cases of systemic lupus erythematosus (SLE), 2 cases of polymyositis, 2 cases of overlap syndrome of SLE and SSc, and a case of Sjögren's syndrome. 2) Eight cases were treated with steroid pulse therapy. Nine cases underwent plasma exchange (PE), and the average number of PE was 16 occasions. Three cases were received concomitant immunosuppressive agents. 3) Five cases died due to multiple organ failure accompanied with TMA, and one patient was dead due to infection. 4) In death group, 3 cases were patients with SSc (3/6; 50%) and all cases required dialysis. On contrast, survival group consisted of 3 cases of SLE, and a case of SSc, PM, and overlap syndrome. Only one case needed dialysis. <CONCLUSION> Coexistence of SSc and renal insufficiency might denote a poor prognosis of CTD-TMA.

W87-4

Study on the preventive pharmaceutical factors of NSAIDs induced gastroduodenal injury in RA

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Conflict of interest: None

Objective. NSAIDs is often used in patients with RA for its pain control. NSAIDs might induce gastrointestinal (GI) injury and the incidence is reported about 10~30% in previous articles. Prevention of GI injury by NSAIDs is important. We investigated incidence of GI injury induced by NSAIDs in RA and preventive effects of different type of NSAIDs and GI drugs in our hospital. Methods. 560 RA patients who were prescribed NSAIDs in our hospital were conducted upper GI endoscopy during 2009-2015. We classified above patient's endoscopic finding into mucosal injury group and normal group. We investigated and compared two groups of clinical features and especially pharmaceutical backgrounds (kinds of NSAIDs, use of PPI, H2 blocker (H2RA), gastric coating agent (GCA).) Results. 1. The incidence of GI injury decreased 19.6%(2009) to 13.7%(2015). 2. The rate of using selective COX-2 inhibitor (COX2i) increased (2009;58.1% vs. 2015;88.2%), and PPI use increased (2009;32.4% vs 2015;38.2%). 3. GI mucosal injury decreased by using COX2i (OR 0.58, p=0.014) and PPI (OR 0.62, p=0.045) by Multiple logistic analysis. But no preventive effects have H2RA and GCA. Conclusion. When we use NSAIDs in RA, we should choose COX2i and prescribe PPI together.

W87-5

Positron-Emission Tomography Images With an Amyloid-Specific Tracer 11C-BF-227 in six Amyloidosis patients

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Conflict of interest: None

[Object] In order to visualize amyloid deposition in the specific organs, the patients with amyloidosis underwent PET with 11C-BF-227 that specifically binds to aggregated amyloid. 11C-BF-227 was previously developed, and succeeded in vivo detection of amyloid in Alzheimer's disease and familial systemic amyloidosis (Kudo Y. J Nucl Med 8: 2007). Here, we investigated patients with AA and AL amyloidosis, utilizing this strategy. [Methods] We obtained 6 patients diagnosed as amyloidosis with biopsies and 4 controls. The types are 3 of AA and 3 of AL amyloid. We analyzed with PMOD software, merging the PET and MRI images into the three-dimensional space. We evaluated SUV. The ratio of regional SUV to lung SUV (SUVR) was calculated. [Results] Amyloid was deposited in the knee in a patient, and in the heart in another one. They were definitely detected by PET-image. On the other hand, amyloid nodules in the lung were slightly detected. Some patients showed relatively higher SUVR in the kidney but pathogenic role was not clear. [Conclusion] We clarified that our newly developed amyloid pet tracer, 11C-BF-227, can detect the amyloid deposition specifically, and it is a useful technology to detect the amyloid in the whole bodies, although the sensitivity might be different in each organ.

W87-6

Clinical Factors Associated with Anxiety and Depression in Patients with Rheumatoid Arthritis -Study using KURAMA cohort-

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Conflict of interest: None

【Purpose】The prevalence of anxiety and depression among Rheumatoid Arthritis (RA) is higher than that in the general population and has been associated with increased pain, functional disability, stress, and psychosocial factors. In this study aimed to investigate the factors that influence their anxiety and depression.【Methods】The Hospital Anxiety and Depression Scale (HADS) was used to measure anxiety and depression of RA patients (N=517). The correlation between anxiety and depression

and increased disease activity, functional disability, pain were assessed. 【Results】Of all patients, 18.1% were found to have anxiety; 28.0% to have depression. In multiple logistic regression analysis, no correlation was observed between DAS28 and anxiety and depression. However both increased PGA and no-HAQ-remission were significantly associated with anxiety (OR=1.19, p=0.01; OR=3.29, p=0.001) and depression (OR=1.20, p=0.02; OR=2.21, p=0.01). 【Conclusion】 Higher PGA and no-HAQ-remission were found to be predictive factors for anxiety and depression. In order to identify anxiety and depression in the diseases' early stages as well as prevent them and improve their course, it should be important to improve PGA score and achieve HAQ remission.

W88-1

Disseminated nocardiosis in patients taking immunosuppressive agents: a report of two cases

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Conflict of interest: None

We report two cases of disseminated nocardiosis in patients taking immunosuppressive agents. Case 1 was a 47-year-old woman who was diagnosed as having systemic lupus erythematosus and treated with prednisolone (PSL) and tacrolimus. She presented with pneumonia and multiple subcutaneous nodules. Skin biopsy samples and bronchoalveolar lavage cultures were positive for *Nocardia asteroides*. Brain MRI showed multiple abscesses. She responded to treatment with trimethoprim/sulfamethoxazole (TMP/SMX). Case 2 was a 74-year-old man who was diagnosed as having relapsing polychondritis and myelodysplastic syndrome and treated with PSL and cyclosporine. He developed pneumonia, and blood cultures were positive for Nocardia species. Treatment with TMP/SMX was started but discontinued because of hypersensitivity pneumonitis. Because brain MRI revealed an abscess, aspiration biopsy was performed, with the isolate confirmed to be *Nocardia nova*. Brain MRI performed after administration of imipenem/cilastatin showed improvement of the abscess. Clinicians should be aware of the possibility of nocardiosis in patients taking immunosuppressive agents. Cerebral MRI should be performed in patients with pulmonary nocardiosis as 20% to 35% of cases have central nervous system dissemination.

W88-2

Investigation of preoperative intranasal colonization in patients with orthopedic surgery

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Conflict of interest: None

From July to October 2016, nasal cavity culture was performed within one month prior to hospitalization for patients scheduled to undergo orthopedic surgery. There are 270 cases of continuous cases. There were 58 males, 212 females, average age 65.8 years, 51 cases of rheumatoid arthritis. In the results of intranasal culture, Staphylococcus aureus, Staphylococcus epidermidis, CoNS (excluding S. Epidermidis) and culture negative were 11.4%, 26.7%, 5.5% and 24.5%, respectively. MRSA, MRSE, MRCoNS (excluding MRSE) with methicillin resistance were 3.3%, 26.0%, 1.5%. It was found that 30.8% of methicillin-resistant Staphylococcus aureus was present. Especially in patients with rheumatoid arthritis, methicillin - resistant bacteria was significantly more than 43.1%(22 out of 51) and 28.3%(62 out of 219 patients) other than rheumatoid arthritis patients. In the future, we need to consider the selection of perioperative preventive antibacterial drugs.

W88-3

Glucose intorelance by steroid tharapy during treatment of rheumatic diseses

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Conflict of interest: None

[Object] We carried out this study to assess influence of steroid on HbA1c and Diabetes Mellitus (DM). [Methods] We retrospectively investigated HbA1c of cases newly treated with steroid in our hospital from August 2012 to August 2016. Cases without HbA1c before treatment and followed less than 4 weeks were excluded. DM were defined as HbA1c more than 6.5%. Amount of steroid, HbA1c and treatment for DM for 48 weeks were assessed. [Results] We analyzed 75 cases. Average±SD of age, height, body weight and BMI were 59.2±19.6 years old, 156.4±9.1cm, 50.4±9.7kg and 20.5±3.2, respectively. Major basic diseases were Polymyalgia Rheumatica (16 cases), Vasculitis (13), Rheumatoid Arthritis including Rheumatic Vasculitis (9), Systemic Lupus Erythematosus (9) and Dermatomyositis/Polymyositis (8). We divided all cases into 4 groups; non-DM (49 cases), already-diagnosed DM (7), just-diagnosed DM (8), newly-diagnosed DM (11). Fifteen percent of the cases were diagnosed as DM. Almost all of them were diagnosed within 12 weeks. HbA1c before treatment of newly-diagnosed DM (5.9±0.38%) was significantly higher than that of non-DM (5.6±0.42%) (P=0.044). [Conclusions] It is important to evaluate risk of DM before treatment and to observe carefully during initial 12 weeks.

W88-4

Certain autoimmune inflammatory manifestations are associated with WT-1 mRNA in patients with myelodysplastic syndrome

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Conflict of interest: None

【Purpose】Autoimmune inflammatory manifestations (AIMs) are common in patients with myelodysplastic syndrome (MDS). This study aimed to investigate with the clinical aspects and complications of AIMs in patients with MDS. 【Methods】A total of 51 MDS patients with AIMs and 13 MDS patients without AIMs, all of whom received medical care at our hospital from April 2014 through November 2016, were enrolled. SLE:2, RA:2, PsA:1, cutaneous PAN:1, intestinal BD:1, hypertrophic pachymeningitis:1, Hashimoto disease:2, neutrophilic dermatoses:1, membranous nephropathy:1, cryptogenic organizing pneumonia:2 are included in MDS patients without AIMs. Age, Sex, WBC, Neutrophils, Lymphocytes, Hb, PLT, WT-1 mRNA, Myeloblasts, Karyotype, and IPSS score were determined in both groups. 【Results】The mean time (±SD) at the time of MDS diagnosis was 71.6±1.9 years, and 69.2% of patients were male. Neutrophils (p=0.048) and WT-1 mRNA (p=0.0025) in MDS with AIMs were significantly higher than in MDS without AIMs. 【Conclusion】The amount of WT-1 mRNA in MDS patients appeared to be related to the complication of AIMs.

W88-5

Acute calcium pyrophosphate (CPP) crystal arthritis in hospitalized elderly patients: its induction and clinical characteristics

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Conflict of interest: None

[Objectives] It is not rare that Acute CPP crystal arthritis affects elderly persons. We determined the induction and clinical characteristics of

this arthritis in our hospitalized patients. [Methods] 29 patients admitted in our hospital during 2011-2015 were diagnosed as acute CPP crystal arthritis according to the 2011 EULAR definition. [Results] 29 patients included 7 males and 22 females, and the average age at diagnosis was 85.9 years (69-102 years). 25 cases showed fever over 37.5°C, and the average CRP level of 26 cases was 13.7mg/dl (2.96 - 23.59 mg/dL). Joint aspiration was done in 14 cases, proving the existence of CPP crystal in 11 cases. calcification was confirmed in 19 cases of 22 X-ray performed cases. 24 cases received treatment, including 17 cases treated with NSAIDs, 3 cases with intraarticular steroid injection, 2 cases with oral steroid (4-30mg/day), and 6 cases with colchicine. 12 patients were admitted with infections, 6 cases with cerebral infarction, 4 with malignant tumors, and 3 with gastrointestinal hemorrhage. [Conclusions] Acute CPP crystal arthritis occurred with fever ant acute arthritis in elderly patients hospitalized with diseases with inflammation, such as infections, cerebral infarction or malignancy, which likely induce pre-IL-1b synthesis.

W88-6

Four cases of senile systemic amyloidosis diagnosed in a regional medical center in 2 years

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Conflict of interest: None

Senile systemic amyloidosis is characterized by deposition of wild-type transthyretin (TTR*wt*) mainly in myocardium of elderly, thus it is now termed as ATTR*wt* amyloidosis. Carpal tunnel syndrome (CTS) often proceeds several years to the onset of heart failure. The exact prevalence of this amyloidosis is still unknown. We report 4 cases of ATTR*wt* amyloidosis diagnosed in our regional medical center between 2014 and 2016. All the cases were referred to us since amyloidosis was suspected in pathological examination after open carpal tunnel release surgery. All of the patients were men, and their age at the time of diagnosis was 69, 78, 84, and 73 years old, respectively. We sent the sample to Shinshu University, where immunohistochemistry and genetic testing confirmed the diagnosis of ATTR*wt* amyloidosis. Amyloid deposition in myocardium was detected by MRI in 2 cases. Two patients had lumbar canal stenosis (LCS). Surprisingly, 2 patients were neighbors without familial relationship. Although Japanese pathological study previously reported that 11.5% of autopsied cases older than 80 years old had TTR*wt* deposition, few of the subjects showed symptoms of amyloidosis while alive. ATTR*wt* amyloidosis might be a common cause of CTS, LCS and heart failure of unknown origin in elderly men.

W89-1

The Identification of STEAP4-splice variant and its possible suppressive role in rheumatoid arthritis

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Conflict of interest: None

Background and Objective TIARP is a negative regulator in arthritis model mice. In human, STEAP4 (human counterpart of TIARP) is also expressed in CD14+ monocytes from patients with rheumatoid arthritis (RA). Recently, STEAP4-splice variant (v-STEAP4) has been found to be highly expressed in porcine lung. The aim of this study is to elucidate the role of v-STEAP4 in the pathogenesis of arthritis. **Methods** 1) To detect and compare the expression of v-STEAP4, CD14+ monocytes that collected from patients with RA and healthy subject (HS) were analyzed by qPCR. 2) The correlation between the expression of v-STEAP4 and clinical information of RA patients was analyzed. 3) We produced v-STEAP4 overexpressed cell lines to analyze the function. **Results** 1) The splicing form of STEAP4 was higher expressed in RA patients than that in HS. 2) The expression of v-STEAP4 was positively correlated with RF and CRP. 3) The production of inflammatory cytokines such as IL-6 and IL-1β by LPS was suppressed in v-STEAP4 overexpressed monocytic cell lines. **Conclusion** v-STEAP4 was identified in patients with RA, and might have a regulatory role in the generation of arthritis through the suppression of IL-6 and IL-1β.

W89-2

T cell development abnormality of rheumatoid arthritis

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Conflict of interest: Yes

[Object] Recently, the least developed memory T cell subset, stem cell memory T (Tscm), was found among cells with naive (Tn) phenotype, therefore, peripheral blood (PB) T cells can be divided into Tn, Tscm, central memory (Tcm), effector memory (Tem), and CD45RA+ effector (Temra). The purpose of this study was to elucidate the T cell developmental abnormality in RA patients, including newly identified Tscm. [Methods] PB samples from 56 untreated RA patients and 38 healthy controls (HC), and 14 synovial fluid (SF) with paired PB from RA patients were collected. T cell development and activating status was analyzed by flow cytometry. Tn, Tscm, Tcm, Tem, and Temra subset from PB of 6 RA and HC were sorted, and analyzed by microarray. [Results] The proportion of CD4 Tscm was high in RA, and CD8 Tscm also tended to be high. In comparison of PB and SF, the proportion of developed and activated cells was high in SF. In addition, the activation status of CD4 Tscm and several CD8 subsets in SF were correlated with RA activity. In transcriptome analysis, remarkable differences were observed among CD8 Tem and Temra between RA and HC. [Conclusions] Although the PB T cell in RA had smaller differences with that of HC than expected, several signatures were found in CD8 Tem and Temra of RA.

W89-3

The low mitochondrial biogenesis induces synovial cell proliferation and enhances joint destruction in in RA

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Conflict of interest: None

[Objectives] One of mitochondrial functions was apoptosis sensor. Therefore, we measured the expression levels of mitochondria-biogenesis related genes in RA-FLS and osteoarthritic (OA)-FLS. We tested the effects of 5-Aminoimidazole-4-carboxamide ribonucleotide (AICAR), an enhancer of mitochondrial biogenesis, on cell synovial proliferation in RA-FLS and joint destruction in collagen-induced arthritis (CIA) mice. [Methods] Quantitative PCR was used to assess the expression levels of mitochondria-related mRNA (PGC-1a, NRF-1, and TFAM) and number of mitochondrial DNA (mtDNA) in RA- and OA-FLS. The effect of AICAR (2 mM) in RA-FLS assessed cell proliferation, apoptosis, MMP3/RANKL, microarray. The effect of AICAR in CIA mice (500mg/kg) assessed on the changes of arthritis score, CT, score of inflammatory cell infiltration, synovium and cartilage degeneration, and osteoclast number by histological analysis. [Results] The mitochondria biogenesis was lower in RA-FLS. In RA-FLS, the mitochondria biogenesis enhanced AICAR, inhibited cell viability by inhibited apoptotic resistance and MMP3/RANKL in inflammated RA-FLS, and which reduced the joint destruction in CIA mice. [Conclusion] We strongly suggested that low mitochondrial biogenesis may induce joint destruction in RA.

W89-4

SPACIA1/SAAL1- regulated CDK6 expression could contribute the proliferation of RA synoviocytes _in vitro_

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Conflict of interest: None

Objectives *SPACIA1/SAAL1*(SPACIA1) is a gene associated with the aberrant proliferation of RA synovial fibroblasts (RASFs). We have reported that SPACIA1 transgenic and knockout strains of mice were also involved in the progression of collagen-induced arthritis; however, we conclude that there is almost no potential for SPACIA1 itself as a druggable target. We previously identified CDK6, one of cell cycle regulator genes at G1 phase, which is reduced by half with SPACIA1 siRNA in RASFs. In this study, we examined the effect of siRNA-mediated suppression of CDK6 expression on the proliferation induced by TNF-α. **Methods** To confirm the influence of CDK6 gene-silencing by three specific siRNAs, real-time PCR was used to examine the expression of G1 phase-associated molecule. Cell proliferation was determined by the Cell Counting Kit-8 assay. **Results** We obtained siRNA effectively inhibited endogenous mRNA expression levels of CDK6, but not of CDK4. CDK6 siRNA suppressed the proliferation of RASFs stimulated with TNF-α($P < 0.05$) compared with control siRNA. **Conclusion** CDK6 knockdown results in impaired proliferation of synoviocytes, which is consistent with our previous studies of SPACIA1. We are currently planning to elucidate the rheumatoid pathophysiologic role of CDK6 *in vivo*.

W89-5

Siglec as a new treatment target of rheumatoid arthritis

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Conflict of interest: None

For the maintenance of homeostasis, the balance between activation and suppression of the cells is important. We thought of enhancing the suppressive function as a new treatment instead of blocking the immune activation function. Sialic acid-binding immunoglobulin-like lectin (Siglec) family have molecules which are related to negative regulation of cell activity. In this study, we focused on a certain molecule (Siglec-A) of Siglec family and examined the effect of an anti-Siglec-A Antibody (Ab) on the collagen-induced arthritis (CIA) model mice. We made monoclonal anti-Siglec-A Ab and administered it to the CIA mice. The Ab treatment ameliorated arthritis score and suppressed the bone erosion. The anti-type II collagen (CII) Ab titer and T cell response were down-regulated by the Ab treatment. With the CII stimulation, IL-10 production of the splenocytes was up-regulated. IL-10 is thought to be engaged in the amelioration effect of the Ab. In the CIA model with IL-10 knockout mice, there were no score difference between the Ab treated and control group. Anti-Siglec-A Ab ameliorated arthritis via IL-10 production. The anti-human homologue of Siglec-A Ab will be a new anti-rheumatic drug.

W89-6

A Novel Pharmacological Action of MTX _via_ Circadian PAR bZip Transcription Factors

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Conflict of interest: None

OBJECTIVE: To explore a novel mechanism of Methotrexate (MTX)-induced apoptosis on RA-FLS, we examined the relation between MTX and PAR bZip (proline and acidic amino acid-rich basic leucine zipper) circadian transcription factor family. METHODS: Total RNA was extracted from MTX (10nM:24hr)-treated RA-FLS, and real time PCR was performed to examine expressions of circadian clock genes (*Clock, Bmal1, Cry1 and Per2*), PAR bZip genes (*Dbp, Tef* and *Hlf*), and mitochondria-related pro-apoptotic factor *Bik*. In addition, expressions of PER2 were observed by fluorescent immunostaining and expressions of PER2 / CYTOCHROME C were examined by western blotting. After transfected with *Per2* siRNAs (5nM), RA-FLS were successively treated with MTX (10nM) to examine cell viabilities by WST-8 assay. RESULTS: MTX enhanced mRNA expressions of *Per2, Dbp, Tef*, *Hlf,* and *Bik*. The enhanced expressions of PER2 and CYTOCHROME C were also observed. Cytotoxicity of MTX on RA-FLS was attenuated by *Per2* interfering. CONCLUSION: *PAR bZip* genes affect the transcription of *Per2* and *Bik.* A novel action of MTX that enhanced expressions of *Per2/Bik* through *Dbp/Tef/Hlf* to induce apoptosis, was proposed.

W90-1

Epidemiological survey in the treatment of Juvenile Idiopathic Arthritis-associated uveitis of pediatric rheumatology hospitals in Japan

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Conflict of interest: None

【Method】We retrospectively investigated characteristics of JIA-U patient from 12 pediatric rheumatology hospitals in Japan from January 1, 2006 to December 31, 2015.【Result】There were 34 patients with JIA-U, which were approximately 5% of whole JIA. 16 patients (47.0%) were treated before JIA-U onset (10 NSAIDs, 8 MTX, 3 glucocorticoids (GC), 1 etanercept (ETN)). 10 patients (29.4%) developed during ETN, MTX, GC use. GC instillation was applied in all cases. MTX was used in 20 cases after onset of JIA-U, 2 cases cured of JIA-U without additional drugs. 18 cases (52.9%) used biological agents after the onset of JIA-U (10 infliximab, 9 adalimumab, 4 tocilizumab, 2 ETN). Among 18 cases, 17 cases (94.4%) showed improvement in symptoms, 11 cases (61.1%) cured.【Conclusions】We conducted a survey in the treatment of JIA-U at pediatric rheumatism hospitals in Japan. Biological agents are used in more than half cases and their effectiveness is expected. We will plan the investigation of whole Japan that includes the ophthalmologists in future.

W90-2

Epidemiological survey of Juvenile Idiopathic Arthritis-associated uveitis of pediatric rheumatology hospitals in Japan

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Conflict of interest: None

【Objective】Characteristics of JIA-associated uveitis (JIA-U) are still unclear in Japan, though JIA-U is important complications which can lead to poor visual outcomes, so our aim is to make clear that of pediatric rheumatology hospitals in Japan.【Methods】We retrospectively investigated characteristics of JIA-U patient from 12 pediatric rheumatology hospitals in Japan from January 1, 2006 to December 31, 2015.【Results】There were 34 patients with JIA-U which were about 5% of all JIA. 76.5% were females. 88.2% were oligo. 61.8% were ANA (+) and 97% were RF (-). There were not family histories and episodes of infection. The median age was 5 years old (3-12) and under 7 years old of these were 55.9%. Uveitis occurred before the onset of arthritis in 6%, within the first 4 years after onset of arthritis in 67.6% and after therapy-off of arthritis in 13.2%. 56% was bilateral and 58.8% was anterior. 55.9% had no symptom, but 41.2% had ocular complications (cataracts, posterior synechia of the iris and so on) and 52.9% at the first diagnosis of uveitis. Only 30% had visited constantly ophthalmologist before diagnosis.【Conclusions】Because this investigation limited specialized hospitals, we will plan the investigation of whole Japan which includes the ophthalmologists in future.

W90-3

Clinical outcome in oligoarticular juvenile idiopathic arthritis; single center experience

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Conflict of interest: None

【Introduction】In the literature, half of the patients with oligoarticular juvenile idiopathic arthritis (o-JIA) could achieve complete cure in in the first decade from onset, but there have been little reports regarding relapse rate.【Methods】We retrospectively studied 35 children with o-JIA diagnosed in our institute since 2010. We investigated the risk factor of relapse of arthritis. Initial treatment consists of methotrexate (MTX) and low dose prednisolone.【Results】The median age of onset is 2.7 year-old (0.7~15.0). Seventeen of 35 patients (48.6%) had experienced relapse. Relapse-free survival in three and five years are 48.7% and 26.7%, respectively (Kaplan-Meier method). In the relapsed group, 15 patients (88.2%) relapsed under MTX treatment. Nine among 15 case (52.9%) needed additional biologic agents.【Conclusion】Approximately half of the patients had experienced relapse in the first three years, but all relapsed patients were successfully managed with additional treatment including biologic agent. However, we could not find any risk factors at onset to predict future relapse.

W90-4

16 cases of juvenile spondyloarthritis (SpA)

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Conflict of interest: None

[Objectives] Pediatric patients with psoriatic arthritis (PsA) or enthesitis related arthritis (ERA), which are subtype of Juvenile Idiopathic Arthritis (JIA), were rare in Japan. But the number of patients with these diseases is increasing in recent years. We aimed to clarify the clinical picture of patients with pediatric onset spondyloarthritis (SpA). [Methods] We examined clinical symptoms, examination results and treatment retrospectively using electronic medical charts for JIA treated in our center. We investigated cases of PsA and ERA further and compared with cases with other subtypes of JIA. [Results] Of 46 JIA cases, we had 4 cases (9%) of PsA and 12 cases (22%) of ERA. Patients of both subtype 16 cases (35%) in total were higher than the previous report in Japan (1.6%). The age of onset ware 4 to 15 year of age (median 12), 7 boys and 9 girls. Juvenile fibromyalgia was common (50%). All cases were treated with medicine, NSAIDs 10 cases (63%), MTX 11 cases (69%), TNF inhibitor 6 cases (38%) and steroid 2 cases (13%). [Conclusion] In JIA registry of our center, juvenile onset SpA were found more frequently than in the previous report and were treated with medicine including MTX and TNF inhibitors. Juvenile fibromyalgia was complicated with high rate in these cases.

W90-5

Investigation of clinical manifestation and HLA antigen among juvenile spondyloarthritis patients in our hospital

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Conflict of interest: None

Object: Spondyloarthritis (SpA) is an umbrella term for inflammatory diseases that involve both the joints and the entheses on body ax and periphery. Some type of SpA is not covered by JIA classification, therefore we use the term "juvenile SpA (jSpA)" recently. SpA is HLA-B27 related disease and SpA patients are thought to be few in Japan where the prevalence of HLA-B27 is low. We investigated the clinical features and HLA antigens on jSpA patients in our hospital. Method: We evaluated patients' charts retrospectively. Results: There are 25 jSpA patients. Median age of jSpA-onset is 9 years, and median period till jSpA-diagnosis is 1year. Sex ratio is almost equal and 24% of patients have family history. Most were first diagnosed as oligoarticular or polyarticular JIA. Undifferentiated peripheral type SpA was major, but axial type SpA increased from 16% to 32% in the course. Ankylosing spondylitis counts to 24%. Peripheral arthritis tended to be seen on lower extremities, especially in hip joints. Value of serum CRP, ESR and MMP-3 were within normal range in half of the patients, and all patients were seronegative. Possession rate of HLA-B27, B7, B39, B61, B62, A2 was high. Conclusion: The clinical manifestation showed closer features except sex ratio and HLA antigen rate.

W90-6

Investigation of the treatment and the effect on growth among juvenile spondyloarthritis patients in our hospital

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Conflict of interest: None

Object: Spondyloarthritis (SpA) is an umbrella term for inflammatory diseases that involve both the joints and the entheses on body ax and periphery. Enthesitis related arthritis, psoriatic arthritis and part of undifferentiated arthritis of JIA are included in juvenile SpA (jSpA). Retardation of growth and puberty becomes the problem on JIA patients and it has been improving with progress of treatment. We investigated the treatment and the effect on growth among jSpA patients in our hospital. Method: We evaluated patients' charts retrospectively. Results: There are 25 jSpA patients that count to 20% of JIA patients. NSAIDs are effective on most cases and 92% patients continue. 28% patients are controlled with NSAIDs monotherapy. Methotrexate and salazosulfapyridine are prescribed in 44% and in 32% cases, respectively. TNF-inhibitors are used in 40% patients. Median height at diagnosis was -0.6 SD and it improved to be +0.01 SD after the initiation of treatment. Median Body Mass Index (BMI) percentile at diagnosis was 3.8 and it also improved to be 25.3 with treatment. Conclusion: Growth and nutritional state of jSpA in our hospital improved by the treatment of jSpA.

W91-1

Validation of the ACR/EULAR 2016 classification criteria of macrophage activation syndrome complicating systemic juvenile idiopathic arthritis in Japanese patients

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Conflict of interest: None

[Object] To validate the new criteria of macrophage activation syndrome (MAS) complicating systemic juvenile idiopathic arthritis (s-JIA) in Japanese patients. [Methods] Ninety six s-JIA patients were enrolled. Fifteen experts diagnosed non-MAS or MAS based on the patients' clinical course. MAS was diagnosed as onset of MAS or full-blown MAS. The MAS criteria was validated with the data item during acute phase of s-JIA or MAS. [Results] Four patients with suspected other complications and 7 patients with unavailable data were excluded. Among 85 s-JIA patients, 25 patients were diagnosed as MAS including 6 patients with onset of MAS and 19 patients with full-blown MAS. All non-MAS patients did not fulfill the criteria, whereas all onset of MAS patients and 18 out of 19 full-blown MAS patients fulfilled it. The sensitivity was 100% and specificity was 96%. Compared to onset of MAS patients, full-blown MAS patients fulfilled more data items. Serum TG levels were less frequently measured. Increase of serum AST levels and decrease of plasma fibrinogen levels were observed from onset of MAS phase, whereas decrease of platelets numbers and increase of serum TG levels were observed during full-blown MAS phase. [Conclusions] The new criteria was sensitive and specific to diagnose MAS.

W91-2

The analysis of gene expression in monocytes from Adult-onset Still's disease (AOSD) with DNA microarray

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Conflict of interest: None

[Purpose] Adult-onset Still's disease (AOSD) is a systemic disorder of unknown origin characterized by high spiking fever, rash and arthritis. The purpose of this study is to clarify the expression of specific genes in monocytes from AOSD patients. **[Methods] 1)** Monocytes were isolated from healthy subjects (n=3), active-AOSD (n=3) and inactive-AOSD (n=3). Differentially expressed genes (DEGs) were analyzed by DNA microarray. **2)** DEGs included in these Gene Ontology (GO) terms and validated by quantitative PCR with monocytes isolated from healthy subjects (n=5), active-AOSD (n=3), inactive-AOSD (n=6) and rheumatoid arthritis (n=8). **3)** The correlation between validated DEGs and serum CRP or ferritin among AOSD was analyzed. **[Results] 1)** In monocytes isolated from active-AOSD, 67 genes expressed significantly higher than that from healthy subjects and inactive-AOSD. **2)** After validation with 13 genes (CLU, FCGR1B, PLAC8, TLR1, S100A12, CD55, PIM1, BCL2A1, SOD2, PLSCR1, CYP1B1, STEAP4, IL1RN), PLAC8 was significantly higher in active-AOSD. **3)** In AOSD, the expression of PLAC8 in monocytes and the value of serum CRP and ferritin had positive correlation. **[Conclusion]** The overexpression of PLAC8 in monocytes might involve in the pathogenesis of AOSD.

W91-3

Distinct profiles of myositis-specific autoantibodies in Japanese patients with juvenile idiopathic inflammatory myopathies

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Conflict of interest: None

[Background] Recently, myositis-specific autoantibodies (MSAs) are reported as clinically useful biomarkers. But there are almost no reports regarding Japanese pediatric patients with Juvenile dermatomyositis (JDM). [Objectives] The purpose of this study was to describe the clinical characteristics associated with MSAs in Japanese patients with JDM. [Patients and Methods] Eligible patients were Japanese pediatric patients with JDM who came to our hospital and had onset or exacerbation of JDM from January 2011 to Oct 2016. All patients were tested for MSAs (anti-ARS, anti-TIF1γ and anti-MDA5 antibody) and classified to each group by antibodies. The clinical characteristics of each group were then compared. [Results] In total, 22 children were enrolled. The age of disease onset was 5.9 ± 4.1 years. The number of patients with anti-ARS, anti-TIF1γ and anti-MDA5 antibody was 0, 9 and 5, respectively. The patients in the group with anti-MDA5 antibody had IP more frequently than the other group. The patients in the group with anti-TIF1γ antibody had more extensive skin lesions in their clinical course than the other group. [Conclusion] Japanese pediatric patients with JDM also demonstrated different clinical characteristics dependent on MSAs, similar to those in previous reports.

W91-4

Adaptation of children to adalimimab injection and nurse support intended promotion of resilience

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Conflict of interest: None

Purpose and methods: In case of newly adalimumab applied patients, some have difficulty in set up home-injection by parents/them-

selves and some even have trouble with injections by health professionals. Adaptation of children to biweekly subcutaneous injection of adalimumab was evaluated. **Results:** Thirteen cases (5-7 years, boys: girls= 4:9, two had developmental disorder) were enrolled in the study. Adaption of the patients were following: 4 smoothly applied to home injection with no problem, 1 applied to home-injection by parents by nurse support, 1 switched to self-injection from injection by parent after nurse support, and 7 continued hospital injection by health professionals and nurse support. A 9-year-old boy with developmental disorder, previously received intravenous biological therapy under sedation. Nurse support built relationship with the child and his mother and convinced him of necessity of the therapy resulting in smooth injection by health professionals. **Conclusions** Adaptation of children to adalimumab injection is affected by self-supported degree of each patient. Nurse support intended promotion of resilience is important for not only for adaptation to painful treatment and examination but for preparation of future transition to adult medical care.

W91-5

Awareness survey of rheumatologists in adult department concerning clinical practice after transition of patients with juvenile idiopathic arthritis

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Conflict of interest: Yes

[Object] To clarify the problems concerning transition of patients with juvenile idiopathic arthritis (JIA) in adult department. [Methods] A questionnaire survey was conducted among rheumatologists in NinJa (National Database of Rheumatic Diseases in Japan). [Results] In total 30 rheumatologists answered the questionnaire. Of these, 77% had had a chance to see adult JIA, but 44% felt anxious or resistance for their clinical practice. As a factor to hesitate to see adult JIA, “response to parents”, “lack of patient’s independence”, and “doctor’s lack of knowledge about JIA” were extracted. Sixty-two percent of doctors thought it ideal that JIA patients should transit to adult department through the consultation period of pediatric and adult department, however, almost of them had transited directly. As for the timing of transition of JIA patients, there were many opinions that it should be examined according to treatment contents, and disease condition regardless of age. There were only 16% doctors who can consult pediatric rheumatologist nearby but 93% wanted to interact with pediatric rheumatologists. [Conclusion] For smooth transition of JIA patients, it might be important that education in adult department and cooperation between adult and pediatric rheumatologists.

W91-6

Attitude of non-pediatric rheumatologists from councilors in Japan College of Rheumatology surveys on transitional care

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Conflict of interest: None

Purpose: Attitude surveys of non-pediatric rheumatologists on transitional care were carried out. Method: Non-pediatric rheumatologists from councilors in JCR were enrolled in the surveys. Experiences of grown-up patients with childhood-onset rheumatic diseases, ideal medical care in adult age, and factors to make difficulty with transition to adult care were examined via e-mail. Results: Two-hundred and one responded to the surveys. Ninety-one percent of them has experiences with childhood-onset patients. Transition to non-pediatric institute as the ideal transition was supported by about 90% of them. However, non-pediatric rheumatologists with no hesitation about taking care of adult childhood-onset rheumatology disorders accounted for only 32% of all. Two main factors preventing from smooth transition to non-pediatric care were noted: inadequacy in non-pediatric care (57%) and patients lack of independence from parents/family (53%). The majority of non-pediatric rheumatologists hesitate about medical care with autoinflammatory syndromes and 93% of all needed more opportunities to learn pediatric rheumatology disorders. Conclusion: Sharing further knowledge of pediatric rheumatology within non-pediatric rheumatology were required.

W92-1

Comparison of the cerebrospinal fluid level of IL-6 in the case of systemic lupus erythematosus with psychoneurotic disorders

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Conflict of interest: None

Objectives: It is reported that IL-6 in the cerebrospinal fluid (CSF) is involved in the pathogenesis of systemic lupus erythematosus with neuropsychiatric disorders (NPSLE). We studied the relationship between the CSF level of IL-6, and MRI findings and clinical course. Methods: We analyzed 20 patients with NPSLE who were divided into 2 groups by CSF IL-6 level (pg/ml);≧4.3: group H (n=14), <4.3: group L (n=6). Results: Abnormal findings in brain MRI were found in 8 out of 14 cases in group H (3 had diffuse lesions), and 1 out of 6 cases in group L showed local abnormal findings. A case with diffuse lesion in group H showed resistance to treatment and died. 3 Cases in group L showed improvement without changing current treatment. Q albumin (spinal fluid albumin/serum albumin) was significantly elevated in group H (0.009 vs 0.004, $P<0.05$). Anti-CL-β2 GPI Ab was positive in 3 out of 14 in group H and 4 out of 6 in group L. Conclusion: It was suggested that IL-6 is directly associated with the pathogenesis of NPSLE, and anti-CL-β2 GPI Ab seemed to cause ischemic disorders. Since those with elevated CSF IL-6 levels tended to show severe courses, it was thought that an intense immunosuppressive therapy was necessary.

W92-2

Examination of the brain MRI of Acute confusional state (ACS) patients in Neuropsychiatric systemic lupus erythematosus (NPSLE)

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Conflict of interest: None

Objective: To explore the characteristics of brain MRI abnormalities in ACS in NPSLE. **Methods:** Thirty-six patients with ACS admitted to our institutions from 1992 to 2015 were enrolled. Their medical charts and brain MRI scans were reviewed. **Results:** Of the 36 ACS patients, 18 patients had MRI abnormalities. MRI abnormalities improved after treatment in 12 patients. MRI abnormalities were not correlated with ages at the onset of ACS, disease durations of SLE, the presence of anti-DNA, anti-phospholipid or anti-ribosomal P antibodies, or IL-6 levels in sera or cerebrospinal fluid. Notably, Positivity of anti-Sm was significantly higher in patients with MRI abnormalities than without MRI abnormalities (77.8% vs 27.8%, P=00067). Finally, 8 of the 18 patients with MRI abnormalities, but none of the other 18 patients without MRI abnormalities, died from active SLE. Thus, presence of MRI abnormalities significantly increased the hazard ratio for death (10.36, 95%CI: 2.487–43.19, p=0.0013). **Conclusion:** Our results demonstrate that patients with ACS with MRI abnormalities have more severe diseases, resulting in poorer prognoses. The data also indicate that anti-Sm is involved in the development of MRI abnormalities in AC.

W92-3

Clinical features of systemic lupus erythematosus patients who developed ischemic stroke

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Conflict of interest: None

[Objective] Systemic lupus erythematosus (SLE) patients sometimes suffer from cerebral infarction (CI). Although this is very serious complication, which is associated with poor prognosis, the clinical features still remain unclear. In this study, we analyzed the clinical features of SLE patients with CI. [Method] We retrospectively evaluated the clinical features and MRI findings of 93 SLE patients with neurological symptoms at Kyushu University hospital between October 2009 and April 2016. 14 of 93 patients were diagnosed as acute CI and the other 79 patients were included for comparison. [Results] The percentage of patients who had T2 high-signal lesion in white matter on brain MRI was significantly higher in patients with CI than in those without CI (p=0.02). No relationship between brain infarction and the presence of antiphospholipid antibodies, disease activity, or the general risk factors of brain infarction (hypertension, diabetes mellitus, and hyperlipidemia) was found. [Conclusion] The presence of T2 high-signal lesion in white matter seems to be the predictive factor of brain infarction in SLE patients.

W92-4

Positive direct Coombs' test in the absence of hemolytic anemia predicts high disease activity and poor renal response in systemic lupus erythematosus

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Conflict of interest: None

Objectives: Direct Coombs' test in the absence of hemolytic anemia was newly included in the immunologic criterion of the SLICC/ACR 2012 criteria for SLE. In this study, we determined its clinical significance in Japanese SLE population. **Methods**: Patients who fulfilled SLICC/ACR classification criteria of SLE and visited St. Marianna University Hospital during Jan to Nov 2016 were prospectively evaluated with direct Combs' test. Hemolysis was defined as lower haptoglobin concentration than the normal limit. Clinical features including SLEDAI, treatment, renal response, and laboratory findings were examined. **Results**: Among 122 patients enrolled, 9 (7.1%) patients were positive with direct Coombs' test in the absence of hemolytic anemia. They had higher SLEDAI (p<0.01), lower CH50 (p<0.01), higher anti-DNA titer (p<0.01) and lower cumulative complete renal response rate (p=0.03) comparing to those who were negative. Multivariate analysis indicated that SLEDAI was the independent factor strongly correlated with the direct Coombs' test (OR 7.4, 95%CI 1.66-4.98, p<0.01). **Conclusions**: Direct Coombs' test in the absence of hemolytic anemia might be correlated with high disease activity and poor renal response in SLE.

W92-5

The investigation of treatment intensification in serological positive SLE patients

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Conflict of interest: None

[Purpose] In this study, we investigate the effect of sustained serological positive to the subsequent treatment of SLE patients in our faculty. [Method] In our faculty, 124 patients were serological positive over a period from August 2012 to October 2012 (Period1). We excluded the patient who had increased prescription or new case over a period from February 2012 to July 2012. Consequently, 95 patients was included. The treatment of these patients until October 2014 was investigated. We used C3, C4, and anti-dsDNA antibody as serological marker. We defined serological positive as any one of three markers was positive and serological negative as all of them were negative. [Result] Patients who needed treatment intensification in a year was 12%(25%, in two year) but needed prednisone over 30mg/day was only five. In intensification group, the mean of anti-dsDNA antibody in Period 1 was higher than non-intensification group (49 vs 26mg/dl). There is no significant difference with C3 and C4. [Conclusion] A fair percentage of patients didn't need treatment intensification at least two years in conditions of serological positive. Aiming at serological remission may be over treatment but we note that with high baseline anti-dsDNA antibody group, they may need intensification treatment.

W92-6

The relationship between disease activity of systemic lupus erythematosus and cystatin C

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Conflict of interest: None

Objective: To investigate relationship between SLEDAI and cystatin C (CyC) as well as creatinine (Cre). **Methods:** Data were collected from 52 patients (50 women and two men, 47.9±13.2 years old) with SLE who had been examined their CyC at least once. **Results:** The average CyC and Cre of maximum level in each individual was 1.27±0.71 mg/L and 0.82±0.74 mg/dL, respectively. Comparing 20 patients with CyC ≧1.2 mg/L and 32 patients with CyC <1.2 mg/L, SLEDAI was significantly higher in the former group, while the dose of corticosteroids did not differ significantly. The ratio of CyC to Cre was significantly higher in 25 patients with SLEDAI ≧3 than in 27 patients with SLEDAI <3. CyC levels and disease flares went parallel in some cases. Eight patients showed eGFRcyc/eGFRcre <60% and their SLEDAI was 10.6±10.9. Organ involvement was found in 7 (87.5%) patients (2 with retinopathy, 1 with cerebral hemorrhage, 1 with myositis plus nephritis, 1 with hemolytic anemia, 1 with pleuritis, and 1 with enteritis). In contrast, SLEDAI of 44 patients with eGFRcyc/eGFRcre ≧0.6 was 3.6±4.3 and organ involvement was found in 11 (25.0%) patients. **Conclusion:** SLE patients with increased ratio of CyC to Cre had high disease activity and organ involvements with high frequency.

W93-1

The correlation between renal pathology and clinical course of lupus nephritis: single center study

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Conflict of interest: None

[Objectives] 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] 58 patients with LN proven by renal biopsy from 2001 to 2016 were enrolled. We assess the correlation between clinical features and pathohistological findings. [RESULTS] Female were 47 (83.3%). Mean age was 44.0±2.3 years old. According to ISN/RPS classification, I, II, III, IV, III/IV+V, and V were 3, 3, 13, 9, 25 and 4 cases, respectively. Intensive therapies included mPSL pulse therapy (34 cases; 58.6%), IVCY (12; 20.6%%) and IVIG (3; 5.1%), following oral PSL. After 1 year, 52 pa-

tients had remission, but 6 had poor prognosis. In LN I or LN II, proteinuria level was less than 1.0g/gCr and renal dysfunction was mild. In LN III/IV+V and LN V, the Sm antibody levels were significantly lower and proteinuria levels were higher than those in LN III/IV only. In LN III/IV+V, renal dysfunction tend to be severe and resistant to treatment. [CONCLUSIONS] In LN exhibiting LN V, severe proteinuria was observed, so we suspected that this result might result from podocyte damage. In LN III/IV+V, renal dysfunction tended to be more severe.

W93-2

Prognosis of lupus nephritis with unknown pathology patients in our department

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Conflict of interest: None

[Object] Patients with lupus nephritis (LN) are recommended to be treated according to their renal pathology. However, not all the patients could undergo renal biopsies. Here we investigate the prognosis of LN patients with unknown pathology in our department. [Methods] This retrospective analysis was conducted on LN patients with unknown pathology who were treated in 2015 in our out patients department. [Results] In total of 343 patients with systemic lupus erythematosus (SLE), 119 patients (35%) have LN. Among them, 47 patients (39%) have not been evaluated their renal pathology. The most common reason not undergoing renal biopsies was bleeding tendency (11 patients), and the second was no consultation to Nephrologist (10 patients). At the time of January 2016, among LN patients who were treated at least one year, one patient have progressed to end stage renal failure, but 22 patients (50%) had no LN activities. [Conclusions] Although it could be difficult to treat some LN patients with unknown pathology, about a half of LN patients with unknown pathology could be manageable with proper therapy according to their laboratory data.

W93-3

Analysis of clinical features of systemic lupus erythematosus complicated by lupus nephritis

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Conflict of interest: None

【Objectives】We evaluated clinical features of systemic lupus erythematosus (SLE) complicated by lupus nephritis (LN).【Methods】79 cases of SLE including 38 cases of LN who received examination in our department from April to July, 2016.【Results】LN was complicated by 48% of SLE. Significantly higher rates of dyslipidemia and hyperuricemia and anti-cardiolipin antibody (aCL antibody) positive were observed in cases with LN than those without LN, whereas the value of complements and autoantibodies was rather low in the former. The sustained proteinuria did not relate to occult hematuria but to urinary casts. Negative conversion of proteinuria was confirmed in all cases of class II and III, 60% of class IV, and 50% of class V according to the ISN/RPS classification.【Conclusion】These data indicated that therapy for hyperuricemia and dyslipidemia was important to maintain the renal function and aCL antibody positive related to the renal involvement. However, no relation between the sustained proteinuria and the value of complements or autoantibodies was revealed.

W93-4

Association between pregnancy and chronic damage index in systemic lupus erythematosus

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Conflict of interest: None

[Objectives] To evaluate association between pregnancy and chronic damage index in systemic lupus erythematosus (SLE). [Methods] Female SLE patients at Okayama University Hospital and Showa University Hospital from January to June 2016 were enrolled. Associations between pregnancy or perinatal complications and irreversible organ damage using SLICC/ ACR Damage Index (SDI) were evaluated. [Results] Of 222 enrolled patients, median age at registration was 44 years, median disease duration was 12 years, and median SDI score was 1. One hundred twenty-six (56.8%) patients experienced pregnancy exhibited older age (49 vs 37 years, $p< 0.0001$), higher levels of CH50 (37 vs 33 U/ml, $p= 0.005$), and high SDI score (1 vs 0, $p= 0.0105$) than those not experienced pregnancy. After adjusting age and levels of CH50 using multivariate analysis, pregnancy had not statistical association with increasing SDI score. Of 126 patients had pregnancy, 44 patients experienced perinatal complications such as abortion, premature birth, stillbirth, and termination due to maternal condition. There was no significant difference in SDI score between the patients with or without perinatal complications. [Conclusions] The pregnancy or perinatal complications might not increase chronic damage index in SLE patients.

W93-5

The outcomes of pregnancy in patients with systemic lupus erythematosus

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Conflict of interest: None

Objectives: The patients with systemic lupus erythematosus (SLE) are associated with increase in obstetric complications. Recent foreign reports were shown that disease flare up occurred in about 50%. To clarify influence of pregnancy with SLE, We retrospectively reviewed the outcomes of pregnant patients. **Methods:** Patients that 26 cases (21 patients) of pregnancy complicated with SLE who were seen at St. Marianna University Hospital from Sep. 2010 to Aug. 2016. The cases include 20 birth, 1 artificial abortion, 4 miscarriages, 1 case born dead. All patients met 1997 revised American College of Rheumatology criteria for SLE. Five cases of non-reassuring fetal status, 2 cases of disease worsening patients are defined abnormal delivery. **Results:** The average age of 26 cases is 31.6±5.4 and primipara is 32.2±5.2 years old. Mean birth weight is 2571.5±673.9 g. Disease flare up occurred in 11.5%. SLEDAI whom abnormal delivery group was significantly high level as compared with normal delivery group. **Conclusions:** As for the SLE merger pregnancy case, age of primipara is older than normal Japanese. It suggests that time before pregnancy being admitted by patients with SLE. We should carefully evaluate disease activity, and should cooperate with obstetrician during pregnancy.

W93-6

Long term efficacy and safety of tacrolimus for patients with systemic lupus erythematosus

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Conflict of interest: None

Purpose: Tacrolimus (TAC) has been approved for rheumatoid arthritis and lupus nephritis since 2007 in Japan. We presented in EULAR 2009 the short term results of efficacy of TAC, as results 82.7% patients showed some efficacy. Long term efficacy and safety of TAC were evaluated. Method: We picked up the SLE patients treated with TAC in our hospital started from 2007 to 2009. We checked the reason of adding TAC, steroid dose, clinical data, and SLEDAI. Results: We found 60 patients treated with TAC from 224 patients. They were 8 males and 52 females, and their average age was 37.8 + 12.2 years-old. The reasons of adding TAC were mainly the difficulty to decrease steroid dose. The persistence cases of TAC were 37 (61.7%) and five years persistence rate was 65.0%. The reasons of cessation of TAC were change of the movement for 3 cases, stop to come to our hospital for 4 cases, change to the clinical study for 2 cases, death for 6 cases, the adverse effects for 3 cases, relapse for 4 cases, and the patients' will for 3 cases. The sparing effect of steroid was observed that prednisolone 11.1 + 6.2 mg/day as initial dose could be decreased to 6.8 + 3.2 mg/day. Conclusion: We considered that TAC was very effective for the many clinical features and was relatively administered in safe.

W94-1

The rheumatoid arthritis (RA) case may cause a liver function disorder during follow-up. I evaluate liver fibrosis and report it for 7 cases with the liver damage using Transient Elastography

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Conflict of interest: None

(Outcome) ALL Female, Average age 72 years old, Average BMI 22.3 Fatty liver was diagnosed in 4 cases during 7 cases and doubted cirrhosis in 1 case. (CASE) 64years old, female, RA of The 1991 onset The patient was under the medical treatment with tocilizumab and bucillamine. However, I introduced me to a liver specialist because I accepted a liver damage. The patient performed abdominal echo and Transient Elastography and had a diagnosis of Non-alcoholic steatohepatitis (NASH). It was an evaluation the liver hardnessresult was 8.5, CAP were 290, and was more likely to shift to cirrhosis. I gave nourishment instruction, kinesitherapy for a patient and became the follow-up every one year. (Conclusions) Transient Elastography can diagnose fibrosis of the liver noninvasively.

W94-2

Examination of the autoantibody for the Amyloid peptide in patients with rheumatoid arthritis

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Conflict of interest: None

Objective: The accumulation of Amyloid-β is considered as an onset factor of dementia. We develop the measurement system of the autoantibody for Amyloidβ peptide (Aβ-40) and reported it (J Neurol Neurosurg Psychiatry. 2016). We examined serum anti Aβ-40 antibody concentrations using the ELISA method for rheumatoid arthritis (RA) patients. **Subjects and Methods:** The subject intended of 104 patients with arthralgia. The diagnoses were 53 RA; age 55.5 ± 17.2 years old, and 51 undifferentiated arthritis (UA); 59.1 ± 12.8 years old. **Results:** AntiAβ-40 antibody concentrations (Mean ± SE) unit (u) were RA group 17.0 ± 2.3u, UA group 11.2 ± 0.95u, and control group 8.3 ± 0.87u. RA group has significantly higher concentrations than UA group ($p<0.02$) and healthy control group ($p<0.002$). In both RA group and UA group, there were no correlations between AntiAβ-40 antibody concentrations with the CRP, and anti-CCP antibody. **Discussion**: It was suggested that there were significantly higher concentrations of the autoantibody for the Aβ-40 peptide in RA patients. However, the range of concentrations of the autoantibody for the Aβ-40 peptide is wide, we need detailed considerations of RA patients backgrounds.

W94-3

A Research on Variation of Anti-citrullinated Protein Antibody and Rheumatoid Factor by Using Biological Originator Disease-Modifying Antirheumatic Drugs (DMARDs) and Targeted Synthetic DMARDs

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Conflict of interest: None

[Object] This study aimed to investigate changes in anti-CCP and RF serum levels in patients with RA on biological drugs and targeted synthetic DMARDs as compared to disease activity. [Methods] We studied 103 patients with RA (Male: Female=24:79, Age (years): 59.4, Duration of disease (years): 9.2, MTX (%): 68.0, the dose of MTX (mg/week):10.1±2.7 [mean± SD]) tested anti-CCP just before started a first biological drug or targeted synthetic DMARDs (53 anti-TNF drug (6 infliximab,14 etanercept,4 adalimumab,6 golimumab,23 certolizumab pegol), 16 tocilizumab,20 abatacept, 14 tofacitinib), and 12 months after each therapy. [Results] 1)80 patients (77.7%) were positive for anti-CCP, and 79 patients (76.7%) were positive for RF. 2) The anti-CCP levels decreased from 220.8±235.6 to 172.0±214.4 ($p=0.001$) in patients taking anti-TNF drugs. 3) RF serum levels decreased from 115.7±137.1 to 74.5±86.3 ($p=0.012$) in patients taking anti-TNF drugs, and from 221.8±419.0 to 85.7±80.4 ($p=0.011$) in patients taking ABT. 4) DAS28-CRP decreased from 4.11±1.28 to 2.19±0.92 ($p<0.001$) in all patients, and there was no significant difference among each therapy ($p=0.106$). [Conclusion] Our study showed that anti-CCP levels decreased by anti-TNF drugs and ABT, RF levels decreased by anti-TNF drugs correlate with disease activity.

W94-4

Screening for novel autoantibodies in rheumatoid arthritis using a high-throughput protein synthesis and AlphaScreen method

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Conflict of interest: None

[Object] Because it is sometimes difficult to diagnose anti-cyclic-citrullinated-peptide (aCCP)-antibody-negative rheumatoid arthritis (RA), we tried to find new autoantibodies which is useful for diagnosing RA. [Methods] 2273 proteins were synthesized by the wheat cell-free protein synthesis technology. Citrullinated protein series was also prepared by using peptidyl arginine deiminase. Screening for antibodies against both unmodified and citrullinated proteins was performed by AlphaScreen method, and divided into 2 steps; primary screening by the sera from 4 RA patients and 2 healthy controls (HCs), and secondary screening by the sera from 66 RA patients, 20 various collagen tissue disease patients, and 10 HCs. Finally, 3 proteins were evaluated by ELISA using 489 RA patients' and 56 HCs' sera. [Results] Anti-citrullinated leucine zipper

protein 1 antibody was detected in 65.1 and 8.9% of aCCP-positive and negative RA patients, respectively. Anti-citrullinated tumor suppressing subtransferable candidate 4 antibody was detected in 82.2 and 7.2% of aCCP-positive and negative RA patients, respectively. On the other hand, anti-delta like non-canonical Notch ligand 1 antibody was not diagnostic. [Conclusions] We found novel autoantibodies using a high-throughput method.

W94-5

Antinuclear antibody found in peri-/post-menopausal women—the clinical significance of anti-dense fine speckled (DFS) 70 antibody—

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Conflict of interest: None

(Object)Peri-/post-menopausal women visit the clinic with complaints of MS and joint arthralgia. Some of them presented neither RF nor CRP, but positive ANA with homogenous pattern. They don't have any significant manifestation. In this study, anti-dense fine speckled (DFS) 70 antibody was tested in menopausal women and RA. (Method) 40 patients visiting the clinic were randomly enrolled in October, 2016. Blood examination included ANA, anti-DFS 70 (tested by ELISA kit. MBL), RF, anti-CCP, anti-SS-A and so on. Further, E2 and follicule stimulating hormone (FSH) and patient-VAS were obtained before and after treatment of hormone replacement therapy. (Results) The presence of anti-DFS70 antibody was 25%(10 of 40) and the mean age of 56 in positive patients were significantly younger than that of 64.7 in 30 negative patients. This antibody was found in 41.7%(5 of 12) in peri-/post-menopausal arthralgia women, however, it was found in only 10%(1 of 10) in RA (Discussion) In this small study, anti-DFS70 antibody was relatively high percentage in menopausal women, in contrast to the low positivity of RA. The determination of anti-DFS70 antibody found in menopausal arthralgia women is useful for differentiation of homogenous pattern indicating anti-DNA/histone antibody found in SLE.

W94-6

The analysis of clinical and therapeutic course of idiopathic interstitial pneumonia with anti-ARS (aminoacyl-tRNA synthetase) antibodies

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Conflict of interest: None

Objective: AntiARS antibodies can be detected in part of patients with idiopathic interstitial pneumonia (IIP), but standard therapeutic strategy of them has not been established. We investigated the clinical and therapeutic course of such patients. **Methods:** We analyzed clinical charts of 17 anti-ARS-positive patients with IIP since 2007 excluding those who were diagnosed or suspected of polymyositis/ dermatomyositis in their clinical course. Anti-ARS antibodies were detected with RNA-immunoprecipitation using Hela cell extracts. **Results**: There were 5 with anti-KS, 5 with anti-PL-12, 3 with anti-EJ, 3 with anti-PL-7, and 1 with anti-OJ. 94.1% of anti-ARS-positive IIP patients received glucocorticoids, and some of them received additional immunosuppressive therapies (cyclosporine 4, cyclophosphamide 1, and tacrolimus 1). 6 (35%) relapsed when glucocorticoid had been tapered, and anti-EJ-positive patients relapsed significantly more frequently than other anti-ARS patients. (p=0.0294) **Conclusions:** Most of anti-ARS-positive IIP patients were treated with immunosuppressive agents and showed favorable responses. However, some, in particular anti-EJ, seemed to be a risk of relapse. Prospective studies are needed to clarify clinical course and establish therapeutic strategy of them.

W95-1

The impact of DMARDs on employment status and work impairment in rheumatoid arthritis-KURAMA cohort study

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Conflict of interest: Yes

Objective: This study is aimed to investigate how DMARDs affect employment status and work impairment in rheumatoid arthritis (RA). Methods: We chose the 548 of consecutive RA patients in our clinical cohort study and assessed clinical variables, disease activity, HAQ, and WPAI-RA. Results: The number of employees was 29.2%. DAS28 was 2.50 in paid worker (PW), and 2.95 in not-employee (NE). Mean age was 54.6 years in PW and 66.6 years in NE. Mean disease duration was PW 8.2 years, NE 14.8 years. DAS28ESR was PW 2.50, NE 2.95. HAQ-DI was PW 0.54, NE 0.70. boDMARDs was PW45.6%, NE36.9. MTX was PW77.5%, NE63.4%. sDMARDs without MTX was PW37.5%, NE39.4. PSL was PW26.9%, NE34.8%. Absenteeism was 6.2±16.9%. Presenteeism was 18.6±25.4%. Work impairment (WI) was 21.9±28.7%. In multivariate analysis, there were associations between employment status and MTX (ODs1.90, 95%CI 1.09-3.42). Moreover, there were associations between WI and bDMARDs (t value=1.98). Conclusion: In Japanese RA cohort study, MTX was predictor of employment status. In addition, bDMARDs influenced work impairment.

W95-2

Analysis of the Current Treatment Status in Patients with Rheumatoid Arthritis Receiving Public Assistance Using the IORRA Cohort

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Conflict of interest: Yes

[Objective] To investigate clinical features and treatment status of RA patients receiving public assistance. [Method] We identified RA patients who were receiving public assistance since April 2011. A cross-sectional analysis was performed in these patients using the IORRA. Each RA patient on public assistance was followed up for two years including status of public assistance. [Results] A total number of RA patients on public assistance was 127 (mean DAS28, 3.5; mean J-HAQ, 1.20: biologics use, 21.2%). In comparison to all RA patients (n = 5,661; DAS28, 3.0; J-HAQ, 0.65: biologics use, 14.2%), RA patients on public assistance had higher disease activity, advanced functional disability, and higher use rate of biologics. At two years of follow-up, RA patients on public assistance (DAS28, 3.0; mean J-HAQ, 1.13: biologics use, 28.0%) improved disease activity with increase in the biologic use. Eight patients (6.3%) had stopped receiving public assistance at two years. None of the patients stopped receiving public assistance with working. [Conclusion] RA patients on public assistance had advanced functional disability, and higher biologic use rate. None of the patients stopped receiving public assistance with working. These findings seem to be important socioeconomic issues.

W95-3

Safety outcomes associated with rituximab therapy in the treatment of autoimmune diseases: systematic review and meta-analysis

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Conflict of interest: None

Objective: Treatment with rituximab (RTX) has demonstrated efficacy for patients with several autoimmune diseases. However, safety evidence of RTX is still lacking. We conducted to evaluate the safety of RTX for autoimmune diseases. Methods: A literature review was performed based on the randomized clinical trials (RCTs) that assessed adverse events (AEs) by comparing RTX and placebo or no treatment. Meta-analyses were performed for each outcome separately using fixed model and generic inverse variance method. Results: 16 eligible RCTs, with a total of 4147 patients for 5 autoimmune diseases (n=8: rheumatoid arthritis, n=3: Sjogren syndrome, n=1: SLE, multiple sclerosis, ulcerative colitis, Graves orbitopathy, immune thrombocytopenia) were analyzed. The incidence of infusion related reactions and the human antichimeric antibody (HACA) were higher in RTX group (OR 1.49, 95%CI 1.25-1.77 and OR 2.25, 95%CI 1.35-3.76, respectively). However, there were no significant differences in the odds of total AEs, serious AEs, withdrawal for AEs, infections, serious infections, malignancy, and all-cause death between two groups. Conclusion: Our meta-analysis revealed that RTX was not associated with an increased risk of AEs except for infusion related reactions and the incidence of HACA.

W95-4

Clinical characteristics and prognosis of community acquired pneumonia in patients with rheumatoid arthritis treated with tocilizumab

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Conflict of interest: None

Purpose: To examine the clinical characteristics and prognosis of community acquired pneumonia (CAP) in patients with RA treated with tocilizumab (TCZ). **Method**: We extracted the patients who developed CAP in RA patients with biological DMARDs from the database in our hospital between 2003 and 2015. We compared patient background, duration from onset of symptoms to diagnosis and severity of CAP between the patients who developed CAP with TCZ and TNF inhibitors. **Result**: Of 98 patients who were treated with TCZ, 7 cases developed CAP (IL-6 inhibitor group). Of 560 patients with TNF inhibitors, 27 cases developed CAP (TNF inhibitor group). Between two groups, there were no differences in the age (66 years [61-80], 66 years [40-83]), the duration from onset of symptoms to diagnosis (7 days [4-21], 7days [1-15]) and admission rate (57.1%, 70.3%). IL-6 inhibitor group was lower in body temperature at the diagnosis (36.5℃ [36.4-36.8], 37.8℃ [35.9-40.5]) and CRP level (0.09mg/dl [0.02-2.5], 6.76mg/dl [0.63-15.2]) than TNF inhibitor group. In CURB-65 and A-DROP which were severity index of CAP, there were no differences between two groups. **Conclusion**: In our study, the prognosis and severity of CAP in RA patients treated with TCZ was not worse than TNF inhibitor groups.

W95-5

Comparative risk of hospitalized infection between biological agents in rheumatoid arthritis patients: A multicenter retrospective cohort study in Japan

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Conflict of interest: None

[Objectives] To examine comparative risk of hospitalized infection between biological agents (BIOs) used for rheumatoid arthritis (RA) patients. **[Methods]** We conducted a retrospective cohort study with a follow-up time of up to 2 years, using data from 2009–2014 for all RA patients who had first received BIOs at eight community hospitals. New treatment episodes with etanercept, infliximab, adalimumab, abatacept, or tocilizumab were included. Incidence rates (IRs) of hospitalized infection were examined. Cox regression analysis was used to calculate hazard ratios (HRs), adjusting for confounders. **[Results]** A total of 1596 new treatment episodes were identified. A crude IR during the first year was 7.4 per 100 person-years (PYs). No significant difference in HRs was observed between BIOs. Advanced age (HR 2.09) and concurrent prednisolone (PSL) use (≥ 5 mg/day) (HR 3.79) were true confounders. In subgroup analyses for advanced age, first BIO use, and concurrent methotrexate or PSL use, similar results were obtained. A crude IR during the second year was decreased (3.0 per 100 PYs). **[Conclusions]** The magnitude of the risk of hospitalized infection is not determined by the type of BIOs. Advanced age and PSL use are important factors to consider when starting treatments with BIOs.

W95-6

Pregnancy plan and perinatal management in rheumatic disease

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Conflict of interest: None

Objectives: Child birth in older aged women and prognostic improvement of rheumatic diseases would contribute to the increase of the number of patients who plan pregnancy. This study was performed in order to study the problems in pregnancy plan and perinatal management in rheumatic diseases. Methods: Patients with rheumatic diseases from teenage to 50th were subjected for the study. The inclusion period was from Jan 2010 to Mar 2017. Information concerning pregnancy or perinatal management of study subjects was retrospectively collected and analyzed. Results: Pregnancy was planned 68 cases. All cases were in remission status of the disease when pregnancy was planned. 33 cases become pregnant and 8 patients gave normal birth. There were 8 cases of low-birth-weight baby, however, no malformation was seen. Cesarean section was performed in 11 cases because of pregnancy high blood pressure syndrome etc. 2 ectopic pregnancy, 3 miscarriages, 2 fatal death were noted. 3 artificial abortions were performed by the reason of unwanted pregnancy. Exacerbation or newly development of rheumatic diseases was recognized in 8 cases. Conclusions: Pregnancy plan is preferable when patients maintain low disease activity or remission.

W96-1

Efficacy of iguratimod in patients with rheumatoid arthritis

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Conflict of interest: None

Objective. The purpose of this study was to investigated the efficacy of iguratimod (IGU) in patients with rheumatoid arthritis (RA). *Methods*. One hundred fifty-three RA patients (123 females) who received IGU were observed in this retrospective study. The improvement and efficacy were evaluated by the disease activity score (DAS28) at baseline, 12, 24, and 52 weeks. The efficacy of IGU between patients with or without MTX were also evaluated. *Results*. The retention rate at week 52 was 73%. Seventy-six patients (50%) received methotrexate (MTX: 8.4mg/week), 61 patients (40%) used prednisolone (PSL: 3.5mg/day) at baseline. The doses of MTX and PSL at 52 weeks (8.1mg/week and 2.9 mg/

day) were significantly decreased from baseline (p<0.01). The mean DAS28 was significantly improved from 4.1 at baseline to 3.2 at 12 weeks (p<0.01). The effect of IGU was maintained thereafter, with the mean DAS28 of 3.0 at 24 weeks and 2.9 at 52 weeks. DAS28 did not show significantly difference between the patients treated with or without MTX from baseline by 52 week. *Conclusion*. Effect of IGU was maintained through 52 weeks in RA patients in spite of the presence of concomitant MTX intake. Our results suggested that IGU treatment may decrease the doses of MTX and PSL.

W96-2

Condition factors affecting achievement of remission of Iguratimod in patients with rheumatoid arthritis

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Conflict of interest: Yes

[Objective] To investigate the condition factors affecting achievement of remission by Iguratimod (IGU) in patients with the rheumatoid arthritis (RA). [**Methods**] One hundred eleven patients (21 males and 90 female) treated with IGU were examined. DAS28ESR was assessed. Among them, in 85 cases at moderate or high disease activity at starting IGU (MDA or HAD cases), we compared the patient backgrounds between the group of achievement of remission (group A) and that of non-achievement remission (B group) after 1 year IGU therapy. [**Results**] Mean DAS28ESR (at week 0, week 12, week 24 and week 52) was 4.1/3.3 (p<0.001)/3.2 (p<0.001)/3.1 (p<0.001). In MDA or HAD cases, 28 (33%) of 85 patients achieved remission. Compared with group B, ages ware significantly younger (A; 63 vs. B; 72, p<0.001). MMP-3 (A; 126 vs. B; 209, p<0.05), IgG (A; 1275 vs. B; 1455, p<0.05), CRP (A; 0.72 vs. B; 2.03, p<0.01), ESR (A; 23 vs. B; 47, p<0.001) and DAS-28ESR (A; 4.00 vs. B; 4.82, p<0.001) were significantly lower at the time of starting IGU in group A. [**Conclusion**] To achieve remission by IGU, younger cases, lower inflammatory marker and DAS28ESR at the time of starting IGU may be considered.

W96-3

Factors predicting efficacy of iguratimod for rheumatoid arthritis

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Conflict of interest: None

[Object] To extract factors predicting efficacy of iguratimod (IGU) for rheumatoid arthritis (RA). [Methods] Medical records of 261 RA cases treated with IGU by Sep 2016 were reviewed. As disease activity markers, swollen joint count (SJC) and tender joint count (TJC) out of 28 joints, CRP, ESR, physician's global visual analog scale (VAS), patient's pain and global VAS, DAS28ESR, CDAI and SDAI were collected. Cases with newly initiated/increased antirheumatic drugs since 3 months before or glucocorticoid since 1 month before were excluded. [Results] Data from 54 cases were analyzable. Among them, IGU was discontinued before 3 months in 7 cases. All the activity markers above significantly improved at 3 months. Compared to the nonresponders according to EULAR criteria for DAS28ESR, the good and moderate responders had significantly greater SJC (median 4 vs 2 joints, p=0.010), TJC (3 vs 2 joints, p=0.006), DAS28ESR (3.75 vs 3.23, p=0.017), CDAI (14.5 vs 9.6, p=0.010) and SDAI (14.9 vs 11.1, p=0.035) at baseline and following tendencies: older onset (60.6 vs 50.2 years old, p=0.053), lower dose of tacrolimus (mean 0 vs 0.25 mg/day, p=0.054) and higher dose of bucillamine (36.4 vs 6.3 mg/day, p=0.063). [Conclusion] IGU may be more effective for patients with older onset active RA.

W96-4

The Evaluation of Disease Activity, Safety and Radiographic Efficacy by Adding Iguratimod for Treating 89 Rheumatoid Arthritis Patients with Inactive Response to csDMARDs

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Conflict of interest: None

OBJECTIVES: To investigate clinical and safety data about adding iguratimod (IGU) on RA patients with poor response to csDMRADs in a single-center, open label and retrospective study. **METHODS:** Clinical and radiographic efficacy was assessed by disease activity score of 28 joints (DAS28) ESR (n=68) and the modified total Sharp score (mTSS) (n=24), respectively. We **evaluated** which **factors** are important in determining a **prognosis of clinical response and mTSS.** For safety, adverse events (AE) were investigated on all patients (n=89). **RESULTS:** 89 RA patients were recruited. Mean age was 61.5 years old and mean of disease duration was 87 months. Main csDMARDs were MTX (72%). The mean dose of MTX was 7mg/week. Observational period was 13 months (range, 1 to 30). DAS28-ESR changed from 4.3 ± 1.1 to 3.6 ± 1.2 after adding IGU for 6 months (P < 0.0001). Yearly mTSS was 0.60 and rate of structural remission **was** 87%. Adverse AE were observed such as transaminase elevation, stomatitis and dizziness. All AE were not serious. DAS28-ESR, CRP, ESR and swelling joint were prognostic factors of the group of good and moderate response against no response group. **CONCLUSIONS:** Adding IGU to csDMARDs with poor response in RA patients is effective, but AE should be considered.

W96-5

Efficacy of adding iguratimod therapy in rheumatoid arthritis patients who had inadequate response to biologic DMARDs

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Conflict of interest: None

Objective Iguratimod (IGU) was approved in June 2012 and recommended by guideline 2014 in the treatment of rheumatoid arthritis (RA). Although there have been efficacy of monotherapy and concomitant MTX in clinical trials, however, there have been no reports of concomitant biologic DMARDs (Bio). Therefore, we investigated efficacy of concomitant IGU therapy in RA patients who had inadequate response to Bio at the author's institution. **Methods** IGU were prescribed to 62 RA patients from August 2012 to June 2016, subjects were 57 patients adding IGU who had inadequate response to Bio. Previous treatment Bio was ADA. And concomitant MTX (mean 12 mg/week) of 54 patients (94%). Baseline characteristics were Mean age 53 years, mean duration of illness 5.5 years, corticosteroid use 14%. The course of DAS28, SDAI, CDAI and remission rates were analyzed. **Results** Mean DAS28-ESR, DAS28-CRP, SDAI, CDAI were significantly decreased from the initiation of IGU treatment at 24 weeks (3.07→2.27, 2.55→1.63, 6.94→2.21, 6.23→1.95). Remission rates of DAS28-ESR, DAS28-CRP, SDAI, CDAI were 67%, 82%, 72%, 74% at 24 weeks. There were almost no side-effect after adding IGU. **Conclusion** IGU might be a new RA treatment option for aiming remission in patients who had inadequate response to Bio.

W96-6

The efficacy of Iguratimod adding on Abatacept in patients with rheumatoid arthritis with the efficacy of Abatacept decreasing

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Conflict of interest: None

[Object] The purpose of this study was to investigate the efficacy of Iguratimod (IGU) adding on Abatacept (ABT) in patients with rheuma-

toid arthritis (RA) with the efficacy decreasing. [Methods] Eight patients in whom IGU added on ABT due to the efficacy of ABT decreasing were included in this study (2 males, 6 females, average age 62.3 years). Average disease duration was 15 years. MTX was used for 5 patients (average 7.2 mg/week) and PSL was used for 1 patient (average 2.5 mg/day). Before IGU adding on, the patients were treated with ABT for average 41 months. DAS28CRP, CDAI and SDAI at baseline, 4 weeks, 12weeks and 24 weeks were used as the values for the estimation of the efficacy of IGU adding on. [Results] At baseline the mean values of DAS28CRP, CDAI and SDAI were 2.21, 6.59 and 7.33. These values were improved to 2.07, 4.50 and 4.65 at 24 weeks respectively. Two patients achieved remission in CDAI and SDAI criteria. Bleeding from the duodenum ulcer was developed in one patient as an adverse event. [Conclusions] As the efficacy of IGU has been reported in the combination therapy with biologics and in the patients with the efficacy decreasing of biologics, this study indicated the efficacy of IGU adding on ABT for the patients with the efficacy decreasing.

W97-1

Bortezomib Treatment Exerted a Lethal Toxic Effect on Lupus Model Mouse with High Disease Activity

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Conflict of interest: None

Object Recently, we reported that Bortezomib (Bz) had therapeutic effects on 14-wks-old MRL/lpr mice. We also reported high complication rate of Bz on refractory SLE. In this study, we compared the immunological activity of 10-wks- and 14-wks-old MRL/lpr mice. The effect of Bz on the survival curve and toxicity of these two-age mice. Methods (1) Cell number of lymph nodes and spleens, serum immunoglobulins and anti-dsDNA antibody titer of 10-wks- and 14-wks-old MRL/lpr mice were compared, (2) Survival curve of MRL/lpr mice initiated with Bz from 10-wks- and 14-wks-old were compared, (3) After two injections of Bz (day1 and day4), blood count, renal and kidney function, and serume cytokines were measured. Results In 14-wks-old MRL/lpr mice, cell number of spleen and lymph nodes, serum IgG3 and anti-dsDNA antibody titer were significantly elevated than 10-wks-old. Among MRL/lpr mice initiated with Bz from 14-wks-old, 33% of the mice died until 18-wks-old, while no mice died in control and 10-wks-old Bz mice until 18-wks-old. After two Bz injections, serum IL-6 and TNF-α were significantly increased in 14-wks-old mice than 10-wks-old. Conclusion In spite of its therapeutic effect, Bz exerted lethal toxic effects in MRL/lpr mice with high disease activity.

W97-2

Role of mucosal-associated invariant T (MAIT) cells in lupus pathogenesis

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Conflict of interest: None

[Background] Mucosal-associated invariant T (MAIT) cells are innate T cells restricted by MHC-related molecule-1 (MR1) and express a semi-invariant TCRα chain. We previously revealed that the activation state of MAIT cells correlated with disease activity in patients with systemic lupus erythematosus. Therefore, we conducted this study to clarify functions of MAIT cells in lupus by using a FcγRIIB$^{-/-}$ Yaa mouse model. [Methods] FcγRIIB-/- Yaa mice were crossed to MR1 deficient mice lacking MAIT cells, and disease progression was compared between MR1KO FcγRIIB$^{-/-}$ Yaa and FcγRIIB$^{-/-}$ Yaa mice at 1-4 months of age. [Result] MR1KO FcγRIIB$^{-/-}$ Yaa mice showed a reduction of anti-dsDNA antibody levels and an increase of survival rate. There was a trend of less proteinuria and less severe nephritis in MR1KO FcγRIIB$^{-/-}$ Yaa mice. MR1KO FcγRIIB$^{-/-}$ Yaa mice developed exacerbated inflammation in the skin lesions with a significant higher histopathological dermatitis score compared to FcγRIIB$^{-/-}$ Yaa mice. [Discussion] These data suggest that MAIT cells exhibit the dual roles in lupus pathogenesis. Further studies are undergoing to understand the mechanisms by which MAIT cells are involved in each pathological condition in lupus.

W97-3

Establishment of model rat with anti-phospholipid antibody syndrome using anti-rat phosphatidylserine/prothrombin monoclonal antibodies

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Conflict of interest: None

[Objectives] To demonstrate the pathogenicity of antiphosphatidylserine prothrombin complex antibody (aPSPT antibody) [Methods] We established aPSPT monoclonal antibodies from autoimmune disease-prone rats that produce aPSPT antibody. Next, cultured rat vascular endothelial cells (REC) were exposed to histones. Two hours later, lactate dehydrogenase release from the REC and expression of PS on the cell surface were assessed using annexin V that can bind to PS. We administered histones into Wistar rats, and 2 hours later, they were given intravenous injection of aPSPT antibody (n=6) or an equal dose of rat IgM as controls (n=5). Three days later, histological examination was conducted. [Results] We established aPSPT antibodies, which immunoglobulin class is IgM. Calf thymus-derived histones could injure REC in vitro. Simultaneously, annexin V could bind to the REC; thereby, this result indicated that histone exposure of vascular endothelial cells induced cell surface expression of PS, which is naturally present inside the plasma membrane. Thrombosis developed with higher frequency in the rats given intravenous injection of aPSPT antibody than in controls. [Conclusions] We established thrombotic rat models induced by aPSPT antibodies.

W97-4

Investigating GWAS loci using splicing QTL analysis of human immune cells

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Conflict of interest: None

[Introduction] Although genome-wide association studies (GWAS) have identified many susceptibility loci for autoimmune diseases, the mechanisms of disease are almost unknown. Here, we examined the role of alternative splicing in GWAS loci by performing splicing QTL (sQTL) analysis focusing on loci that change the protein structure. [Method] We collected peripheral blood from 105 healthy Japanese volunteers (80% female). Five immune cell populations (B cells, CD4$^+$ T cells, CD8$^+$ T cells, Monocytes, NK cells) were isolated by FACS. RNA-seq was conducted using a Hiseq 2500. We quantified isoform expression using HISAT2 and Cufflinks. We integrated transcripts that had the same ORF sequence in a gene and calculated the transcript ratio. Then, we tested the correlation between this ratio and SNP genotype (trQTL analysis). GWAS SNPs were extracted from ImmunoBase. [Result] Of 11,438 genes examined, 830 genes were identified as sQTL (FDR <= 0.05). Among them, 67 sQTLs had GWAS SNPs in strong linkage disequilibri-

um (r2 > 0.8). [Discussion] Our new approach is unique in that we focused on sQTL that change the protein structure. Functional analysis of these proteins would lead to understanding pathogenesis of diseases.

W97-5

Association between serum insulin-like growth factor-binding protein 2 and systemic lupus erythematosus: A retrospective study

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Conflict of interest: None

【Objectives】insulin-like growth factor (IGF) is polypeptide and looks like insulin. There are 6 types of IGF and it was bound to IGF-binding protein (IGFBP). Recently, correlation of serum levels of IGFBP2 with LN activity and response to treatment was reported in Europe. But it is unclear there is correlation of the serum levels of IGFBP2 with activity of SLE except LN or not. We aimed to evaluate the correlation of serum IGFBP2 and activity of SLE. 【Methods】We measured the levels of IGFBP2 by enzyme-linked immunosorbent assay (ELISA)kit in SLE patients with and without active LN (n=44, 27) and healthy controls (n=40). Clinical and laboratory data were retrospectively collected from the electronic medical records and statistically analyzed. 【Results】The levels of serum IGFBP2 in SLE patients with and without active LN were higher than healthy controls (mean 440 ng/ml, 347 ng/ml, 162ng/ml $p<0.001$)There was no significant difference in SLE patients with or without active LN ($p=0.33$). There was no significant difference in class of LN too. In SLE patients, the levels of serum IGFBP2 were mildly correlated with titers of anti-ds DNA antibodies and the levels of C3. 【Conclusion】The present study suggested that serum IGFBP2 increased in SLE patients and associated with activity of it.

W97-6

The relevance of P-glycoprotein$^+$CD27$^-$ B cells to clinical manifestation in systemic lupus erythematosus

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Conflict of interest: None

[Objectives] P-glycoprotein (P-gp) expression on activated lymphocytes is associated with active efflux of intracellular drugs, resulting in drug resistance in SLE. CD27$^-$IgD$^-$B cells are reported to be increased in SLE patients. We have investigated the relevance of P-gp expression on each B cell subsets to clinical features. [Methods] Flow cytometry analyzed molecules on CD19$^+$cells were performed. [Results] CD27$^+$IgD$^-$B cells ratio was highest in B cell subsets of SLE patients (n=39), but had only marginal expression of P-gp. P-gp was expressed on CD27$^-$IgD$^{+/-}$B cells. P-gp$^+$CD27$^-$IgD$^{+/-}$B cells ratio were increased in non-proliferative lupus nephritis (LN) and NPSLE. P-gp$^+$CD27$^-$IgD$^{+/-}$B cells ratio correlated with SLEDAI, especially in serositis, and were increased in corticosteroid -low responders with serositis. P-gp$^+$CD27$^-$IgD$^-$B cells ratio correlated with SLEDAI in NPSLE. P-gp$^+$CD27$^-$B cells ratio has no relevance to proliferative LN. Immunosuppressive therapy resulted in reduction of CD27$^-$IgD$^-$B cells ratio and P-gp$^+$CD27$^-$IgD$^{+/-}$B cells ratio associated with improvement in clinical manifestation in highly active serositis. [Conclusion] P-gp$^+$CD27$^-$IgD$^{+/-}$B cells might be involved in non-proliferative LN, NPSLE, and especially refractory serositis.

Poster Session

P1-001

Association between MTX doses and clinical variables in patients with RA who achieved remission with MTX monotherapy: A study using the IORRA cohort

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Conflict of interest: None

[Object] We aimed to study the association between MTX doses and clinical variables in patients with RA who achieved remission with MTX monotherapy. **[Methods]** Among the participants of the IORRA cohort (2011-15), 603 patients fulfilled the ACR/EULAR Boolean-based definition of remission in RA at least once with MTX monotherapy. Associations between MTX doses and gender, disease duration, height, body weight, BMI, BSA, serum creatinine (Cr), eGFR, CCr, RF, and ACPA when remission was first reached by each patient were analyzed by univariate analyses. Ultimately, a multiple regression analysis was performed. **[Results]** Univariate analyses detected several candidate clinical variables associated with MTX monotherapy doses in RA patients who achieved remission: height, body weight, BSA, Cr, eGFR and CCr. Subsequently, a multiple regression model developed a best-fit model with these variables; age, height, body weight and Cr (B_i = -0.20, 0.10, 0.07, -0.22), while its adjusted R^2 value was 0.114. **[Conclusion]** There were significant associations between MTX monotherapy doses and age, height, body weight, and renal function in RA patients who achieved remission. However, the low coefficient of determination indicated the model accounted for limited variability with the specified variables.

P1-002

Change in RF Titers Reflects RA Disease Activity and Predicts Therapeutic Response during Tocilizumab Therapy

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Conflict of interest: None

[Objectives] To determine whether change of RF levels reflects RA disease activity and predicts therapeutic response in RA treated with Tocilizumab (TCZ). [Methods] Subjects were 41 RA patients who filled ACR RA criteria 1987, were treated with TCZ, and had moderate to high disease activity and high titer of serum RF (≧45 IU/ml). Their medical records were reviewed retrospectively. Serum RF levels were measured every 3 month during TCZ treatment. When RF levels were changed more than 10%, the change was judged as significant. RA disease activity was measured by DAS28-CRP. [Results] TCZ reduced both serum RF levels and DAS28-CRP at 12Mo, but decrease of RF levels has no correlation with reduction of RA disease activity. Change in RF levels during first 3Mo showed "elevation" in 10.3% and "no elevation" in 89.7%. Patients without elevation of RF levels during first 3Mo showed lower DAS28-CRP and rate of "No Response" in EULAR response criteria at 12 Mo than those with elevation. Change in RF levels during 3-12Mo did not reflect RA disease activity and failed to predict therapeutic response at 12Mo. [Conclusion] Change in RF titers during first 3Mo reflects RA disease activity and predicts therapeutic response in RA treated with TCZ.

P1-003

Prediction of Joint Damage Progression and Flare after Adalimumab Discontinuation by serum 14-3-3η levels in patients with RA (post hoc analysis of HONOR study)

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Conflict of interest: Yes

[Background] The HONOR study investigated discontinuing adalimumab (ADA) therapy in RA. Serum 14-3-3η, a mechanistic serum marker, was investigated as a predictor of joint damage & flares. **[Methods]** Serum 14-3-3η levels were measured in 62 RA patients. **[Results]** At baseline and discontinuation of ADA, median 14-3-3η levels were 0.28 and 0.22 ng/ml, with 26 (59%) of 44 and 29 (54%) of 54 patients being positive (≥0.19 ng/ml). 14-3-3η levels were significantly different between baseline and ADA-discontinuation, p=0.030. Baseline 14-3-3η levels were associated with changes in modified Sharp score (ΔSHS) at 12 mo and at the time of flare, p=0.038. Bivariable modeling revealed that baseline 14-3-3η together with the change in 14-3-3η had a significant interacting effect onΔSHS at 12 months and the time of flare, p=0.02. Although baseline 14-3-3η levels alone was not associated with flares at 12 months (p=0.15), when combined with CRP, a significant interaction was present (p=0.03). **[Conclusion]** To reduce the risk of flare in patients who are candidates for discontinuation of ADA, CRP and 14-3-3η measurements should be considered in combination as markers of flare prediction.

P1-004

A Study on Characteristics of Rheumatoid Arthritis Patients Achieving HAQ remission with 6 Months of non-TNF Biologic Treatment

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Conflict of interest: Yes

Objectives We aimed to investigate factors to predict if a patient can enter remission based on the HAQ by treating non-TNF biologics for 6 months before they start their treatment in RA patients. Methods The subjects were 75 RA patients treated with Tocilizumab or Abatacept for 6 months. The following characteristics were investigated in the follows; age, gender, BMI, steroid and MTX dosage, serum MMP-3 levels, SDAI, the HAQ (for ADL) and the short form (SF)-36 (for QOL) of the RA. Remission based on the HAQ is defined as HAQ≦0.5 after 6 months of the treatment. The subjects were divided into two groups: patients with a HAQ ≦0.5 and >0.5, and a retrospective study was conducted. Results The group of RA patients who entered remission based on the HAQ (44 patients) had a lower SDAI than the group of patients who couldn't enter remission (31 patients), and they had lower TJC and HAQ scores and higher patient global assessment (PGA). The PCS and RCS of the SF-36 summary score showed higher scores. Before the start of the treatment, HAQ score, TJC and PGA were detected based on logistic regression analysis. Conclusions It was suggested that RA patients with lower HAQ scores, higher PGA and ADL at baseline are more likely to achieve HAQ remission with non-TNF biologic treatment.

P1-005

Factors that influence on pain control for rheumatoid arthritis patient

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Conflict of interest: None

[Objective] Pain control is the most important theme for rheumatoid arthritis (RA) patient. Factors that affect on pain control were evaluated statistically from small cohort data. [Methods] In 685 RA patients who have been treated for more than 1 year, 500 were monitored their disease activity, Pain VAS (PS-VAS), mHAQ. In these, 14,005 times from 495 patients were enrolled in this study. PS-VAS at the reference demonstrated no more than 10mm, and less than last time, and more than 30mm at first time was evaluated as positive. Patients sex, ACPA titer, joint destruction (SHS), patients current age, history length, DAS28-CRP and its components, PS-VAS at first, last, and current time, drug usage and its dosage were evaluated statistically with Binary Logistic Regression Analysis. Significant level was set within 5%. [Results] Current age, age no less than 65, SHS at first time, DAS28-CRP at every time of first, last, and current time, MTX thrown dose at current time, glucocorticoid use, compound of weak opioid and acetaminophen use, start of tofacitinib at last time, were picked up as significant factors. [Conclusions] Pain control in RA is mostly influenced by patient's age and disease activity control. And it is also suggested specific drugs have higher effect on pain control.

P1-006

Factors influencing functional disability in elderly patients aged 75 or over with rheumatoid arthritis

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Conflict of interest: None

Objective: The aim of this study are to identify influencing factors to maintain the functional ability in elderly patients with rheumatoid arthritis (RA). Methods: A retrospective chart review was conducted in elderly patients aged 75 or over with RA. A total of 77 patients (13males and 64females, mean age, 80.7±4.0 years; mean disease duration, 12.8±11.2years) were identified. To explore the influencing factor, we divided the patients into two groups depend on the value of mHAQ (group A, mHAQ≦0.5; group B, mHAQ>0.5), and tested the differences for statistical significance using t test or chi square test. Results: Lower Steinbrocker stage, dosage of steroid group (A, 4.6±2.8; B, 5.4±2.1mg/day), and DAS28-CRP (A, 2.4±0.8; B, 3.1±1.0) were associated with lower mHAQ. The adverse event of infection (A, 46%; B, 74%) and comorbidity of respiratory disease (A, 30%; B, 59%) were associated with higher mHAQ. Disease duration (A, 11.7±10.2; B, 14.7±12.8 years), use of MTX (A, 7.6±2.0; B, 8.4±2.2mg/w) or bDMARD (A, 20%; B, 15%) were not associated with functional disability. Conclusion: To maintain the functional ability, we should pay attention to decrease the pain due to joint destruction, and care the respiratory condition.

P1-007

Analysis of rheumatoid arthritis patients that did not achieve the treatment goal by the treat-to-target strategy

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Conflict of interest: None

[Objective] The treatment goal of rheumatoid arthritis (RA) is to achieve remission or low disease activity with the treat-to-target (T2T) strategy. This study was performed to determine the reasons why the patients do not achieve the treatment goal. [Methods] Patients with moderate or high disease activity according to the simple disease activity index (SDAI) in 2014-2015 were evaluated. Each item of SDAI, patient background, and treatment content were investigated. [Results] Sixty patients had moderate or high disease activity. They had an average age of 70.2 years, average disease duration of 17.8 years, average SDAI of 19.6, and mean CRP of 1.27 mg / dl. As disease activity did not decrease, 21 patients were considered to have been treated insufficiently with the T2T strategy. 21 patients had joint pain without arthritis. Eighteen patients were not treated sufficiently for complications, such as 6 elderly patients and respiratory complications in 8 patients. [Conclusion] Although the treatment goal of the T2T strategy in RA is remission or low disease activity, this goal is often not achieved in daily clinical practice. Additional T2T is necessary.

P1-008

Body Mass Index and response to conventional synthetic disease-modifying antirheumatic drugs in early onset rheumatoid arthritis

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Conflict of interest: None

Objectives: Obesity has worsened disease activity of rheumatoid arthritis (RA). RA patients with high body mass index (BMI) also showed worse responses to biological disease-modifying antirheumatic drugs (bDMARDs). The objective of this study was to assess whether BMI affects response to conventional synthetic DMARDs (csDMARDs) and differences of affected joint regions. Methods: BMI was categorized into two groups: normal (BMI<25.0 kg/m^2) and obese (BMI≥25.0 kg/m^2). After 12 and 24 weeks of csDMARDs treatment, changes in disease activity were assessed with SDAI. Results: A total of 336 patients with RA were included. The mean ± SD BMI was 21.6 ± 3.2 kg/m^2. Methotrexate was first-line DMARD for 68.8% patients. We found no differences in rates of remission between the 2 BMI groups in 12, and 24 weeks. However, we found marginal difference in rates of remission between obese group complicated with knee swollen and normal group with knee swollen (19.6% vs 0%, p=0.069). Conclusions: Response to csDMARDs in early onset rheumatoid arthritis was not influenced by BMI, however, high BMI might be associated with lower response to csDMARDs in RA complicated with knee swollen.

P1-009

Do amounts of drugs required to achieve low disease activity in EORA and YORA patients differ?

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Conflict of interest: None

Elderly onset rheumatoid arthritis (EORA) is reported to differ from young onset rheumatoid arthritis (YORA) in regard to both patient background and drug treatment. We examined drug amounts given to those patients who achieved low disease activity (LDA) for rheumatoid arthritis at our hospital. Background and treatments were compared between EORA (n=70) and YORA (n=190) patients. There were no significant differences in regard to background, as average age was 73.8 and 57.8 years, disease duration was 6.66 and 14.7 years, female ratio was 62.9% and 83.7%, RF positivity was seen in 85.3% and 80.7%, ACPA positivity was seen in 86.5% and 87.7%, SDAI was 4.28 and 4.59, and DAS28 (CRP) was 1.99 and 2.04, respectively. As for treatment, there were no significant differences for prednisolone (PSL) use (37.1% vs. 36.3%), amount of methotrexate (MTX) (1.45 vs. 1.41 mg), and MTX use (55.7% vs. 65.3%). However, MTX dose (2.89 vs. 4.09 mg/week, p=0.011) and biologics use (32.9% vs. 56.3%, p=0.0012) were significantly lower in the EORA cases. Our results indicate that EORA patients may be able to achieve LDA with lower drug amounts as compared to YORA patients.

P1-010

Study of quality of life (QOL) assessment by EQ5D in the patients with rheumatoid arthritis (RA)

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Conflict of interest: None

Objective: To evaluate the QOL in the patients with RA, EQ5D questionnaire was conducted. Methods: In ninety-nine RA patients whose female was 76 cases, average age was 64 years, average duration was 13 years, EQ5D questionnaire was investigated. At the same time, the situation of anti-rheumatic drugs and biologics dosing, DAS28CRP were investigated retrospectively. Results: Average EQ5D price was 0.71. 36 RA cases showed less than 0.7 EQ5D price whose ages were older, long duration and high application of anti-rheumatic drugs and biologics and high volume of prednisolone dose compared with the patients who showed EQ5D 0.7 or more. In low EQ5D group, DAS28CRP was significantly higher ($p<0.05$) compared with high EQ5D group. Conclusion: EQ5D questionnaire was one of the excellent tool to assess the RA patients QOL. By using EQ 5 D tool, more delicate treatment will be possible in the patients with rheumatoid arthritis.

P1-011

Correlation of improved disease activity with decline of rheumatoid factor in patients with early rheumatoid arthritis

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Conflict of interest: None

Objective:To investigate an association between disease activity after treatment and a decline of rheumatoid factor (RF) in patients with early rheumatoid arthritis (RA). **Methods**:We enrolled 24 patients with untreated-RA and a positivity of RF at first visit to our hospital between 2014 and 2016. RF and simplified disease activity index (SDAI) were evaluated during 6 months after the commencement of DMARDs. The decline ratio of RF was calculated as follow:([RF titer at baseline]-[RF titer at 6month after initiation of treatment])x 100/(RF titer at baseline) **Results**:The mean age at diagnosis of RA was 60.7 years. The median value of RF before treatment (IQR) was 120 (36-189) IU/ml. Methotrexate and biological DMARD was received in 14 (58%) and 7 patients (29%), respectively. The remission rate in SDAI was 50% at 6 months after initiation of treatment regardless of treatment regimens. At that time, the median decline ratio of RF was 61%. The cut-off value of the decline ratio of RF for remission was calculated as 45% using ROC curve. SDAI was significantly lower in the subset with the decline ratio of RF≥45% than in the other subset (2.5 vs 7.4, p=0.03). **Conclusion**:Regardless of treatment regimens, improved disease activity was correlated with a decline of RF titer in early RA.

P1-012

Effect of tapering of MTX for RA patients with low disease activity

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Conflict of interest: None

Purpose: Among all rheumatoid arthritis patients (n=301), we use MTX for 173 patients (57.1%). In this study, we evaluate effect of tapering of MTX. Methods: For MTX utilized low disease activity 72 patients (DAS28-CRP < 2.7) showing negative echo signal of finger joints, we decreased dose of MTX. We classified the patients into 4 groups; MTX alone (n=23), MTX + csDMARDs (n=20), MTX + bDMARDs (n=14), and MTX + csDMARDs + bDMARDs (n=15). Six month later, we evaluated disease activity and retrospectively analyzed the effect of tapering of MTX. Results: Average tapering rate was 50.6 +/- 32.4%, and 19 patients (26.4%) were free for MTX. In 4 groups, MTX free rates were as followings; MTX alone (13%), MTX + csDMARDs (25%), MTX + bDMARDs (50%), and MTX + csDMARDs + bDMARDs (26.4%). Among

groups using bDMARDs (n=29), we can stop using MTX in all TOC cases; MTX + bDMARDs (n=5), MTX + csDMARDs + bDMARDs (n=1). However, another bDMARDs used cases, 21.7% were free for MTX. In 3 patients (4.2%), tapering of MTX worsened activity of disease. Conclusions: We can decrease MTX for patients showing low disease activity and negative echo signal of finger joints. Moreover, in case of MTX + TOC therapy, we can stop using MTX if disease activity was low and echo signal of finger joints was negative.

P1-013

Comparison of Disease activity score (DAS)28-erithrocyte sedimentation rate and DAS28-C-reactive protein in patients with rheumatoid arthritis (RA) – Data from Kansai consortium for well-being of rheumatic disease patients (ANSWER cohort)-

Koji Nagai[1], Shuzo Yoshida[1], Motomu Hashimoto[2], Moritoshi Furu[2], Wataru Yamamoto[2,3], Ryota Hara[4], Takanori Fujimura[4], Akira Onishi[5], Kengo Akashi[5], Masaki Katayama[6], Yonsu Son[7], Hideki Amuro[7], Kosuke Ebina[8], Toru Hirano[9], Ayaka Yoshikawa[1], Yuko Kimura[1], Yoko Matsumura[1], Shigeki Makino[1]

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Conflict of interest: None

[Object] To analyzed the factors that contribute to the differences between DAS28-ESR and DAS28-CRP in patients with RA. [Methods] A total of 1,341 patients except for ones administered Tocilizmab (TCZ) from 2011 to 2016 were included in this study. We defined a variable DIFDAS=DAS28-ESR – DAS28-CRP to analyze which independent variables account for differences between the two index. We use data on age, gender, disease duration, disease activity score (DAS28CRP, DAS-28ESR) and their components (TJC, SJC, PtVAS, CRP, ESR), and HAQ. [Results] The correlation coefficient of DAS28-ESR versus DAS28-CRP was 0.805, indicating that the DAS28-ESR and DAS28-CRP were strongly linearly correlated. There was a statistically significant correlation between DIFDAS and age, female, SJC, CRP, ESR, HGB, ALB ($p<0.001$) and HAQ ($p=0.003$). Serum HGB level was an independent factor of DIFDAS significantly under various conditions except for elderly age groups and high disease activity groups in RA patients. [Conclusion] Various background factors influence the difference between DAS28-ESR and DAS28-CRP in RA patients. We have to evaluate the disease activity of RA patients with anemia carefully.

P1-014

Effect of poor-prognostic factors (ACPA/RF) on Adalimumab treatment outcome (3 years)

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Conflict of interest: None

Objective: To investigate whether adalimumab (ADA) treatment in rheumatoid arthritis (RA) patients affects the effect of poor-prognostic factors on clinical outcome. Methods: Enrolled were 191 analyzable patients introduced to ADA treatment at our hospital from May 2009 to November 2013. We examined retrospectively, whether poor-prognostic factors at baseline affected clinical progress. For ACPA, the +ve group was set as the quartile, and for RF, intergroup comparisons were made between the+ve and -ve groups. Efficacy index was assessed by DAS28 (CRP) and remission achievement rate. Results: Mean patient age was 54 yrs, and mean duration of illness was 6.8 yrs. Overall DAS28 (CRP) reached clinical remission in 43% of patients from 4W of treatment, in 75% at 52W and sustained to 152W. Significant decrease in DAS28 (CRP) was confirmed in the ACPA -ve and +ve groups (quartile). Remission achievement rate showed no interquartile difference for both groups. For RF, there was no difference between both groups; significant decrease in DAS28 (CRP) and a remission achievement rate of 80%, were confirmed. Conclusion: Best use of ADA is in combination with the maximum MTX dose possible for each patient. ADA can be an effective drug regardless of ACPA and RF, by maximizing its potential.

P1-015

Is it possible to estimate future efficacy based on the blood concentration at the time of the fourth administration of Infliximab?

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Conflict of interest: None

Purpose: To investigate the efficacy in patients with rheumatoid arthritis (RA) treated with Infliximab (IFX) based on the IFX concentration at the time of the 4th administration. **Materials and Methods:** The subjects were 56 RA patients (13 male and 43 female) who ranged from 26 to 81 (mean: 60.3) who were treated with IFX. We measured the IFX concentration prior to the 4th administration (8 weeks after the 3rd administration) and examined the correlation with subsequent efficacy. **Results:** At 4th administration the IFX concentration was higher than 1 μg/ml (higher group) in 32 cases and lower (lower group) in 24 cases. In the higher group the drug was effective in 30 cases (93.8%), with the average concentration at 5.18. The average in the 2 ineffective patients was 5.69. In the lower group the drug was effective in 21 cases (87.5%). At this point there were 5 cases of primary ineffectiveness. At this point efficacy was 58.8% in the higher group and 41.2% in the lower group and therefore no correlation between efficacy and IFX concentration was observed. **Conclusions:** During IFX treatment there are many effective cases in which the IFX concentration is lower than 1 μg/ml, and therefore measurement of the IFX concentration is not considered necessary for a clinical assessment.

P1-016

Statistical analysis of mHAQ in patients with rheumatoid arthritis - Attempt of correction to linear score –

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Conflict of interest: None

[Object] Purpose of this study was to clarify statistical structure of mHAQ of patients with rheumatoid arthritis. Based on the results, I aimed to create the calculation formula for linear evaluation and correct mHAQ so that linearity is guaranteed. **[Method]** mHAQ obtained from 83 patients with rheumatoid arthritis in our department was considered. First, the factor structure of mHAQ was determined using factor analysis. Since the contribution ratio of the first factor was sufficiently high, the factor loadings and the weights of the eight items of mHAQ were calculated based on the first factor. From the weights of first factors, the score point of mHAQ with linearity can be calculate. Next, a total of 24 points of mHAQ was proportionally allocated to the 8 items of original mHAQ according to factor loading. Furthermore, each point within eight items were determined by using the quantification theory 1 with the factor scores of each case as objective variables and the original mHAQ score as explanatory variables. **[Results] [Conclusion]** The weights of the first factor were the maximum in “common daily activity” 0.21807 to the smallest “walking” 0.07892. A calculation formula for linear mHAQ score point and a corrected mHAQ with linearity could be established.

P1-017

Keeping remission in RA patients at a high level of anti-cyclic citrullinated protein antibodies titer over 500

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Conflict of interest: None

[Objectives] We investigated a factor of keeping remission in RA patients at a high level of anti-cyclic citrullinated protein antibodies (anti-CCP) titer over 500. [Methods] 25 patients (7males and18 females, mean age 58.3 years old) among 725 RA patients in out-patient clinic by September 2016 were analyzed, retrospectively. [Results] 20 patients (80%) had complication diseases, lung for 9, HT for 6, HL for 6, Gastrointestinal for 5, Orthopedics for 4, SjS for 3, CNS for 2. The average level of anti-CCP titer were 1070.2 (507.4-4050), CRP were 0.98, RF were 150.0 and MMP3 were 103.21 patients (84%) reated MTX and the average dose are 5.3mg/w.11 patients (44%) treated DMARD except MTX (SASP for 7, Bu for 6, Tac for 5, MZB for 2).10 patients (40%) treated Bio therapy (ETN for 6, TCZ for 1, GLM for4).7patients (28%) treated PSL and the average dose are 5.3mg. 15 patients (60%) achieved keeping remission. In keeping remission group (15 patients) in comparison with Non-keeping remission group (10 patients) Bio therapy are higher rate (9 patients:60% vs 1patient:10%). [Conclusion] Our data suggested that in keeping remission Bio therapy were most important factor for RA patients at a high level of anti-CCP titer but it was difficult to treat Bio therapy for patients with lung disease.

P1-018

Mental Effects of Neuropathic Pain in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Objectives] It has been reported that the pain of rheumatoid arthritis (RA) may include elements of neuropathic pain (NP) as well as nociceptive pain. We investigated the mental effects of NP in RA patients. [Methods] Eighty-seven RA patients who visited outpatient in October 2016 were included. NP used painDETECT Japanese version (PD), nociceptive pain group (non-NP group) of 12 points or less and neuropathic pain group (NP group) more than 13 points. Catastrophic factors were evaluated by Pain catastrophizing scale (PCS), and self-efficacy factors were evaluated by Pain self-Efficacy Questionnaire (PSEQ). In addition, pain VAS and disease activity were evaluated and compared between the two groups. [Results] There were 79 cases in non-NP group and 8 cases in NP group. Pain VAS, DAS 28-ESR and DAS 28-CRP did not show any significant difference between the two groups. PCS was significantly higher in the NP group (26.8±7.7 points) than non-NP group (14.7±11.2 points) ($p < 0.01$). There was no significant difference between the two groups in PSEQ. [Conclusion] RA patients with similar pain and disease activity were shown to be more pessimistic in NP patients. For patients with NP, it is necessary to actively treat NP, and in some cases mental care should also be considered.

P1-019

Study of the correlation between ultrasonography, serological marker and periodontitis in RA patients

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Conflict of interest: None

[Objectives] The aim of this study was whether the findings of ultrasound (US) associated with clinical and laboratory findings including plasma IgG antibody titers to periodontal bacteria in rheumatoid arthritis (RA) patients. [Methods] Eleven patients underwent US and assessed clinical and laboratory findings including plasma IgG antibody titers to periodontal bacteria of 4 species; Aa, Pg, Pi, Ec. Twenty-eight joints were evaluated by semi-quantitatively Gray Scale (GS) and Power Doppler (PD). In addition, the periodontists made some examinations of their teeth. [Results] Of the all patients, nine patients had periodontal disease (81.8%) with the median age of 53 years old and the median disease duration of 14 months. Total GS and total PD score have high correlation with CRP and ESR (γ =.94, $P<0.05$). In addition, the median plasma IgG antibody titer of Pg was higher than the titers of the other 3 bacteira (31.2 [10.6-48.2]). The median of the deepest pocket proving level was 5 [4-9] mm. Total GS score have the tendency of correlation with the deepest pocket level in their teeth (γ =.58, P=0.06). [Conclusion] Total GS score have the tendency of correlation with the deepest pocket proving level, suggested that the severity of periodontitis is related to synovial thickening.

P1-020

The serum albumin value is is useful for MMP-3 and equality in order to evaluate the disease activity of rheumatoid arthritis

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Conflict of interest: None

[Objectives] We reported on the usefulness of serum albumin value in disease activity evaluation of rheumatoid arthritis at the 59th Scientific Meeting of JCR. Although MMP-3 is useful as an index of arthritis in daily practice, it was examined whether serum albumin value is as useful as MMP-3 in disease activity evaluation. [Methods] We analyzed 2138 data of 123 patients with rheumatoid arthritis with DAS 28-CRP, serum albumin value and MMP-3 value. Correlation between serum albumin value and DAS 28-CRP was examined. The correlation between MMP-3 value and DAS 28-CRP was investigated [Results] the correlation coefficient between DAS 28-CRP and MMP-3 value was 0.35, whereas the correlation coefficient between DAS 28-CRP and serum albumin value was -0.42. Serum albumin value showed higher correlation with DAS 28-CRP than MMP-3 value. Albumin is synthesized in the liver, and the inflammatory disease such as rheumatoid arthritis develops hypoalbuminemia by promoting the degradation of albumin by the inflammatory cytokine IL-6. The serum albumin value that can be easily measured in the hospital is considered to be a good auxiliary tool for evaluating disease activity in daily practice.

P1-021

Treatment process of elderly-onset rheumatoid arthritis in our department

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Conflict of interest: None

Objectives: We treat Elderly-onset RA (EORA) patients (pts) toward Treat to Target with consideration of complication, and so on. We examined treatment process. Method: We investigated 39 RA pts who were diagnosed as RA developing after the age of 70 years in our department between Jan 2012 and Oct 2016. Mean age of onset was 76.1 years. Mean duration of disease was 5.7 months. Mean follow-up duration was 25.8 months. We examined disease activity at the first visit and the latest, and the process. Results: Mean DAS28-CRP at the first visit was 4.6, 25 pts showed high activity and 12 pts did moderate. RF were positive in 27 pts, and anti-CCP antibody in 26 pts. Mean CRP was 3.4 mg/dl, 34 pts showed high value of MMP-3. At the initiation, 4 pts suffered interstitial pneumonia, 3 pts NTM and 4 pts CKD stage more than 3b. We administered MTX to 15 pts, SASP to 17 pts, TAC to 11 pts, and PSL to 3 pts. 14 pts were treated with biologics including 3 pts with monotherapy. At the latest observation, 29 pts were in remission and 3 pts had low disease activity. As complications 2 pts developed pneumonia, 1 pt lung cancer, 1 pt thyroid cancer and 2 pts vertebral fracture. Conclusions: Treatment with appropriate DMARDs from the initial could bring EORA good con-

trol.

P1-022

The assessment about the relationship between anti-citrullinated peptide antibody and clinical response to biologics in rheumatoid arthritis

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Conflict of interest: Yes

【Objective】Anti-citrullinated peptide antibody (ACPA) is known diagnostic serological markers of rheumatoid arthritis (RA), and some reported that positivity or high titer of ACPA are associated with a better response to some biologics. Now we assessed retrospectively about the efficacy of biologics in RA and the ACPA status in the real world.【Methods】Enrolled 139 patients with RA who could measure ACPA in the start of biologics were classified into the presence or absence of ACPA status. We compared with the ACPA status and disease activity, rate of remission in 6M and12M and biologics retention rate.【Results】ACPA positive was 84.1%. There were no differences between ACPA status and DASESR, the achievement rate of low disease activity and remission, HAQ and the retention rate. In each type of biologics, ACPA positive were ABT:TCZ:TNF=71/81:18/25:28/33. There were also no differences about any type of biologics under the status of ACPA.【Conclusions】In this study, we found no difference in the response of biologics and the ACPA status in the start of biologics. But we need to assess more additional data because of small samples of ACPA negative in this study.

P1-023

A Comparison of the Effects of Biologics Depending on Age of Onset of RA

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Conflict of interest: None

Purpose: Average onset of RA is in the 40's and 50's, as are many patients in this facility's biologics cohort group. Late-onset RA is increasing. Research on biologics' effects in these age groups is lacking, and the level of efficacy is not clear. We studied the effects of biologics in late-onset RA patients. Methods: Patients of the bio cohort group were divided into three age-of-onset-based groups-ages 20-64 (standard group), 65-74 (older onset group) and over 75 (advanced-age onset group). Patients had used a biologic for over one year, and the results were compared using DAS28-CRP and HAQ. Results: The SG was 376 patients, the OOG 48, the AAOG, 13. Etanercept was used most often, but abatacept more often as age increased. DAS28-CRP scores of the three groups were 4.81, 4.84, and 4.84, with no large differences. One year later they were 2.73, 2.67, and 2.79. Pre-administration HAQ values were 0.959, 1.276, and 1.212; one year later they were 0.643, 1.058, and 1.174, with the average change 0.32, 0.22, and 0.04, clearly lower in the advanced age group. Results: Due to complications in late-onset RA cases there are also treatment limitations. Low disease activity is attainable, but a resultant improvement of physical functions was not seen. Treatment strategies must be reconsidered.

P1-024

Investigation of the usefulness of "revised HAQ" fits with everyday life in patients with rheumatoid arthritis

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Conflict of interest: None

【Introduction】HAQ (Health Assessment Questionnaire) is used as an important index for evaluating joint function in RA patients. Last year, we reported that some of motions in HAQ are not actually done in everyday life and devised alternative actions on them.【Object】To investigate the usefulness of "revised HAQ" we reported last year.【Method】A total of 45 patients with RA who treated with our hospital and Osaka Medical College were analy. They were asked to have the answer conventional HAQ and "revised HAQ" and analy the relationship with RA disease activity index (DAS28CRP, PGA, EGA). And the results for the two groups, group A (≧65 y.o) and group B (≧75 y.o) were analyzed separately.【Result】12 men, 33 females, average age 62.3 years old, average DAS28-CRP 2.85, average PGA 27.2, average EGA 14.6. As a whole, both conventional HAQ and "revised HAQ" showed significant correlation with DAS28-CRP, PGA and EGA. (respectively, Conventional HAQ:$p<0.001$, $p=0.008$, $p=0.040$ revised HAQ:$p<0.001$, $p=0.007$, $p=0.027$)【Conclusion】The "revised HAQ" is highly correlated with RA disease activity index compared to conventional HAQ. It was suggested that dysfunction accompanied with aging affects the difference between HAQ and RA disease activity index.

P1-025

Can rheumatoid factor be used for determining the therapeutic effects of the administration of abatacept?

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Conflict of interest: None

[Purpose] Abatacept is thought to inhibit the activity of T cells, and furthermore working to inhibit autoantibody production in plasma cells located downstream. In this report, we examined the administration of abatacept and the changes in RF that it caused. [Method] Our subjects were 9 patients who were able to continue the abatacept for more than 52 weeks. We evaluated the inflammatory markers (ESR60, MMP-3, CRP, and RF), DAS28-ESR and CDAI in these patients on the 0th, 3rd, 6th and 12th month. Furthermore, we focused on only the RF, and compared the inflammatory markers and performed a clinical evaluation between a group in which the RF decreased during the 12 months and a group in which the RF was unchanged or increased during the same period. [Results] All markers decreased by the 12th month for all 9 patients. However, the RF decreased in four patients, whereas it was increased in five patients. The four patients whose RF decreased attained low disease activity or clinical remission; however, there were no significant statistical differences in all factors between two groups. [Conclusion] Our study suggests that if the RF decreases, we may assume that the clinical effect has been obtained; however, if it does not decrease, further verification will be necessary.

P1-026

Clinical features of patients with monoarticular rheumatoid arthritis and comparison of monoarthritis between of small joint and of large joint in patients with rheumatoid arthritis

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Conflict of interest: None

We did this study to investigate the clinical characteristics in rheumatoid arthritis (RA)patients with monoarthritis and to evaluate the differences those with monoarthritis of large joint and those of small joint.

Among 2200 RA patients of NHO Sagamihara hospital,1756 are without prosthetic joint and 269 are with single joint (assessed in DAS28) swelling and/or pain. We compared these 3 groups. DAS28-ESR, DAS-CRP, SDAI CDAI scores are largest in patients with single joint of swelling and pain. And the frequencies of remission of all four composite measures are almost the same. We also investigated the differences in patients with single joint and/or swelling of large joint and those of small joint in each these 3 groups. There were statistically significant differences between those of large joint and those with small joint as bellows. MDGA, CRP, ESR in a group with single joint of swelling and pain. DAS28-ESR and DAS28-CRP in a group with single joint of swelling and pain and a group with single joint of pain without swelling. SDAI, CDAI in a group with single joint of swelling and pain. There weren't satastically significant differences PGA and medication (biologics, methotorexate, oral steroid, NSAIDs) between those with large joint and those with small joint.

P1-027

Examination between Boolean remission and ultrasound remission about rheumatoid arthritis (RA) patients in our hospital

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Conflict of interest: None

Boolean remission criteria are most strict criteria for RA treatment. In the meantime, the elderly RA patients are likely to be infected and suffer from the side effects. We investigated the relationship between Boolean remission and ultrasound remission, and considered the validity of Boolean remission in the elderly RA patients. As of October 2016, we analyzed the 31 RA patients (4 men, 27 women, average age 69.1 years old, average DAS28-CRP 2.23) who had the ultrasound test. We classified the 31 RA patients to the group under 75 years of age and the group over 75 years of age, and investigated the relationship statistically between the disease activity indexes containing Boolean remission and ultrasound remission. In the group under 75 years of age, Boolean remission related to ultrasound remission (P=0.0237*), but in the group over 75 years of age Boolean remission didn't related (P=0.1213). And tender joint count (TJC) (P=0.2448), CRP (P=0.4712), and the patient's VAS (P-VAS) (P=0.7508) included Boolean remission didn't related to ultrasound remission. In the patients over 75 years, TJ, CRP, and P-VAS may not correspond with the ultrasound findings. In the elderly RA patients, Boolean remission criteria may not be suitable for the therapeutic target.

P1-028

Polymorphism analysis to predict anti-TNF biologics efficacy in rheumatoid arthritis

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Conflict of interest: None

[Object] When patients inadequately responded to anti-TNF biologics, a switch to other bDMARDs is necessary as early as possible in RA treatment. The objective of this study is to analyze genetic polymorphisms associated with the response to anti-TNF biologics [Methods] The subjects consisted of 84 cases (9 male cases, average age: 60.1 years old) of patients. The subjects were divided into two groups; the responder (n=56) who achieved low disease activity or remission with anti-TNF biologics and the non-responder (n=28) who were remained moderate/high disease activity or stepped up to other bDMARDs. Ninety-six candidate SNPs were examined with the association of the groups. The significance of the association between the trait and genotype was evaluated using the Wald test under the trend mode for minor allele. [Results] The rs1045642 on the gene *ABCB1* encoding p-glycoprotein was suggestively associated. The frequency of minor allele in the responders was higher than one in the non-responders (odds ratio; 2.96, 95% CI;1.46-6.52, P=0.004). [Conclusions] ABCB1 is a membrane transporter which is involved in the DMARDs efflux mechanism. ABCB1 polymorphisms could be a useful tool to predict patients at risk of non-responder to anti-TNF biologics in RA patients.

P1-029

Perioperative course of RA patients underwent orthopedic surgery under disease control by tofacitinib

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Conflict of interest: None

Background: Tofacitinib (TOF) is oral Janus kinase (JAK) inhibitor approved for the treatment of rheumatoid arthritis (RA). There is no available data to support the management of TOF during perioperative period. Methods: We reviewed clinical course of 7 orthopedic surgeries in 5 RA patients. Surgical procedures included one toe plasty, two open reduction and internal fixation for femoral trochanter fracture and humeral proximal fracture, one removal implant for humeral proximal fracture, one synovectomy of wrist, one wrist arthroplasty, and one total knee arthroplasty. The surgical-site infection (SSI), delayed wound healing (DWH), and abnormal blood test values were investigated. Results: SSI was not identified. DWH was observed in one case underwent toe plasty. Lymphonemia was observed in 3 patients (4 surgeries), and recovered within 30 days. Conclusions: The JCR guidelines for TOF recommended careful management of TOF during perioperative course. However, drug withdrawal may not be reasonable for TOF, because of its short half-life (3 hours). The flare-up of disease might be a concern about discontinuation. We did not experience severe adverse event after the surgery, however further accumulation of evidences and experiences are needed to reach the acceptable conclusion.

P1-030

Perioperative management in RA treated with Tofacitinib

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Conflict of interest: None

[Object] Tofacitinib (TOF) is a Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). TOF inhibits the multiple cytokines involved in the inflammatory cascade, hence there is concern over the side effect of infection. On the other hand, it is unknown about surgical site infection and flare up of rheumatic symptoms in RA treated with TOF during perioperative period. The purpose of this study is to investigate surgical site infection and flare up of rheumatic symptoms in RA treated with TOF to make an useful perioperative guideline. [Methods] Between January 2015 and November 2016, we experienced 10 operations in RA treated with TOF. In the current study, we set the cessation of TOF at 3 days before the operation day and prescribed TOF after removal of sutures. [Results] In this study, 1 of 10 patients had surgical site infection. Rheumatic symptoms flared up on 3 of 10 patients during the cessation of TOF. [Conclusions] We require further investigation about surgical site infection and the flare up of rheumatic symptoms during perioperative period in RA treated with TOF.

P1-031

Perioperative management of biological DMARDs in patients with rheumatoid arthritis

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Conflict of interest: None

Objective: To identify retrospectively perioperative complications of arthroplasty employing bDMARDs in patients with RA. **Methods:** This was a study on 63 patients with RA who underwent surgeries involving bDMARDs. We investigated a total 88 arthroplasties. They were evaluated for surgical site infection (SSI) and arthritis recurrence. Of all the bDMARDs, infliximab (IFX) was used in 15 surgeries, etanercept (ETN) in 35, adalimumab in 16, golimumab in 3, certolizumab-pegol in 1, abatacept in 4, and tocilizumab (TCZ) in 12. The surgeries included TKA (n=33), TEA (12), THA (10), wrist arthroplasty (4), arthrodesis of the thumb (1) and ankle joints (6), synovectomy (3) and, forefoot arthroplasty (19). Administration of bDMARDs were discontinued for four weeks from a several days. **Results:**Deep infection developed in three cases of TEA (3/12) whereas TKA and THA group had no SSI. Recurrence of arthralgia during the perioperative period in 10.2%: 7 cases in the ETN group, 1 in IFX group and 1 in the TCZ group. **Conclusion:** Infection rate of TEA is higher than THA and TKA generally. These results suggest that use of bDMARDs may not affect the incidence of SSI after elective orthopaedic joint surgery in RA patients by appropriately discontinuing the administration of bDMARDs.

P1-032

Surgical improvement of occipital pain in patients with atlantoaxial disorder due to rheumatoid arthritis

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Conflict of interest: None

Introduction: We conducted a retrospective study to evaluate the characteristics of occipital pain in patients who underwent atlantoaxial posterior fusion surgery with RA. Methods: From April 2012 to December 2015, 6 patients of atlantoaxial disorder due to RA underwent surgery. The characteristics of occipital pain were checked from the medical record. VAS and NDI were measured to evaluate the degree of occipital pain. The degree of atlantoaxial osteoarthritis (OA) and compression of C2 nerve root were evaluated using CTM. The follow-up period is 1 year. Results: The characteristics of occipital pain are lancinating pain in 3 cases, pain with click in 2 cases, and dull pain in 1 cases. The significant improvements of VAS (75.0±16.4 to 30.8±19.6) and NDI (62.7±15.8 to 34.2±13.5) were detected after surgery. 2 cases of pain with click showed hemi atlantoaxial OA and no compression of C2 root. In case of lancinating pain, the CTM showed C2 root compression by C1 posterior arch and outgrowth of osteophyte of hemi-atlantoaxial joint. Conclusion: In AAS of RA, the occipital pain with click firstly arises due to hemi-atlantoaxial OA. Secondary, the progression of OA and outgrowth of osteophyte in hemi-atlantoaxial joint results in C2 radiculopathy that causes the occipital neuralgia.

P1-033

The historical review of the rheumatoid cervical surgery in our hospital

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Conflict of interest: None

Objective:We reviewed the cases of the RA cervical surgery over 25 years. Methods: 40 RA cases were included. The operation was performed in upper cervical spine in our hospital since1991. We compared 35 cases in which wiring fixation was provided, and 5 cases in which screw fixation was provided since2008. Results:The number of RA cervical spine surgeries increased most in about 1995, but has been decreasing since then. There was no significant differences in patient characteristics of both groups (age, sex, RA disease duration, rate of occipital bone fixation, the number of fusion levels, preoperative halo-vest utilization). There was significantly more usage of the biological preparations in the Screw group. (Wiring group was 5.7%, and the Screw group was 60%, $p<0.01$)In the Screw group, the operative time was significantly shorter, and the postoperative halo-vest utilization was significantly lower and the bone union rate tended to be higher. Conclusion: Recently the number of the RA cervical spine surgery decreased since biological preparation was introduced in Japan. Due to development of upper cervical spine operations, the complications of the operation decreased, and the postoperative external fixation method became quite simple.

P1-034

Clinical outcome of surgery for cervical spine lesions in progressed Rheumatoid Arthritis

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Conflict of interest: None

【Objects】We report clinical results of surgery for cervical spine lesions in progressed Rheumatoid Arthritis (RA).【Methods】We reviewed 14 patients performed surgery in our institute from 2008 to 2015. There were 3 men and 11 women. The mean age was 68.4 (range 40-75) years. They were followed up for a mean duration of 8.4 (1-24) months. We retrospectively investigated disease types, operative methods, pre- and postoperative JOA score (the Japanese Orthopaedic Association score for cervical myelopathy), complications after surgery.【Results】On plain X-ray, 6 cases had atlantoaxial subluxation, whereas 7 cases had atlantoaxial subluxation with vertical subluxation, another one case had atlantoaxial subluxation accompanied with subaxial subluxation. 9 cases were performed decompression and fusion, only decompression in 5 cases. The mean JOA score improved from 7.2 (range 4-12.5) preoperatively to 10.0 (0.5-17) at the final follow-up. There were 6 cases with complications after surgery. Complication rate after surgery was 42.9%(6/14).【Conclusions】Though about a half of these progressed RA patients sustained various complications after surgery, their QOL improved. Our relatively minimal invasive operations with careful perioperative management were effective.

P1-035

Patient reported outcome of the upper extremity surgery for the patients with rheumatoid arthritis using the Japanese DASH and our original questionnaire

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Conflict of interest: None

Objectives: To clarify the effect of the wrist, the hand and the elbow surgeries, we evaluated the patient reported outcome using Japanese version of DASH and our original questionnaire. Methods: A prospective cohort study was performed on 70 patients who underwent the upper extremity surgery. They were evaluated by the DASH and DAS28-CRP (4) at just before surgery and one year after surgery. Postoperatively, original questionnaires were sent to patients to reveal patient's satisfaction. The strength of association between original satisfaction score and each score of DASH items was measured using Spearman's rank-order correlation test. Results: The mean DASH score before surgery 47.3 decreased to 39.5 ($p<0.01$) at one year after surgery. The mean DAS28-CRP (4) de-

creased from 3.3 to 2.4 ($p<0.01$). 86% of patients were "most satisfied" or "satisfied" with the surgically-treated site. The score of "Weakness in your arm, shoulder or hand." and " tingling" had a correlation with the satisfaction level. Conclusion: The wrist, the hand and the elbow surgeries for the patients with RA improved specific function of the surgically-treated site as well as the disease activity. The power in the upper extremity without pain appeared to be the determinant of the patient's satisfaction.

P1-036

RA related orthopedic surgery for patients in clinical remission

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Conflict of interest: None

[Objectives] To investigate the outcome of RA related orthopedic surgery in the patients with RA in clinical remission. [Methods] A total of 276 RA patients were scheduled to undergo RA related orthopedic elective surgery between October 2012 and September 2014. They were divided into remission group (RG) of 61 patients and non-remission group (NG) of 215 patients. Clinical remission was defined using DAS28-CRP (4) less than 2.3. They were assessed and compared at baseline (preop.), 6 months and 12 months after surgery. [Result] There was not a significant difference between two groups in age, disease duration, stage, class, and use of MTX, PSL, and bDMARD. Forefoot ($p<0.01$) and fingers ($p<0.05$) in RG, and wrists ($p<0.05$) and knees ($p<0.05$) in NG were frequently surgically treated. At 6 months after surgery, CDAI, DASH score, EQ-5D, and BDI-II in RG improved significantly. There was not a significant change in SDAI, GH (patient VAS, Dr. VAS), J-HAQ, use of MTX and PSL. [Conclusion] The need of orthopaedic surgery for the small joint in the hand and the foot is high, even if the patient is in clinical remission. ADL and QOL are possible to improve more by the surgical intervention.

P1-037

Investigation on the postoperative range of motion of metacarpophalangeal joints treated with silastic joint replacement or soft tissue reconstruction in the patients of rheumatoid arthritis who were suffering from ulnar deviation of the fingers

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Conflict of interest: None

[Object] Silastic joint replacement (SJR) of metacarpophalangeal (MCP) joint is applicable to advanced ulnar deviation deformities in rheumatoid arthritis (RA), but we treat them by soft tissue reconstruction (STR) when deformity can be repositioned passively. In this study, we report on the results of the procedure. [Methods] We examined the postoperative range of motion (ROM) of the involved joints of the RA patients who underwent SJR (R group) or STR (S group) of MCP joint. [Results] Ninety-seven hands of 82 patients were included. The SJR were performed in 329 joints, and STR were performed in 50 joints. Postoperative joint ROM was evaluated 25.0 (2.0-64.0) weeks after surgery on average. In index to little finger, ROM of R group/S group was flexion 60.4° / 61.3° and extension -13.7° / -19.3°, flexion 60.7° / 65.3° and extension - 11.4° / - 10.3°, flexion 58.4 / 60.1 and extension - 8.1° / - 6.9°, and flexion 47.8° / 53.1° and extension -1.28° / 2.52°, respectively. No significant difference was found in all joints. [Conclusions] There was no significant difference in postoperative range of motion between MCP joints treated with SJR and STR. STR, which can preserve joints, was thought to be useful for advanced ulnar deviation when indication was decided carefully.

P1-038

The Usefulness of wrist block in the surgical reconstruction of finger tendon rupture in RA patients

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Conflict of interest: None

【Purpose】We studied the short term usefulness of wrist block in the surgical reconstruction of finger tendon rupture in RA patients.【Methods】Objects were 4 RA patients performed reconstruction of finger extensor tendon rupture under wrist block anesthesia. Controls were 4 RA patients performed the same operation under general anesthesia. We compared operation time, blood loss, limitation of finger extension and deep flexion between both groups.【Results】There were no differences of mean operation time (wrist block group: general anesthesia group; 148 min.: 160min.) and mean blood loss (66ml: 56ml) between two groups. On the other hand, the limitation of finger extension was significantly lesser in the wrist block group than the general anesthesia group (6.3° : 10 °). The case of limitation of finger flexion was observed only one case in general anesthesia group.【Conclusion】 The wrist block in the surgical reconstruction of finger tendon rupture in RA patients was useful for the decision of tendon suture tension and low risk of the limitation of finger motion.

P1-039

Clinical results of wrist fusion for the patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] In wrist severely affected by rheumatoid arthritis (RA), wrist fusion is a reliable procedure to achieve a painless and stable joint. There are several techniques described for wrist fusion. We report clinical results of wrist fusion. [Methods] The subjects were 9 wrists in 8 patients with RA. The mean age was 64 years at the time of surgery. Six patients had extensor tendon rupture. Preoperative Larsen grades were IV or V. Intramedullary rod or wire supplemented with UniClip was performed in 5 wrists, and the other techniques in 4. The follow-up periods ranged between 5 and 42 months. The evaluation was performed by the period for bone union and the clinical scores. [Results] The average periods for bone union were 79.6 days in intramedullary implant, and 120 in other techniques after excluding two cases who have not achieved bone union. Grip strengths were improved from 9.3 kg to 19.1 in intramedullary implant, while from 9.6 to 15.8 in other techniques. [Conclusion] Intramedullary rod or wire supplemented with UniClip provided reliability for bone union and shortened the period for bone union. Rigid stability provided by UniClip might enable early postoperative exercise, which further enhanced finger function, even though tendon rupture is combined.

P1-040

Plural subcutaneous flexor tendon ruptures caused by dislocation of carpal bones associated with rheumatoid arthritis : case report

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Conflict of interest: None

We experienced a rare case of plural subcutaneous flexor tendon ruptures caused by dislocation of carpal bones associated with RA. A 86 year-old female (stage3 class2) presented with inability to flex her right index and middle finger gradually, and uncomfortable feeling to flex ring

finger. The wrist joint was volar dislocated, but was reduced easily. Surgical exploration revealed complete tear of flexor digitorum profundus (FDP) (2,3), flexor digitorum superficialis (FDS) (2,3), partial tear of FDP (4) in carpal tunnel, and few tenosynovitis by RA. But at deep layer in the tunnel, joint capsule was ruptured and lunate that was defected cartilage was volar dislocaded easily. We considered that the tendon ruptures had been caused by direct friction with dislocated injured lunate. We excised the lunate and closed the capsule strongly. The FDP (2) distal tendon was sutured to the FDP (3) with palmaris longus tendon as a bridge graft, and the FDP (3) distal tendon was transferred to repaired FDP (4) by interlacing suture. At present, range of motion of the fingers were recoverd before the rupture. In X-ray, there were no dislocation of the wrist joint. We can achieve good result for poorly treated plural flexor tendon ruptures by combined technique of tendon graft and transfer.

P1-041

Treatment outcomes with volar locking plate fixation for distal radius fractures in rheumatoid arthritis patients

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Conflict of interest: None

Purpose: The number of surgeries and treatment outcomes with internal fixation using a volar locking plate (VLP) for distal radius fractures (DRFs) in the Akita Orthopedic group on the rheumatoid arthritis registry were investigated. Methods: The subjects were RA patients (2,142 patients in 2016), and the number of DRF surgeries done with internal fixation using VLP and the treatment outcomes were investigated. Results: Internal fixation with VLP was done in 6 subjects, 7 hands (2 men, 4 women, age at surgery 65–84 years). At final observation, bone union was obtained in all subjects. In 2 subjects, correction loss had occurred at final observation compared with immediately after surgery, and ulnar pain remained. In one of the 2 subjects, the screw on the central side had broken and severe shortening occurred. Conclusion: The treatment outcome with VLP fixation for DRFs in RA patients was generally good. A case of severe postoperative shortening was also seen because of bone fragility in the distal radius, and during surgery it is important to be aware of subchondral support for distal bone fragments. In cases when people need to bear weight on their upper limbs when standing or walking, after treatment, such as combination postoperative external fixation, should be kept in mind.

P1-042

Mid-term results of semiconstrained total elbow arthroplasty in patients with rheumatoid arthritis

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Conflict of interest: None

Objective: To investigate mid-term results of semiconstrained total elbow arthroplasty (TEA) in RA patients. **Method:** Semiconstrained TEA were performed on 29 elbows in 26 patients (3 males and 23 females) with severe destructive elbows between September 2001 and December 2011. The mean ages at operation was 65.2 years old and the mean duration of follow-up was 93.5 months. All patients were examined preoperatively and at 5 or more years postoperatively. **Results:** JOA elbow score were significantly improved from 44.3 points to 82.6 points at the latest survey. The ROM were improved from -24.3˚ to -20.7˚ in extension angles, and from 102.6˚ to134.4˚ in flexion angles. Postoperative complications were detected in 12 cases (7 humeral condylar fractures, 2 ulnar paresthesia, 2 superficial infections and 2 deep infections). All humeral condylar fractures healed without invasive treatments. In one deep infection the removal of prosthesis was required. **Conclusion:** In our study excellent pain relief and good functional can be achieved in the mid-term with semiconstrained TEA in, however the rate of postoperative complication was relatively high.

P1-043

Reverse shoulder arthroplasty with intraoperative O-arm navigation in patients with rheumatoid arthritis

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Conflict of interest: None

Reverse shoulder arthroplasty (RSA) is useful for rheumatoid arthritis. It is important to implant the glenoid component appropriately for procedure success. Our objective was to report two cases of RSA using intraoperative O-arm navigation in patients with rheumatoid arthritis. A 77 years-old woman who had been diagnosis with rheumatoid arthritis underwent RSA with intraoperative O-arm navigation. We used a standard deltopectoral approach. We attached the reference array for O-arm navigation at the coracoid process. Then, the glenoid component placed under O-arm navigation. The glenoid version angle was 12˚ of retroversion preoperatively, compared with 6˚ of retroversion postoperatively. A 71 years-old woman who had been diagnosis with rheumatoid arthritis underwent RSA with intraoperative O-arm navigation as mentioned above. The glenoid version angle was 2˚ of retroversion preoperatively, compared with 7˚ of anteversion postoperatively. There were no perioperative complications in two cases. This is the first report of RSA with intraoperative O-arm navigation in patients with rheumatoid arthritis. O-arm navigation permits more accurate and safer instrumentation for RSA in patients with rheumatoid arthritis.

P1-044

Treatment of humeral fracture after linked total elbow arthroplasty

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Conflict of interest: None

Introduction: Total elbow arthroplasty in patients with rheumatoid arthritis is a useful treatment for reconstruction of upper limb function. But periprosthetic fractures are difficult to treat. We report on cases where the bone cement filling was devised in order to strengthen the fixation of the humeral implant on the humeral fracture after linked total elbow arthroplasty. Subject: Internal fixation, bone graft, and bone cement filling were performed on 3 cases who had a humeral fracture after linked total elbow arthroplasty. Bone cement was filled from the distal part of humerus. In addition, the proximal part of humerus was fenestrated and bone cement was also filled from the proximal side so that the humeral stem could be sufficiently fixed. Result: Bone union were obtained in all three patients. Conclusion: In the treatment of humeral fracture after linked total elbow arthroplasty, internal fixation by plates, bone grafting is used in combination. The bone cement fills from the distal part of humerus, but it is difficult to fill the bone cement to the tip of the long stem. In these cases, bone cement can be sufficiently filled up to the tip of stem by fenestration of humerus and injection of bone cement. By firmly fixing the implant, bone union was obtained.

P1-045

The Graft Site Hernia after Iliac Crest Bone Harvest in Rheumatoid Arthritis: A Case Report

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Conflict of interest: None

We report a case of iliac crest bone hernia in a 77-year old female with rheumatoid arthritis who was underwent revision total elbow arthroplasty of the right elbow with iliac crest bone from the right side. Two months after revision surgery, the patient complained swelling at the right iliac crest bone harvest area. A CT of the abdomen confirmed graft site hernia. An intraperitoneal onlay-mesh repair was performed, but the hernia recurred. Six month after mesh repair, revision surgery for iliac crest bone hernia with Suture Anchors. The recovery was uneventful.

P1-046

Long-term clinical results of Kudo total elbow arthroplasty with allo bone graft for patients with Mutylans rheumatoid arthritis

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Conflict of interest: None

Objective; We studied the clinical long-term results of TEAs with allo-graft for patients with Mutylans rheumatoid arthritis. **Methods;** 2 elbows were replaced using K-Elbow prostheses with allo-bone graft. After a follow-up period of least 10 years, they were assessed about clinical condition before and after surgery, radiographic changes. **Results;** These patients were satisfied for results of K-Elbow arthroplasty. Radiological loosening was none. **Conclusion;** K-Elbow with allo-graft for patients with Mutylans rheumatoid arthritis provide good pain relief in the arthritic elbow leading to high patient satisfaction and long-term survivorship.

P1-047

Changes in the background characteristics of rheumatoid arthritis patients who underwent total hip arthroplasty and total knee arthroplasty

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Conflict of interest: None

[Objectives] We investigated the background characteristics of RA patients who had undergone total hip arthroplasty (THA) or total knee arthroplasty (TKA) in our hospital. **[Methods]** Subjects were 245 RA patients (357 joints) with a mean age of 64.8 years who underwent primary THA and TKA from 2000-2015. Changes in the number of surgeries, patient background characteristics and preoperative X-ray images were investigated. **[Results]** The number of surgeries in the second 8-year period was decreased compared with that in the first 8-year period. The mean age in the second period was significantly higher than that in the first period. There was no significant difference in disease duration between the two periods. The incidence of other arthropathies was significantly decreased from 84.6% to 68.0%. There was no significant difference in the proportion of patients who were on corticosteroids, while those on methotrexate and biological agents were increased from 13.7% to 36.6% and from 0% to 11.4%, respectively. **[Conclusion]** Medication for RA has changed, and a decrease in the number of surgeries. The age of patients who required THA and TKA has risen. Such trends will continue and decreases in the number of THA and TKA cases are expected in the future.

P1-048

Middle to long term survival of revision THA with GAP II Aacetabular Shell

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Conflict of interest: None

Purpose: We examined the survival of the revision THA with GAP II Acetabular Shell in our hospital. Methods: We retrospectively reviewed 18 patients, 3 males and 15 females, mean age was 61 years old. We performed the total of 21 operations from 2002 to 2011. 5 patients were RA. Results: 17 patients were followed up more than 5 years, and moreover, 8 patients were more than 10 years. One patient was already dead 4 years after operation with other reason. Implant failure were occurred in 8 patients. Revised operations were performed in 5 patients at the last follow up. 3 patients within 5 RA patients received revised operations. Mean duration we found out implant failure with X-ray was 31.5 months (4-64 months), and mean duration we performed revised operations was 65 months (6-112 months). We keep on following up carefully 3 patients with implant failure but not performed additional operations. Only 1 patients occurred obvious but little implant displacement and had no complaints. Discussion: Implant abnormalities occurred at 43% and revised operations were performed at 24%. The survival of the revision THA with GAP II Acetabular Shell proved unsatisfactory results, especially RA patients.

P1-049

Clinical result of total hip arthroplasty using tapered wedge-shaped stem for the rheumatoid arthritis patients

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Conflict of interest: None

[Object] We investigated results of total hip arthroplasty (THA) using taperd wedge-shaped cementless stem for the RA patients. [Methods] Thirteen patients (all women with an averege age at operation of 67.7 years) underwent THA using Taperlock Hip System (made in ZIMMER BIOMET) between 2011 to 2016. The examples which we can follow up to date were 11 cases. We investigated these examples on clinical or radiographic evaluation. [Results] The complications of all cases were one fracture of femur. Final average of Japan Orthopaedic Association score was 72 points. In X ray, Canal Flare Index was 2.3 to 4.0 (averege 3.3), femoral cnanal shape (Noble) was stovepipe in 4 cases, normal in 7 cases. Stem aligment was middle posion: 9 cases, varus position: 1 case, valgus posion: 1 case from AP view, and middle posion: 4 cases, flection posion: 7 cases from lateral view. Stem stability was establishied through bone ingrowth fixation (Engh)for all canal shaped except femoral fractue case. [Conclusions] Short-term results of THA using Taperlock Hip System for the RA patient are satisfied for clinically and in X-ray.

P1-050

Genome-wide search for SNPs associated with remission, adverse events or infection risk in anti-TNF-treated RA patients using multiple medical cohorts

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Conflict of interest: None

Purpose: Achievement of remission, occurrence of adverse events and infection risk in anti-TNF treatment is currently one of the most important matters in RA treatment. In this study, we searched for SNPs associated with remission, occurrence of adverse events or infection risk in anti-TNF treated RA patients by using multiple medical cohorts. **Patients and Methods:** Infliximab-treated patients included 285, etanercept, 263 patients, adalimumab, 45 patients, certolizumab-pegol, 30 patients, and golimumab, 35 patients, for a total of 658 patients from eight hospitals in different regions of Japan. Remission was determined by DAS28 (CRP)

around 24-30 weeks after the initiation of treatment. Association analyses between 285,548 SNPs and medical record were examined by Fisher's exact tests. **Results:** We found, in part, *ADAMTS17* in remission, and *IGSF11* in infection risk. Common SNPs among anti-TNF, TCZ and ABT analyses showed *TCF7L1*, *IL20RA* in remission, *ADAMTS20* in adverse events, and *HS3T1* in infection risk. **Conclusion:** Genome-wide SNP analysis may be useful in the prediction of remission, adverse events, or infection risk before treatment with anti-TNF biologics. Common SNPs among anti-TNF, TCZ and ABT analyses may be useful for switching of these biologics.

P1-051

Genome-wide search for SNPs associated with remission, adverse events or infection risk in tocilizumab (TCZ) or abatacept (ABT)-treated RA patients using multiple medical cohorts

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Conflict of interest: None

Purpose: Achievement of remission, occurrence of adverse events and infection risk in TCZ or ABT treatment is currently one of the most important matters in RA treatment. In this study, we searched for SNPs associated with remission, adverse events or infection risk in TCZ- or ABT-treated RA patients by using multiple medical cohorts. **Patients and Methods:** TCZ-treated patients included 244, and ABT, 161 patients, for a total of 405 patients from eight hospitals in different regions of Japan. TCZ remission was determined by CDAI. ABT remission was determined by DAS28 (CRP). Association analyses between 285,548 SNPs and medical records were examined by Fisher's exact tests. **Results:** We found, in part, *ADAMTSL1* in remission, *ADAM33* in adverse events, and *CD163* genes in infection risk in TCZ. In ABT, we found *CD109* in remission, *PCDH7* in adverse events, *CD83* in infection risk. Common SNPs between TCZ and ABT analyses showed *ADAM29* in remission, *IL20RB* in adverse events, and *COL6A1* in infection risk. **Conclusion:** Genome-wide SNP analysis may be useful in the prediction of remission, adverse events, or infection risk before treatment with TCZ and ABT. Common SNPs among anti-TNF, TCZ and ABT analyses may be useful for switching of these biologics.

P1-052

Effect of CTLA4-Ig (Abatacept) on cell proliferation state (Ki67 expression) of CD4$^+$T cell subsets in rheumatoid arthritis patients

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Conflict of interest: Yes

[Object] The immune response of CD4$^+$T cells (cell proliferation and cytokine production) plays an important role in the pathology of rheumatoid arthritis (RA). We compared the effects of CTLA4-Ig (Abatacept, ABA) on the cell proliferation state of CD4$^+$T cell subsets using the cell cycle related nuclear protein Ki67. **[Methods]** PBMC of RA patients were collected before ABA administration and 4 weeks after, respectively. Changes in Ki67 expression rate (ABA 0, 4 wks) in each CD4$^+$T cell subsets (Th1, Th2, Th17, Th17.1, and Treg) were analyzed by multicolor flow cytometry by intracytoplasmic staining of Ki67. **[Results]** The percentage of Treg in CD4$^+$T cells (0→4wks,4.2%→ 3.3%, p=0.003) decreased significantly, but the proportion of Th1 (CXCR3$^+$CCR4$^-$CCR6$^-$; 12.1%→11.7%), Th2 (CCR4$^+$CXCR3$^-$CCR6$^-$; 17.5%→17.6%), Th17 (CCR6$^+$CCR4$^+$CD161$^+$; 5.1%→5.1%), and Th17.1 (CCR6$^+$CD161$^+$ CXCR3$^+$CCR4$^-$; 1.49%→1.52%) did not change. However, in Th2, Th17, Treg, the proportion of Ki 67$^+$ was markedly reduced (Th2; - 56%, Th17; -39%, Treg, - 55% reduction rate). On the other hand, in Th1 and Th17.1, the decrease in Ki67$^+$ was slight (Th1; -1.7%, Th17.1; -14%). **[Conclusions]** The effect of ABA on cell proliferation may differ depending on the Th subset, especially in the CXCR3$^+$ T cells with little effect.

P1-053

Clinical efficacy of abatacept in rheumatoid arthritis patients with interstitial pneumonia

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Conflict of interest: None

[Purpose**]** To evaluate the clinical efficacy of abatacept in patients with rheumatoid arthritis (RA) who had interstitial pneumonia as pre-existing pulmonary disease. **[**Methods**]** Among the RA patients registered to ACAGI who had been treated with abatacept, we selected 45 patients who had interstitial pneumonia as pre-existing pulmonary disease and retrospectively analyzed their data on RA disease activity markers (DAS28-CRP, DAS28-ESR, CDAI, SDAI, CRP, ESR, andMMP-3) at the start and after 52 weeks of abatacept treatment. **[**Results**]** Patients' mean age was 72 years and mean duration of the disease was 14 years. The proportion of those who concomitantly received methotrexate was 27%, proportion of those who concomitantly received prednisolone (PSL) was 84%, and mean dose of concomitant PSL was 4.3 mg/day. DAS28CRP was 4.10 at the start of treatment, which improved to 2.84 after 52 week. CDAI also improved from 18.1 to 9.08. At week 52, CDAI remission rate was 13.6% and low disease activity rate 50%. The treatment continuation rate at week 52 was 86%; there were 6 withdrawal cases (4 due to insufficient efficacy and 2 due to personal reasons). **[**Conclusions**]** Abatacept can be considered one of the treatment options for RA patients with interstitial pneumonia.

P1-054

The investigation of patients treated with Infliximab (IFX) in Akita Registry in 2016

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Conflict of interest: None

[Object] To investigate the patients treated with IFX who registered with the Akita Orthopedic group on Rheumatoid Arthritis (AORA). [Methods]: Two thousand and forty-two patients were registered with AORA in 2016. Of these, 140 patients were treated with IFX who comprised the subjects of this study. [Results] The patient characteristics were follows: there were 28 males and 112 females, the mean age was 59.5 year and the mean disease duration was 129.3 months. The DAS-28ESR could be calculated in 99 patients, and the mean was 4.88 (REM: 3, LDA: 7, MDA: 46, HDA: 38). The mean CRP was 2.24 mg/dl, and the mean MMP3 was 250.4 ng/ml. One hundred and twenty-eight patients had been prescribed methotrexate (MTX) with a mean dose of 6.9 mg, and 95 patients had been prescribed prednisolone (PSL) with a mean dose of 5.6mg. Nine patients were administrated IFX as a second biologics. Thirty-two patients could continue IFX treatment during the investigation. In DAS28ESR, MDA and HDA which accounted for 90% at the

start were decreased. On the other hand, REM and LDA were increased, and were accounted 60% at the investigation. One hundred and ninety-nine patients could not continue IFX treatment, because of a decreasing effect (44 patients) and adverse events (42 patients).

P1-055

14 cases pregnant during rheumatoid arthritis treatment

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Conflict of interest: None

We examined 14 patients who gave birth to pregnancy during the treatment of rheumatoid arthritis (RA) in our hospital. We will report about the actual safety of pregnancy therapy from our analysis of RA pregnancy cases. We will report pregnancy cases of RA patients who visited our hospital from April 2013 to November 2016. The number of cases was 14 cases, the age at pregnancy was 30 to 40 years, and the disease duration was 1 to 18 years. Before pregnancy treatment, 11 cases biological products alone (ETN 7, CTP 1, ADA 1, GLM 1), 2 cases PSL + biological products (CTP 1, TCZ 1), 2 cases of PSL + SASP. Prior to pregnancy, through pregnancy the disease was controlled with less than low disease activity. The treatment at lactation was 3 cases of drug free, 1 case of PSL alone, 1 case of PSL + SASP, and 10 cases of PSL + biological preparation. One case of cesarean section with birth, one case of placenta remnant, and two cases of low birth weight infants. There was no birth defect in the baby child, and there was no abnormality in both the mother and the child medical examination for 1 month after birth. However, antiTNF preparation is said to delay wound healing and considering that it's necessary to take a drug holiday period in consideration of the observational treatment at birth.

P1-056

Long-term outcome of tocilizumab in patients with rheumatoid arthritis in real-world clinical setting ~ focusing on disease activity, activity of daily living, change of concomitant drugs and prevention of joint destruction~

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Conflict of interest: Yes

[Objectives] To investigate longterm outcome of TCZ in disease activity, activity of daily living, changing of concomitant drugs and prevention of joint destruction in RA patients. [Methods] 65 cases were used for patients' characteristics and drug retention rate (Kaplan-Meier) and 31 cases who continued TCZ for 2 years and more were used for detailed analysis. [Results] Baseline Characteristics (n=65): Mean age 58.8 yo, Female 70.8%, RA duration 9.0 y, MTX concomitant 58.5%, PSL concomitant 63.1% and bionaïve 35.4%. Drug retention rates of TCZ were 86.3% at 1 year, 77.7% at 2 years, 74.5% at 3 years and 71.2% at 4 years. In 31 RA patients who continued TCZ for 2 years, DAS28-CRP, CDAI and mHAQ had significantly decreased over time. DAS28-CRP: 4.98-2.03-1.79, CDAI: 23.3-6.8-5.0, mHAQ: 0.85-0.45-0.38. Mean RF (IU/mL) was not decreased over time (93-183-116). Rates (%) of concomitant MTX, PSL and TAC at baseline, 1-year and 2-year were 74.2-45.2-29.0, 64.5-45.2-22.6 and 6.5-25.8-19.4, respectively. [Conclusions] Drug retention rate of TCZ in RA patients with high disease activity in average was very good. In RA patients who continued TCZ for 2 years, MTX and PSL was decreased. Although concomitant drugs were decreased, prevention of joint destruction was improved over time.

P1-057

High Retention Rates and Clinical Efficacy of Tocilizumab As First-Line Biologic Treatment in Patients with Rheumatoid Arthritis

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Conflict of interest: Yes

[Object] This study aimed to investigate optimal treatment strategy with tocilizumab (TCZ) as a first-line bDMARD treatment in comparison with second-line treatment for RA patients. [Methods] All RA patients who treated with TCZ in Osaka City University RA registry (including 1070 patients eith RA and 353 patients using bDMARDs) were included in this analysis. These patients were divided into two groups that TCZ was used as a first-line bDMARDs (1st group) and a secondline or more treatment (2nd group). Retention rates and clinical efficacy assessed from week 0 to week 52. Furthermore, the discontinuation ratio of glucocorticoid was also evaluated. [Results] Sixty-two patients in 1st group and 75 patients in 2nd group were analyzed. Retention ratio at week 52 was 85.5% in 1st group and 64.0% in 2nd group (p=0.01). DAS28 remission rates were 23.5, 47.0, 49.1, 41.2 and 35.3% in 1st group and 8.3, 22.9, 29.2, 33.3 and 37.5% in 2nd group at week 4, 12, 24, 36 and 52, respectively. During 52 weeks, the dose of glucocorticoid was reduced in 18 patients and withdrawal in 12 patients between 22 patients of 1st group using glucocorticoid at week 0. [Conclusions] High retention rates and clinical efficacy of TCZ as a firstline biologic treatment was found in this research.

P1-058

Efficacy and safety of abatacept treatment in rheumatoid arthrtiis patients with severe lung diasease

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Conflict of interest: None

[Objectives] The aim of this study is to evaluate the efficacy and safety of abatacept treatment in RA patients with severe lung diasease. [Methods] Abatacept was administrated to eighteen RA patients with severe lung diasease intravenously or subcuteneously. Lung diseases in eighteen RA patients were included in 10 interstitial pneumonia, 4 chronic obstructive pulmonary diseases, 2 bronchiectasis, 1 nontuberculous mycobacteriosis, 2 post-pneumocystis pneumonia. [Results] Overall DAS28-ESR was significantly decreased from 5.25±0.31 to 3.65±0.33 ($p<0.01$). Especially, patient's global assessment of disease activity was clearly diminished from 45±5 mm to 24±5 mm ($p<0.01$). According to the EULAR improvement criteria based on DAS28, six patients (34%) achieved good response and nine patients (50%) achieved moderate response. Moreover, serum matrix metalloproteinase-3 and rheumatoid factor were clearly reduced after abatacept treatment in RA patients ($p<0.05$). In contrast, severe adverse effect of abatacept treatment was not in RA patients with lung disease. [Conclusions] Abatacept was effective and safe in RA patients with severe lung diasease, possibly suggesting that it is useful in conventional synthetic DMARD-resistant RA patients with lung disease.

P1-059

A simulative attempt for optimization of choosing biologic DMARDs in treatment of rheumatoid arthritis

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Conflict of interest: None

[Objective] A simulation for correct choice of biologic DMARDs (bDMARD) in rheumatoid arthritis (RA) treatment is performed. There have been introduced some part of this attempt. [Methods] From our clinical results of 190 bDMARD used cases, choice of bDMARD was evaluated as success as achieved remission or low disease activity, while other was evaluated as failure at three years later from the start. Based on data what were already reported in journals and our clinical data, odds ratio

for risk of bDMARD for discontinuity was calculated with multiplication on each bDMARD on our clinical results. The highest drug was chosen. Then if it was corresponded, it was evaluated as true, and if not as false. Concordance ratio, false ratio, sensitivity and specificity were evaluated. [Results] TNF inhibitor had shown 80.4% of concordance ratio. However, false choice ratio had demonstrated 16.8%. On the other hand, nevertheless different drug was chosen, success cases demonstrated 33.2%. Sensitivity was 69.7% and specificity was 33.7% in a whole. In failure cases, high risk cases counted 17.5% and severe infection cases counted 9.6%. [Conclusions] If more precise risk calculation were possible, accuracy can be raised. For the time being, 80% of sensitivity and 70% of specificity is aimed.

P1-060

The clinical course of abatacept treatment selected for safety reasons

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Conflict of interest: None

[Objectives] Rheumatoid arthritis (RA) patients with complications or elderly RA patients represent a therapeutic challenge due to the risk of adverse events under immunosuppressive treatment. The aim of this study was to assess the safety profile of abatacept (ABT) in this particular clinical setting. [Methods] 73 RA patients who underwent ABT treatment at our hospital were enrolled in this study. We compared the number of adverse events (AEs) between patients selected for safety reasons (subject group) and another group. [Results] 55 patients were included in subject group. The majority of the reasons were categorized as lung disease (n=38). AEs were 11 cases in subject group and 2 cases in another group. Discontinuation due to AEs were 9 cases in subject group and 2 cases in another group. [Conclusions] Safety as well as efficacy is an important consideration when initiating intensive treatment, especially in patients with serious comorbidity. Our results suggest that careful treatment is needed for patients who have complications.

P1-061

Efficacy and identification of predictive factors for Tofacitinib treatment response ~ Sweet Cohort ~

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Conflict of interest: None

Objectives: A few reports has been described for efficacy and identification of predictive factors for efficacy. Retrospective analysis on clinical characteristics was performed to assess predictive factors for response to TOF treatment. Methods: Thirty seven RA pts treated with TOF who have clinical data through 24 weeks among fifty four pts treated with TOF were target for this retrospective analysis. Predictive factors through cytokine profile analysis associated with DAS remission and EULAR good response were evaluated. Results: All thirty seven patients treated with TOF showed significant improvement in DAS28-CRP after one month. After 24 weeks of treatment, remission rate is 39.3%, and EULAR good response is 56%. Factors associated with remission could not be revealed neither univariate nor multivariate analysis including history of biologics use or MTX combination. Discussion: According to the result that no correlative factor is identified in remission and good-response to TOF treatment, TOF may be effective in patients with any clinical background and history of treatment.

P1-062

Biologic switching from abatacept to tocilizumab in patients of RA

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Conflict of interest: None

[Objective] There are no reports about biologic switching from abatacept (ABT) to tocilizumab (TCZ). We examined the efficacy of biologic switching from ABT to TCZ and analyzed the predictive factor for clinical remission achieved by this switching. [Methods] This study period was 24 week. Eligible patients had to have switched biologics from ABT to TCZ (SC and IV), and was evaluable for their disease activity by DAS28-ESR (3). LOCF was used if TCZ was discontinued before 24 week. [Result] 1)Eighteen patient was include in this study. Persistence rate of TCZ at 24 week was 78 (14/18) %. (Reasons for discontinuation: insufficient response 2, injection reaction 1, infection 1, others 1) 2) DAS28-ESR (3) was significantly improved at 12 and 24 weekbaseline:5.04±1.38, 12w: 3.42±1.6, 24w:3.54±1.63) 3)There was a significant collection between tender joint count of baseline and DAS28-ESR (3) ($r=0.669$, $P<0.005$). ROC analyses suggested that the best cutoff to discriminate patients achieved and not achieved clinical remission at 24 week was tender joint counts of 6 at baseline. (TPF 72.7%, FPF 14.3%, AUC=0.86, 95% CI 0.68-1.00, $p < 0.001$). [Conclusions] Biologic switching from ABT to TCZ was useful and tender joint count of baseline might predict achievement of clinical remission at 24 week.

P1-063

Clinical outcome of rheumatoid arthritis patients who have been administered biologic agents for 10 consecutive years

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Conflict of interest: None

[Objectives] The purpose of this study is to clarify the long-term outcome of bDMARDs treatment in rheumatoid arthritis (RA) patients. [Methods] Twenty six patients (23 women, three men) with active RA who have been treated with any biologic agents for 10 years were analyzed. The mean age of the patients was 55.8 years old, and the mean duration of disease was 11.9 years on average. Five clinical parameters including DAS28-CRP, SDAI, mHAQ, CRP and TSS of hand were continuously measured. There were only six patients to whom a single biologic agent has been continuously administered for 10 years (single treatment group). To the other patients, two or more agents were administered in this period (switching group). [Results] In these patients, treatment of biologic agents for 10 years significantly reduced clinical parameters, including DAS28-CRP (from 4.71 to 2.26), SDAI (from 33.4 to 8.57), mHAQ (from 1.11 to 0.60), and CRP level (from 5.08 to 0.60 mg/dL). TSS of hand deteriorated by an average of 30 in 10 years. There was no significant difference between the single treatment group and the switching group. [Conclusion] Administration of bDMARDs for 10 years maintained low disease activity of rheumatoid arthritis even in the switching group.

P1-064

Ultrasonographic evaluation of Abatacept therapy in patients with rheumatoid arthritis

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sei Hospital, Toyota, Japan

Conflict of interest: None

[Objectives] To evaluate the clinical efficacy of Abatacept (ABT) therapy patients with rheumatoid arthritis (RA) using ultrasonography (US). [Methods] We used ABT treated 12 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] The mean age was 68.0±16.9 years; the mean disease duration was 16.0±15.3 years; the number of MTX and PSL combination was 6 and 4 cases (50% and 33%); and the mean dose of MTX and PSL was 9.3±5.6mg/w and 3.6±1.6mg/d. Clinical findings related to RA were as follows: tender and swollen joint count, 6.3±5.7 and 5.8±3.3; patient's and physician's global assessment of disease activity, 59.8±29.1 and 54.3±25.0mm; CRP, 2.3±1.9 mg/dL; ESR, 40.4±23.4 mm/h; MMP3 231.7±193.2ng/ml; DAS-ESR, 5.19±1.34 and SDAI, 25.8±10.2. The mean GS score changed from 28.0±18.2 at baseline to 29.4±16.2 (p=0.858), 22.8±15.7 (p=0.223) and 22.3±17.1 (p=0.075) at week4, 12 and 24. The mean PD score changed from 14.4±10.5 at baseline to 13.3±7.9 (p=0.449), 9.5±7.6 (p=0.119) and 8.1±6.7 (p=0.028) at week4, 12 and 24. [Conclusion] The present study provides evidence supporting the ABT therapy improved not only the disease activity not also the inflammatory synovitis.

P1-065

Effect of treatment of Golomumab in elderly people

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Conflict of interest: Yes

Objective we analyzed it about the effect of treatment of the elderly (65 years old or older) RA patients treated in Golimumab in this hospital subject and method We evaluated the continuation situation two years later in 73 RA patients treated in Golimumab 65 years or older. Results In the RA patients receiving Golimumab 65 years or older, the patients 70% or more were able to continue administration regardless of a history of treatment for a long term. But the likelihood that periodical side effect monitoring was necessary was suggested in the Golimumab administration to elderly people because the tendency that the incidence of Serious ADR became higher so as to become old was found as even postmarketing surveillance was said.

P1-066

Retrospective Analysis of Efficacy for Disease Activity, Radiographic Outcome and Safety of Abatacept in Patients with Elderly Advanced Rheumatoid Arthritis Accompanied with Comorbidities

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Conflict of interest: None

OBJECTIVES: To evaluate disease activity, radiographic progression for efficacy and adverse events (AEs) for safety of Abatacept (ABT) for elderly advanced rheumatoid arthritis (RA). **METHODS:** A retrospective 1-year study was performed using medical records from Disease Activity Score 28-joint assessment using C reactive protein (DAS28-CRP) to assess disease activity and modified total Sharp score (mTSS) for radiographic assessment. **RESULTS:** 50 RA patients (male 7, female 43). Disease duration, 140 months; DAS28-CRP, 4.91; RF, 242 IU/ml; ACPA, 426 U/ml; MMP3, 257.3 ng/ml; mTSS, 67.4, BIO, 22 patients; MTX, 19 patients (7.4 mg/week). Half of patients had moderate to severe comorbidities (lung, kidney, liver). DAS28-CRP decreased significantly from 4.92 to 4.00 after 6 months and to3.88 after 12 months of ABT treatment (P <0.0001, respectively). Annual progression of mTSS was 1.02 and structural remission rate was 67.4%. The prognostic factor for joint damage are baseline MMP3 and mTSS/y. The AEs were observed in only 5 cases – pneumonia, interstitial pneumonitis, high KL-6 value, disturbance of the sense of smell, deterioration of schizophrenia. Finally, 88% of patients continued ABT. **CONCLUSIONS:** ABT is useful for elderly advanced RA accompanied with severe comorbidities.

P1-067

Use of Biological DMARDs, better timing and adequate background

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Conflict of interest: None

[Object] To learn the best use of Biological DMARDs (Bio) for the patients with rheumatoid arthritis (RA), we analyze the clinical information and disease outcome of them. [Methods] From January 2014 to May 2016, 52 cases of RA were classified into three groups (HDA, MDA, and LDA) by disease activity at the first visit, and examined about the timing of the first Bio-use and their background. The disease activity was indicated by DAS28-CRP etc. [Result] In 29 cases of HDA, 83%(24) were started with Bio within 6 months, and all their disease activity was improved within 24 weeks. In another 3 cases of HDA spending more than 1 year until Bio-use, 2 of them were intolerable for MTX. Resting one case, with effective initial treatment, had to discontinue MTX because of pregnancy. In 8 LDA cases, 50%(4) of them used Bio within 6 months, and were difficult to use MTX due to comorbidities. There were 2 LDA cases, resistant to MTX, and one MTX-effective case. The latter had to stop MTX for preparation for pregnancy, and flared. These three were under 40-year and used Bio within 6 months. [Conclusion] Our results suggest that HDA, MTX and younger age are decisive factors. We should investigate better decisive factors for the administration of Bio.

P1-068

Biologic DMARD mono-therapy for the treatment of elderly onset rheumatoid arthritis

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Conflict of interest: None

[Purpose] Elderly onset rheumatoid arthritis (EORA) tends to develop physical disability rapidly and to disturb patients' QOL because of age- and treatment-related co-morbidities. Our hypothesis is that biologic mono-therapy is effective and safe for EORA. [Methods] From January 2015, RA patients with the onset of 65 years or older were consecutively treated with biologic DMARD alone. Short-term steroid within 3 months was allowed. [Results] Twenty patients (F 13, M 7) with mean age of 76.5 were enrolled. Seven cases had ACPA positivity. Fourteen out of 20 had some co-morbidities. Mean period of 2.5 weeks after the diagnosis, they were treated with either abatacept in 13, etanercept in 3, or tocilizumab in 2. Short-term steroid was administered in 4. Four cases failed to show an optimal response, which required switching to another biologic. Six months after the treatment, they showed an improvement of SJC from 9 to 2.5, CDAI from 27.2 to 10.8, HAQ score from 0.92 to 0.70. There were no serious adverse events observed during the mean observation period of 9.5 months. Kaplan-Meyer analysis showed the treatment success rate of 75% at 6 months. [Conclusion] Biologic mono-therapy seems effective and safe for the treatment of EORA. Long-term outcome will be carefully monitored.

P1-069

Biotherapy in patients with complication/history of malignant tumor

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Conflict of interest: None

Objective: We studied the psychology of patients with malignant tumor complications/history receiving RA biotherapy. **Subjects and Methods:** We interviewed 8 patients who developed malignant tumors during biotherapy and 2 with tumor history, regarding the time of diagnosis, mental state at diagnosis, reasons for biotherapy, and concerns after starting therapy. **Results:** Four patients who maintained remission did not un-

dergo biotherapy, 2 received rituximab for malignant lymphoma and maintained remission, and 4 received biotherapy for intense pain. One and 3 patients on ABA and TCZ biotherapy, respectively, had early stage cancer surgery without postsurgical adjuvant therapy and said they "never want to experience rheumatic pain," just before or after surgery. **Discussion and conclusion:** The guideline for TNF inhibitor use for RA in Japan College of Rheumatology (revised March 12, 2015) prohibits them in patients with complicating malignant tumors. TCZ and ABA are to be avoided, limiting biotherapy in patients with malignant tumor complication or history. We began monitoring malignant tumors just before, and then yearly after biotherapy since IFX was launched. The interview shows that good postoperative prognosis and early discovery by health checkup are decisive biotherapy factors

P1-070

The 5-year survival rate for RA patients treated with Etanercept started with half of usual dosage

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Conflict of interest: None

When physician treat patients with rheumatoid arthritis (RA), biologic DMARD (bDMARD) is very effective. But it is a weak point that bDMARD is expensive. The aim of this study is to investigate of survival rate of long term in treating patients with RA by Etanercept (ETN) started with half of usual dosage (25mg*1/week). RA patients treated in our hospital between 2006~2014 were investigated and 78 patients were enrolled. The overall 5-year drug survival rate for RA patients treated by ETN was 56%. 46 patients were treated with the same dosage of ETN (25mg*1/week), 23 patients were treated with elongation period of ETN (25mg*1/10~14days) and 3 patients were treated with increased dosage of ETN (50mg/week). 5-year drug survival rate was 56% in patients treated with MTX and 61% in patients treated without MTX but there was no significant difference (p=0.63). 5-year drug survival rate was 59% in patients without previous bDMARD and 40% in patients exposed previously other bDMARD but there was no significant difference (p=0.33). Cumulative incidence of discontinuation for inefficacy was 15% and adverse events was 28%. In this study, the overall 5-year drug survival rate for RA patients treated by ETN started with half of usual dosage (25mg*1/week) results comparatively good.

P1-071

Long-term outcome of golimumab in patients with rheumatoid arthritis in real-world clinical setting ~ focusing on disease activity, activity of daily living and change of concomitant drugs~

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Conflict of interest: Yes

[Objectives] To investigate longterm outcome of GLM in disease activity, quality of life and changing of concomitant drugs in RA patients. [Methods] 60 cases were used for patients' characteristics and drug retention rate (Kaplan-Meier) and 26 cases who continued GLM for 2 year and more were used for detailed analysis. [Results] Baseline Characteristics (n=60): Mean age 60.1 yo, Female 85.0%, RA duration 12.5 y, MTX concomitant 90.0%, PSL concomitant 35.0% and bio-naïve 41.7%. Drug retention rates of GLM were 80.1% at 1 year, 75.4% at 2 years, 69.6% at 3 years and 53.0% at 4 years. In 26 RA patients who continued GLM for 2 years and more, DAS28-CRP, CDAI and mHAQ had significantly decreased over time (baseline-1year-2year). DAS28-CRP: 3.26-1.90-1.74, CDAI: 12.5-5.1-4.0, mHAQ: 0.51-0.32-0.29. Mean RF (IU/mL) was significantly decreased (125-81-77). Rates (%) of concomitant MTX, PSL and tacrolimus (TAC) at baseline, 1-year and 2-year were 92.3-88.5-88.5, 38.5-7.7-0.0 and 7.7-15.4-23.1, respectively. [Conclusions] Drug retention rate of GLM in RA patients concomitant to MTX with moderate disease activity in average was very good. In RA patients who continued GLM for 2 years and more, PSL was completely stopped. Although MTX was maintained over time, TAC was added if needed.

P1-072

Long term outcome of abatacept in patients with rheumatoid arthritis in real-world clinical setting ~ focusing on disease activity, activity of daily living, change of concomitant drugs and prevention of joint destruction~

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Conflict of interest: Yes

[Objectives] To investigate long term outcome of ABT in RA patients in real-world clinical setting. [Methods] 46 cases were used for patients' characteristics and drug retention rate (Kaplan-Meier) and 16 cases who continued ABT for 2 years and more were used for detailed analysis. [Results] Baseline Characteristics (n=46): Mean age 68.2 yo, Female 78.3%, RA duration 17.5 y, MTX concomitant 54.3%, PSL concomitant 67.4% and bionaïve 56.5%. Drug retention rates of ABT were 85.8% at 1 year, 68.3% at 2 years, 64.2% at 3 years and 55.3% at 4 years. In 16 RA patients who continued ABT for 2 years, DAS28-CRP, CDAI and mHAQ had significantly decreased over time (baseline-1year-2years). DAS28-CRP: 4.33-2.34-2.40, CDAI: 18.1-6.2-6.3, mHAQ: 0.79-0.48-0.53. Mean RF (IU/mL) tended to be decreased (178-93-79). Rates (%) of concomitant MTX, TAC and PSL at baseline, 1 year and 2 years were 75.0-50.0-37.5, 6.3-25.0-18.8 and 62.5-50.0-37.5, respectively. ΔmTSS was significantly decreased over time (6.6-0.7-0.3). [Conclusions] Drug retention rate of ABT in long standing RA patients was very good. Although MTX and PSL were decreased in RA patients who continued ABT for 2 years, prevention of joint destruction was maintained over time.

P1-073

Efficacy of tofacitinib in patients with long-term rheumatoid arthritis

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Conflict of interest: None

[Objective] To evaluate of tofacitinib in patients with long-term rheumatoid arthritis. [Method] Thirteen RA patients treated with tofacitinib in our department, these were Steinbrocker Stage2 1case, Stage3 3cases, stge4 9 cases, and Class 3 13cases. Mean age was 76.2, mean disease duration was 17.2 years. and six patients were treated with methotrexate (MTX), eight patients were teated with prednisolone. And eight patients were treated with Biologics. Efficacy was evaluated based on tenderness joint count (TJC), swollen joint count (SJC), CRP, PatientVAS (PtVAS), Dr VAS, MMP-3, and we estimated for baseline, after 3 months, and, after 6manth. [Result] Two patients were administered tofacitinib with 10mg/day, eleven patents were with 5mg/day. Mean TJC was 6.54/1.38/0.31 (baseline/3month/6month), SJC was 5.85/ 1.61/0.77, CRP was 3.15/0.34/0.14, PtVAS was 62.4/28.8/19.6, DrVAS was 64.6/32/7/21/5, MMP-3 was 332.1/176.9 (baseline/6month). [Discussion] Inspite of long-term treatment and resistant for biologics, all cases (thirteen patient)were improvement, especially for PtVAS and CRP. We suggested that it is very usuful for long-term RA patients who resistant for biologic and DMARDs to introduce tofacitinib.

P1-074

The efficacy and safety of Abatacept in Elderly Patients with Rheumatoid Arthritis

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Research Center for Allergy and Clinical Immunology, Asahi General Hospital, Asahi, Japan

Conflict of interest: None

Objective: The aim of this study was to analyze the efficacy and

safety of Abatacept in elderly RA patients. **Methods:** We retrospectively analyzed the clinical characteristics of 42 RA patients who had treated with Abatacept from November 2010 to August 2016 in our hospital. The patients were divided into two groups; elderly patients group (≥65 years, n=17) and younger patients group (<65 years, n=25). Disease activity, drug continuation rate and adverse events were evaluated in groups. **Results:** There were no significant factors between groups at the baseline, except for disease duration. Delta DAS28-ESR from 0w to 12 wks was significantly higher in the elderly patients group than in the young patients group (1.53±1.23 vs 0.84±0.84, $p < 0.05$). Two patients (11.7%) in elderly patients group and eight patients (32.0%) in younger patients group discontinued Abatacept with inefficacy. Whereas two patients (11.7%) discontinued due to adverse events (cellulitis and interstitial pneumonia, respectively), there were no patients with adverse events in younger patients group. **Conclusion:** Our study suggests that Abatacept may be effective for treatment in elderly patients with rheumatoid arthritis. However, adverse events of Abatacept must be taken into account.

P1-075

Patient who depeloped sarcoidosis during the treatment with etanercept (ETN) for rheumatoid arthritis (RA), and had resolution without discontinuation of ETN

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Conflict of interest: None

Many cases of sarcoidosis secondary to Tumor necrosis factor (TNF) α blockers have been reported. All reported patients improved after discontinuation of drugs. Herein, we report a patient who depeloped sarcoidosis during the treatment with etanercept (ETN) for rheumatoid arthritis (RA), and had resolution without discontinuation of ETN. A 68 year old woman was diagnosed with RA in 2005, and etanercept was added 5 years later. In 2015, chest CT scan revealed bilateral hilar lymphadenopathy and interstitial nodular changes of the lung. Laboratory tests revealed elevation of serum lysozyme. The bronchoalveolar lavage showed increased lymphocytes (26%) with high CD4/CD8 ratio (11.60). Transbronchial lung biopsies revealed noncaseating granulomas with surrounding lymphocytes, which confirmed the diagnosis of pulmonary sarcoidosis. Because she had no symptom of sarcoidosis, ETN was continued with close observation.3 month later, chest CT showed spontaneous remission of BHL, and her sarcoidosis had been stabilized until now (about 9 months). This rare case hypothesis some patients of sarcoidosis induced by TNFα blockers may have spontaneous resolution without discontinuation of the drugs. Since TNFα blockers are important for controlling RA, we should carefully determine whether to discontinue drugs.

P1-076

The 1year clinical results of biosimilar (IFX-BS) in patients with rheumatoid arthritis

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Conflict of interest: None

Purpose We discuss 1year clinical results from patients who selected IFX-BS treatment and started IFX-BS for MTX-resistant. **Subjects and Methods** 11 of these patients elected treatment with IFX-BS (1 male, 10 females, mean age 65.2±8.0 years, mean disease duration 17.8±10.3 years), and Bio-naïve 3 patients were included IFX-BS. The simplified disease activity index (SDAI) was used to evaluate disease activity at baseline, 0.5year, 1year. Adverse events were studied as well, and drug survival rate was calculated by Kaplan-Meier survivorship analysis. **Results** Mean SDAI was 6.14±3.9 prior to switching, 5.37±2.8 prior to 0.5year following switch, and 6.57±3.6 prior to 1year following switch, revealing no particular changes in clinical symptoms following switching to IFX-BS. However, 1 case was getting worst, after switch, 1 case was complicated MTX-LPD, they were stopped administration of IFX-BS. Two bio-naïve patients were getting better as SDAI and reached low disease activity at 1year. By the way, one bio-naïve patients was complicated PCP at 1month. **Discussion** IFX-BS is Japan's first biosimilar disease-modifying antirheumatic drug (DMARD). Our study demonstrated no effects of switching from IFX in terms of efficacy or safety, and the biosimilar formulation is useful in terms.

P1-077

Effectiveness and safety of tocilizumab therapy for the elderly patients with rheumatoid arthritis

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Conflict of interest: None

Background: Recently ages of patients with rheumatoid arthritis (RA) is increasing. Elderly patients have more comorbidity and disadvantages to the therapy than those whose ages are younger. This study examined whether elderly patients have some disadvantage in tocilizumab (TCZ) therapy. **Methods:** We retrospectively evaluated 104 patients with RA who were observed through 52 weeks of follow-up after TCZ treatment. Clinical efficacy was assessed based on a 28-joint disease activity score using erythrocyte sedimentation rate (DAS28-ESR) remission and adverse effects were observed at 52 weeks after initiating treatment. There were 32 patients older than 65 years and 72 who were less than 65 years. **Results:** There were no significances in MTX intake, GC intake, disease duration, and disease activity at the start of TCZ. Number of female patients was greater in younger group and the number of biologic therapy naïve patients was greater in elder group. Efficacy of treatment was almost the same in the two groups. Remission rate of elder group was higher than that of younger group. There were 3 cases who withdrew the treatment because of the lack of effectiveness and adverse effects. **Conclusion:** It was suggested that TCZ treatment was safe and effective for elderly patients over 65 years.

P1-078

Two cases of Rheumatoid Arthritis (RA) complicated with mesenteric panniculitis treated with Tocilizmab

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Conflict of interest: None

【Case1】The female patient was diagnosed with seronegative RA, StageII, in 42 years. She was diagnosed with vasculitis from skin biopsy in 63 years without leading to remission though it was treated with the first in MTX and Etanercept: ETN. ETN is stopped because of vasculitis. She was treated with MTX, but the effect was insufficient. MTX was stopped with pneumocystis pneumonia. Tocilizumab:TCZ was started. However she was hospitalized in 71 years because of the right lower abdominal pain, diagnosed with mesenteric panniculitis.【Case 2】The patient was diagnosed with RA, StageII, at 28 years old time. In 29 years, Infliximab was used together MTX. However it was changed in ETN. In 31years, after MTX was stopped, she delivered the first child and treated with PSL+MTX. MTX was restarted but it was non-effect. she was treated with TCZ and MTX at 39 years old time. In a haif year she was diagnosed with mesenteric panniculitis of the ascending colon because of lower right abdominal pain. There are some cases of the intestinal tract perforation by the diverticulitis, but we don't know why diverticulitis is many under the TCZ dosage. There is a possibility that the center of the intestinal tract lesion by TCZ is mesenteric panniculitis.

P1-079

3 case reports for emergence of skin lesions (bullous pemphigoid, psoriasis vulgaris, psoriasiform dermatitis) in rheumatoid arthritis patients treated with TNF inhibitors

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Conflict of interest: None

Bullous pemphigoid (BP) is autoimmune bleb caused by autoantibodies against epidermal basal antigen. It is rare to emerge BP upon biologics. TNF inhibitors are effective for treatment of psoriasis. Paradoxically, several reports show new-onset psoriasis in patients treated with TNF inhibitors. We report 3 cases of paradoxical reactions upon TNF inhibitors therapy of rheumatoid arthritis (RA). Case 1: 76 years old female RA patient under treatment with adalimumab and tacrolimus for a few years developed bleb at lower limbs. Skin biopsy revealed findings of BP. Starting at 30 mg/day prednisolone (PSL) improved bleb, then, PSL was tapered. Case 2: 84 years old female RA patient developed psoriasiform rash after a month starting certolizumab pegol treatment. Skin biopsy led diagnosis of psoriasis vulgaris. Case 3: 84 years old male RA patient developed psoriasiform rash after 27 months treating with infliximab in conjunction with methotrexate and tacrolimus. The finding of skin biopsy was compatible with psoriasiform dermatitis. Their rash was improved by stopping TNF inhibitors and by external vitamin D preparation. All patients keep good condition of arthritis and skin lesion by switching to tofacitinib (TOF), suggesting that TOF can provide therapeutic options for such cases.

P1-080

Consideration on the status of biological agent in patients with malignant rheumatoid arthritis

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Conflict of interest: None

PURPOSE: Rheumatoid factor (RF) positive is regarded as a predictor to therapeutic reactivity for ABT. MRA is a condition with extra-articular symptoms due to immune abnormality such as RF elevation and vasculitis. Therefore, we investigated the difference in the status of administration for biological agent (Bio) between in the patients with RA having and not having MRA. METHODS: Twenty-one MRA patients were investigated. RESULTS: They are 10 males and 11 females. Patients at baseline had the mean age at onset of MRA 59.5 years, and the mean titer of RF (highest value) was 1567 IU / ml. Fourteen cases were treated with anti-TNF agents (TNF-i) (IFX: 5, ETN: 6, ADA: 2, GLM: 1, and CZP: 0), 6 cases were treated with TCZ, none cases was treated with ABT, and 1 case was treated without Bio. At November 2016, 5 (24%) cases are treated with TNF-i (ETN: 2, ADA: 1, CZP: 2), 5 (24%) cases are treated with TCZ, 7 (33%) cases are treated with ABT, and 4 (19%) cases are treated without Bio. In whole RA patients of our department, 83 (61%) cases are treated with TNF-i (IFX: 19, ETN: 35, ADA: 13, GLM: 4, CZP: 12), 25 (18%) cases are treated with TCZ, and 28 (21%) cases are treated with ABT. CONCLUSIONs: Although the proportion of TNF-i was high in the whole RA, the ratio of ABT was high in MRA.

P1-081

Clinical effect of certolizumab pegol in patients with rheumatoid arthritis from data registered in the Akita Orthopedic Group on Rheumatoid Arthritis (AORA)

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Conflict of interest: None

[Objectives] To analyze the efficacy of certolizumab pegol (CZP) in patients with rheumatoid arthritis (RA). [Patients and Methods] Among the Akita orthopedic group on rheumatoid arthritis (AORA), twenty-three patients were followed up for at least 52 weeks of treatment with CZP. We evaluated persistence rate, DAS28-CRP and reasons for discontinuing at 52 weeks. [Results] The patient characteristics were as follows: there were 6 males and 17 females, mean age was 61.3 years and mean disease duration was 12.1 years. Nine patients were biologics-naïve, while 14 were biologics-switched. MTX had been administrated to 19 patients (82%), mean dose was 8 mg/week, PSL to 16 patients (70%), mean dose was 4 mg/day and csDMARD to 5 patients (22%). Thirteen patients (57%) were administered continuously in 52 weeks. At 0, 4, 12, 24 and 52 weeks after initiation, the mean DAS28-CRP were respectively 4.36, 3.63, 3.45, 3.43 and 3.41. The reasons for discontinuing were insufficient effect in 9 cases (naïve; 2, switch; 7) and remission in 1 case. [Conclusion] Persistence rate of CZP at 52 weeks was 57%.

P1-082

Akita Orthopedic Group on Rheumatoid Arthritis (AORA) 2016 registry of patients in the Akita Orthopedic Group on Rheumatoid Arthritis (AORA) registry 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 71 patients in the Akita Orthopedic Group on Rheumatoid Arthritis (AORA) registry (mean age, 61.7 years) who received ADA. [Results] The mean disease period was 11 years. The cases had Steinbrocker classification stages I/II/III/IV (15/13/18/25 patients), classes 1/2/3/4 (33/28/9/1 patients). Sixty-two patients (87%) received methotrexate (MTX; mean dosage, 6.3 mg/week); and Forty-two (61.8%), prednisolone (3.3mg/day). The mean DAS28CRP (4) was 3.87 in the first ADA administration. The mean follow-up period was 97 weeks. The cumulative continuation rates were 85%(1 year), 76%(2 years), and 58%(3 years) in the Kaplan-Meier analysis. Eighteen patients had failure of ADA administration. Therapy was discontinued because of primary failure in 5 cases and secondary failure in 6. The mean disease activity score was 1.36, and 48 patients (91%) had good response in the final examination according to the criteria of the European League against Rheumatism. [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.

P1-083

Therapeutic results of Abatacept for Rheumatoid Arthritis with Interstitial Lung Disease in our hospital

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Conflict of interest: None

Purpose: To assess the clinical response of abatacept (ABT) for RA patients with or without interstitial lung disease (ILD) followed in our hospital. **Methods:** We retrospectively evaluated clinical response of ABT for 18 patients in our hospital from March to Sep 2016 and compared the response between 10 cases with ILD and 8 cases without it. **Results:** In 18 patients, 5 were male, average age was 74.1 years, and average duration of disease was 12.9 years. 4 were taking steroids, 4 received monotherapies of ABT, and the details of DMARDs combination were 3 patients. 8 had histories of bDMARD use. Baseline DAS28-ESR and -CRP were 4.91 and 4.41. At the end of evaluation period, there were significant reductions for DAS28-ESR and -CRP. Regarding 10 patients with ILD and 8 without ILD (mean age:76.3 vs 71.3, mean duration of disease:12.6 vs 13.3), there were significant reductions in both groups for DAS28-ESR and -CRP. Average KL-6 of patients with ILD showed a de-

creasing trend (530.7→388.1 U/mL, p=0.12). **Conclusion**: There are several reports that ILD was developed or worsened after TNF inhibitors use. ABT did not show significant reduction on effectiveness and safety for RA with ILD compared to RA without ILD. As previously reported, usefulness of ABT for RA with ILD was suggested.

P1-084

A study of RA treatment using golimumab

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Conflict of interest: None

(Introduction) Biologic agents have been changing dramatically the course of the treatment for rheumatoid arthritis (RA). We can use golimumab as the sixth biologic agents in Japan since September 2011. The purpose of this study is to evaluate the effectiveness of the treatment of RA patients with golimumab (Patients and methods) Forty-seven RA patients treated with golimumab were evaluated. They have been treated with this biologic drug more than 52 weeks at April 2016. The mean age at introduction of golimumab was 61.7 years-old, 20 were over 65 and 27 were under 65, 11 men and 36 women. (Results) At the time of follow-up, DAS28-C reactive protein decreased, although there was the differences among the patients of over 65 and under 65. No serious side effects related to this biologic agents were observed in patients received this treatment. (Conclusion) The effectiveness of golimumab for RA patients was reported. This biologic agents' therapy is thought to be useful for RA patients. This drug will be considered as an option for RA treatment. The experiences and clinical information about this biologic drug will be needed more in future.

P1-085

Outcomes of etanercept without methotrexate use in the treatment of rheumatoid arthritis patients

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Conflict of interest: None

[Objectives] To investigate the outcomes of etanercept (ETN) without methotrexate (MTX) use. [Methods] Forty five patients underwent ETN treatment without MTX. Of these, 39 patients divided into three groups: continuation group (n=22), discontinuation due to lack of efficacy (LOE) group (n=9), and discontinuation due to adverse events (n=8). ETN retention rate and baseline characteristics of the three groups were evaluated. [Results] The cumulative ETN continuation rate was 77.5% and 39.6% after one and five years, respectively. Mean age at initiation of treatment were 61.4, 63.6, 65.7 years, mean duration of illness were 165, 110, 230 months, rate of PSL concomitant use were, 68.2, 88.9, 62.5%, mean DAS28-CRP score were 4.10, 4.65, 4.79, mean CRP level were 1.78, 2.59, 3.03 mg/dl, and mean MMP-3 level were 225, 324, 417 ng/ml in continuation group, LOE group and AE group, respectively. At the final survey, the rate of PSL use were decreased to 45.5% and mean DAS-28CRP was significantly low in the continuation group. [Conclusion] Efficacy and drug retention of ETN treatment without MTX may be expected in case that the patients have shorter disease duration and lower MMP-3 level.

P1-086

Consideration of using Golimumab in elderly patients

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Conflict of interest: None

[OBJECT] To examine the outcome of treatment of Golimumab in patients with rheumatoid arthritis in our hospital. [METHODS] For 104 rheumatoid arthritis patients who received Golimumab at our hospital, we examined the age group among young people, elderly people, and late elderly patients on the continuation rate, usefulness, and serious side effects of Golimumab. For each age groups, comparison was made based on the presence or absence of MTX combination. [RESULTS] There was no difference in utility and safety regardless of the presence or absence of concomitant use of MTX, and the continuation rate was equivalent to 82% of MTX combined group and 80% of MTX noncombined group, respectively. Serious adverse reactions due to age group are young cellulitis flora, elderly aspiration pneumonia is noticeable. [CONCLUSIONS] this results suggesting the necessity of proper use of biological products according to age.

P1-087

Effectiveness of Golimumab in the elderly patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] The effectiveness of anti-TNF blocker is not influenced by age. As the elderly patients are difficult to use MTX in case, effective TNF blockade without concomitant use of MTX is expected. To clarify the profile of validity of Golimumab in the elderly patients as compared with the non-elderly-patients, we investigated the cases newly prescribed Golimumab. [Methods] We enrolled 81 patients with RA, newly prescribed Golimumab in our department. We investigated the achievement rate of DAS remission and the retention rate of Golimumab at 52 weeks after initiation of treatment. Then, we compared the elderly patients (; defined over 70) with the non-elderly-patients (; defined below 70) in these two points. [Results] DAS remission was achieved in 31.3% of the elderly patients, and in 37.5% of the non-elderly patients. Also, retention rate of drug was not so significant between two groups (86.1%, 87.0%, respectively). MTX use was significantly different between two groups (51.1%, 73.7%, respectively). Contributing factor for achievement of DAS remission was concomitant use of MTX, and conditon of biologics naïve. [Conclusion] Golimumab is effective for the elderly patients as compared with the non-elderly-patients.

P1-088

Study of the effects of abatacept SC for elderly patients with rheumatoid arthritis

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Conflict of interest: None

[Purpose] To examine the efficacy and safety of the patients treated with abatacept (ABT) SC against elderly rheumatoid arthritis (RA) patients who are treated in our hospital. [Methods] 12 RA patients over the age of 65 being treated abatacept SC by 24 weeks or more, was studied efficacy (DAS28-ESR) and safety (continuation rate and the side-effects). [Results] As patient background, age is from 65-year-old to 80-year-old (male 6, female 6), RF or ACPA positive patients 10 cases, in 2 cases

switching patients from biologics (GLM1·TCZ1) there were. MTX was used in combination with 5 cases (8mg ~ 12mg). In DAS28-ESR the course of more than 24 weeks after, 4 cases of good response, 6 cases moderate response, 2 cases of no response. All treatment is continued, serious side effects did not. [Conclusion] Abatacept sc is sufficient effect can be expected for the elderly patients with rheumatoid arthritis, has been able to continuously treated in all cases without any side effects.

P1-089

Clinical study of the safety and effectiveness of abatacept for elderly rheumatoid arthritis patients at this clinic

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Conflict of interest: None

Purpose: Here, we report on the safety and efficacy of ABT, when used at this clinic on EORA patients. Methods: The subjects were 15 patients (m,1; f,14) aged ≥65y who received outpatient treatment at this clinic (04/15-08/16) and administered ABT. They were grouped into #1 Effective group (n=11) and #2 Ineffective group (n=4). These were subjected to clinical investigation of age, history of biologics administration, concurrent use of DMARDs, blood serum findings, and complications. They were further divided into a Bio naïve group (#3 n=6) and a Bio non-naïve group (#4 n=5) These were then assessed for improvements in PD with regard to 22 joints using a DAS28CRP and US measurements from 4w to 16w. Results: The bio naïve rate in the #1vs #2 was 68vs25%(P<0.05), the disease duration was 3.24vs9.8 y (P<0.002), DAS in the #3 vs #4 was 2.56vs3.27 (P<0.05), PD of 1 or below on US at 8w was 66vs40% and at 12w and16wwas 83vs80%(n.s). Residual joint inflammation in both groups was treated by localized injection under US which resulted in the disappearance of PD. Discussion: Bio naïve patients experienced significant recovery after ABT administration, and adjunct therapy consisting of localized injection under joint US of residual inflammation after ABT administration was effective.

P1-090

Efficacy and safety of infliximab BS in patient with rheumatoid arthritis in a routine case

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Conflict of interest: None

[Objectives] Infliximab BS (IFXBS) is a biosimilar of infliximab that has been prescribed in a routine care in Japan since 2014. There are a few studies that have examined the efficacy of IFXBS in RA patients in a routine care. In this study, we investigated the efficacy of IFXBS in RA patients. [Methods] RA patients with an inadequate response to methotrexate (MTX) and treated with IFXBS as a first-line biologic agent for longer than 24 weeks were included in this study. We retrospectively reviewed the clinical data (DAS28-CRP, SDAI, CDAI). [Results] Nine patients were included in this study. Mean age was 63 years old and mean disease duration was 12 years. Mean DAS28-CRP, SDAI and CDAI was 4.2, 21.5 and 18.3 respectively at baseline, and 1.6, 3.3 and 3.1 respectively at 24 weeks. The number of patients who withdrew from IFXBS was four (adverse events: two patients, lack of efficacy: two patients). [Conclusion] IFXBS was effective in RA patients in a routine care. This study provides support for the possible use of IFXBS in RA patients with an inadequate response to MTX and biologic naïve.

P1-091

Sustainable Duration of Subcutaneous Tocilizumab for Rheumatoid Arthritis at a Single Center

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Conflict of interest: None

<Object> To clarify an advantage of subcutaneous (sc) tocilizumab (TCZ) for rheumatoid arthritis (RA) care <Methods> We looked up patients with RA who were currently treated with or had a history of administration of sc and intravenous (iv) TCZ in the electronic clinical records since 2010 and reviewed duration of sc injection, methotrexate (MTX) dose, previous usage of other biologic agents and adverse effects. <Results> 39 patients (34 females, 5 males) were listed and the average age was 63 and 74, respectively. 14 patients used MTX and the average week dose was 9.6mg/week. sc TCZ was introduced to 4 of 39 as a first biologic agent, and other patients had been treated with eternacept, iv TCZ, golimumab, adalimumab, infliximab, abatacept or joined other clinical trials. Biweekly sc TCZ was continued in 19 of 31 patients who were observed for 52 weeks or more, and the continuity ratio was similar to iv TCZ. 5 patients discontinued sc TCZ and their average dose/body weight was 2.75mg/kg, which was somewhat less than that of those who successfully continued the agent. The reasons for discontinuation were ineffectiveness in 5 patients, infections in 3, and other events in 4. <Conclusions> In a real-world practice at a single center, sc TCZ was apparently as tolerable as iv one for RA.

P1-092

Treatment of elder patients with rheumatoid arthritis using biologics

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Conflict of interest: None

Objective: To evaluate the characteristics of elderly patients with rheumatoid arthritis (RA) who have been treated using biologics. **Patients:** There were 13 patients with RA whose age were above 70 years old, and have been treated using biologics within recent 2 and half years. We evaluated the characteristics of these elderly RA patients. **Results:** The mean age of the study population was 75.2 years old. There were 3 men and 10 women. The mean disease duration was 12.2 years. Biologics used for these patients were abatacept: 6, adalimumab: 3, tocilizumab: 2, and infliximab and golomumab each 1. Disease activity scores at the start of biologics therapy were relatively high, mean DAS28-CRP: 6.03, DAS28-ESR: 6.74. Methotrexate was used in 6 cases and glucocorticoid in 6cases. Complications of these patients were diabetes, hypertension, cardiac failure and so on. The past history of the malignancies consisted gastric cancer, lung cancer and prostatic cancer. One patient who obtained the clinical remission discontinued the biologics therapy. Other patients are continuing the biologics therapy without serious adverse events. **Conclusion:** Although the elderly RA patients have some complications and serious past history, biologics therapy could be performed with careful attention.

P1-093

A case of the rheumatoid arthritis that gave birth the pregnancy under the Certolizumab Pegol (CZP)

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Conflict of interest: None

(case)A 41 years old woman was treated with etanercept (ETN 50mg/week) for rheumatoid arthritis from 2005 and discontinued in 2012 because of the pregnancy. After having given a baby, because disease activity turned worse, she was reopened ETN, but an effect was insufficient. In addition, she was switched to CZP in 2014 because she hoped a child. She became pregnant in September, 2015 and discontinued CZP. However, she reopened CZP by a self-judgment because disease activity turned worse from the last dosage in (the postpregnancy twelfth week) eight weeks later. She was treated with CZP until pregnancy 36 weeks and delivered a child weighing 2,865 g naturally in pregnancy 40 weeks. The inborn character abnormality did not accept it to a baby. (Discussion) Be-

cause the safety of an antirheumatic drug and the biological agents during pregnancy is not established, It is difficult of treatment of the perinatal rheumatic. Tomor Necrosis Factor Inhibitor (TNFi) biologic agents is regarded as a relatively safe drug for the perinatal period, and there is known to be above all less placenta transitivity in CZP than other TNFi therapy. We report that was able to use CZP safely with reducing disease activity during the pregnancy, and dont recognize inborn character abnormality to a newborn baby.

P1-094

The clinical outcome of certorizumab pegol in patients with rheumatoid arthritis

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Conflict of interest: None

【Objective】To examine the clinical outcome of certorizumab pegol (CZP) in patients with rheumatoid arthritis (RA).【Methods】Eighteen RA patients (16 in female) who were introduced with CZP were registered. The age was 59 years old on average, and RA duration was 5.9 years on average. The follow up period was 0.9 years on average. Steinbroker Stage II/III/IV were 3/9/6 cases, and Class 1/2/3 were 2/6/10 cases, respectively. Bionaive cases were 7. Methotrexate was used in 14 cases and 5.5 mg/week on average. Methylprednisolone was used in 5 cases and 1.3 mg/day on average. The persistency, DAS28, EULAR response, and adverse events were examined.【Results】The persistency rate was 56%(10 cases). DAS28 (4.85 on the introduction of CZP) was decreased to 3.71 (at 3 months) and to 3.07 (at 6 months after CZP). At the final follow up, moderate response was 13 cases and no response was 5 cases. Discontinued cases were 8. Of these, no efficacy was 6 cases, and adverse events were 2 (pain on injection in 1, and itching in 1).【Conclusions】In spite of high rate of refractory RA cases (11 out of 18) in this study, DAS28 showed low disease activity 6 months after CZP treatment. These results suggest that CZP is effective for refractory RA patients.

P1-095

A case of rheumatoid arthritis with AA amyloidosis, whose proteinuria was remarkable during etanercept treatment, but disappeared by tocilizumab treatment

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Conflict of interest: None

A 73-year-old woman without proteinuria was started on adalimumab (ADA) since 6 years ago. She was diagnosed with rheumatoid arthritis at the age of 59. From 4 month before hospitalization, her arthritis were activated with overt proteinuria, so her biologics were changed from ADA to etanercept (ETN), but overt proteinuria had been sustained. On admission, her laboratory data were as follows; proteinuria 2.0 g/gCr, negative hematuria, Cr 0.69mg/dl, eGFR 63ml/min/1.73m^2, CRP 0.85mg/dl, serum amyloid A protein (SAA) 86.6μg/ml. On renal biopsy, amyloid deposition was found at arteriolar wall and vascular pole of glomerulus. She was diagnosed with AA amyloidosis. When the biologics were changed from ETN to tocilizumab (TCZ), her SAA was decreased <10 μg/ml and proteinuria was 0.33 g/gCr after 2 months. One year treatment of TCZ resulted in negative proteinuria, but amyloid deposits were observed in rectal mucosa. This case was AA amyloidosis which became manifested during treatment with TNF inhibitor, remission of proteinuria by changing to TCZ. TCZ have a greater SAA lowering effect than TNF inhibitors, so TCZ should be considered for AA amyloidosis. Proteinuria, SAA, and rectal mucosal biopsy were available as therapeutic markers of AA amyloidosis.

P1-096

Clinical efficacy of Golimumab in patients with rheumatoid arthritis

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Conflict of interest: None

Objective: The purpose of this study was to investigate the efficacy and safety of golimumab (GLM) in patients with rheumatoid arthritis (RA). Methods:17 patients with RA who received treatment with GLM and were followed up for more than 52 weeks were included in this study. There were 14 bionaive patients and 3 switched patients. Average age was 63 years and average disease duration was 13.8 years. Dose of GLM was 50 mg in 15 patients, 100 mg in 1 patient, and converted from 50 mg to 100 mg in 1 patient. CRP, MMP-3, DAS28-CRP, SDAI, CDAI and the adverse event (AE) was investigated. Results: 2 patients did not continue treatment with GLM for economic reason or insufficient drug efficacy, and the continuation rate was 88%. For 15 patients who continued treatment with GLM, the mean values of CRP, MMP-3, DAS28-CRP, SDAI, and CDAI at baseline were 1.36, 162.1, 4.1, 20.0 and 18.7, respectively. These values were improved to 0.55, 59.3, 2.3, 6.1 and 5.6 at 52 weeks. 1 patient developed pneumonia and another patient developed pyelonephritis. However, GLM was resumed after healing of the infections in both patients. Conclusion: Patients with RA treated with GLM had clinically relevant improvement. The AEs of GLM treatment occurred in 2 patients out of 17 patients (11.8%).

P1-097

Correlation between efficacy of biologic DMARDs and antibody value of anti-CCP antibody in our hospital - Comparison at Abatacept and Golimumab

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Conflict of interest: None

[Object] There are some reports that antibody value of anti-CCP antibody influences efficacy of biologic DMRADs. Purpose of this study is to check that by our cases. [Methods] 20 cases of ABT prescription and 37 cases of GLM prescription which accomplished for 52 weeks were made a subject of research. Anti-CCP antibody 100U/mL was made the cutoff value and each was divided into 2 groups. The age, the gender, BMI, a disease period, the MTX prescription rate, MTX prescription dose and disease activity are without the significant differences both at patients background. ⊿ DAS28-ESR and ⊿ SDAI 52 weeks later were compared at each medicine [Results] In cases of ABT prescription, low antibody value group vs high antibody value group is ⊿ DAS:-1.4 vs -1.6 (p=0.51) and ⊿ SDAI:-8.6 vs -10.7 (p=0.36). In cases of GLM prescription, low antibody value group vs high antibody value group is ⊿ DAS:-1.0 vs -1.2 (p=0.56), ⊿ SDAI:-9.9 vs -9.7 (p=0.57). [Conclusions] In our study, correlation was not observed between efficacy of either ABT or GLM and antibody value of anti-CCP antibody.

P1-098

About proper use of certolizumab pegolu in the rheumatoid arthritis treatment

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Conflict of interest: None

【Purpose】certolizumab pegol is the seventh drug among biological preparation by the rheumatoid arthritis treatment, and the only peg is with TNF α preparation. I examined a use example in our House this time. [method] methotrexate combination, two cases were noncombination and weighed patient 18 cases of 20 certolizumab pegolu which I prescribed in Dr. medical corporation Yamaguchi's office in October, 2016 from April, 2013 of those about DAS-CRP, SDAI, HAQ- DI for 12 weeks for eight laps for four weeks for 0 weeks. [result] I got DAS remission in 18 methotrexategroup until four weeks, but recognized a rise of the all cases disease activity in the two weeks group for interdose in-

terval of the maintenance period eight weeks later. (2 vial) maintained all DAS remission for four weeks for five interdose interval. One case looked at the rise of the disease activity eight weeks later every two weeks for the maintenance period, but I recognized a drop of the disease activity when I changed it to / 2 vial for the next four weeks and got DAS remission. [conclusion] It is said that the maintenance of the blood concentration trough value is important to antiTNF said to certolizumab pegol and concluded that you should maintain quantity of drug for the maintenance period this time.

P1-099

The swich study of infliximab biosimilar from innovator infliximab in Japanese patients with rheumatoid arthritis

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Conflict of interest: None

Objective: To examine the 1-year safety and efficacy of switching to a generic infliximab product in 30 long-term forerunner-product infliximab-treated Japanese rheumatoid arthritis patients who, out a total of 70 patients in our hospital, had agreed to the switch. Methods: Patients were evaluated for adverse events (AEs) using the DAS28, CDAI, SDAI and HAQ for 1 year following the switch in drugs. Evaluated hematological test parameters were CRP, ESR, bD, KL-6, IL-6 and TNF-a. Results: No major AEs were seen after patients were switched to the generic infliximab product following long-term treatment with the original infliximab product. No exacerbation of rheumatoid arthritis activity was seen. These results indicate that these patients can be safely switched to the generic product without loss of efficacy.

P1-100

The efficacy and safety of sirukumab in Japanese rheumatoid arthritis (RA) patients who are refractory to TNF inhibitors (TNF-IR): Sub-analysis of CNTO136ARA3003 study

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Conflict of interest: Yes

Background/objectives: Sirukumab is an anti-IL-6 fully-human antibody. In CNTO136ARA3003 study, the efficacy and safety of sirukumab in RA patients with TNF-IR were investigated. The sub-analysis was conducted to evaluate the efficacy and safety for Japanese patients. Results: Of 878 patients, 116 Japanese patients were randomized to placebo (P, n=37), 50 mg q4w (n=35) or 100 mg q2w group (n=44). Patients in P crossed over to sirukumab 50 or 100 mg at week 24. Baseline demographics and disease activity were similar among treatment groups. Mean disease duration was 10.75 years. The ACR 20 response at week 16 (primary endpoint) was significantly higher in both sirukumab 50 mg (57.1%, $p<0.001$) and 100 mg (54.5%, $p=0.001$) compared with P (18.9%). The ACR 20 response was shown as early as 8 weeks and was maintained through 52 weeks. The proportion of DAS28 (CRP) remission at week 24 was 5.4% in P, 37.1% in 50 mg and 38.6% in 100 mg (both $p<0.001$). The change from baseline in HAQ-DI score at week 24 was -0.01 in P, -0.40 in 50 mg, and -0.34 in 100 mg (both $p<0.001$). The safety profile in Japanese population was consistent with those in all population. Conclusion: Sirukumab was efficacious and well-tolerated in TNF-IR Japanese patients.

P1-101

The pooled safety profile of sirukumab in Japanese patients with active rheumatoid arthritis (RA) from Phase III studies (CNTO136ARA3001, CNTO136ARA3002, and CNTO136ARA3003 studies)

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Conflict of interest: Yes

Background/objectives. Sirukumab, an anti-IL-6 fully-human antibody, has been developed for RA. The pooled (n=369) safety analysis of sirukumab through 52 weeks was performed for Japanese patients who participated in 3 independent phase III studies that enrolled DMARD-IR and TNF inhibitor-IR patients. **Results.** The most frequently reported adverse events (AEs) were infection and infestation (65.4% in 50 mg and 59.5% in 100 mg). The incidences of serious AE (SAE) were 17.2% in 50 mg and 19% in 100 mg, and infection was the most frequently reported SAE. The incidence of SAE was slightly higher in patients who used concomitant DMARDs compared to those without DMARDs at baseline. One death due to a traffic accident was reported through 52 weeks. Specific AEs of special interest included 1 case of duodenal perforation, 2 cases of major adverse cardiovascular event, 3 cases of malignancy, 1 case of hepatobiliary abnormality. Grade 3/4 neutropenia was numerically higher in patients with DMARDs compared to those without DMARDs, but no infections were reported in patients with grade 3/4 neutropenia. Grade 3/4 ALT and AST increase were more frequent in patients with DMARDs. **Conclusion.** Sirukumab was well tolerated in Japanese RA patients. No specific signals for Japanese were observed.

P1-102

The efficacy and safety of sirukmab for Japanese patients with DMARD refractory (DMARD-IR) active rheumatoid arthritis (RA): Sub-analysis of CNTO136ARA3002 study

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Conflict of interest: Yes

Background/objectives: Sirukumab is an anti-IL-6, fully-human antibody. In CNTO136ARA3002 study, the efficacy and safety of sirukumab in RA patients with DMARD-IR were investigated. The sub-analysis was conducted to evaluate the efficacy and safety for Japanese patients. Results: Of 1670 patients, 168 Japanese patients were randomized to placebo (P, n=56), sirukumab 50 mg q4w (n=58) or 100 mg q2w (n=54). Due to less than 20% improvement, 27 patients in P were re-randomized to sirukumab group. The ACR 20 response at week 16 (primary endpoint) was 21.4% in P, 69.0% in 50 mg and 66.7% in 100 mg (both $p<0.001$). The median change from baseline in total vdH-S score at week 52 (co-primary endpoint) was 1.27 in P, 0.25 in 50 mg ($p=0.024$) and 0.00 in 100 mg ($p=0.002$). The proportion of DAS28 (CRP) remission at week 24 was 5.4% in P, 44.8% in 50 mg, and 51.9% in 100 mg (both $p<0.001$). Mean change from baseline in HAQ-DI score at week 24 was 0.00 in P, -0.59 in 50 mg, and -0.47 in 100 mg (both $p<0.001$). Safety profile of Japanese population was similar to that of overall. Conclusion: Sirukumab was efficacious and tolerable for Japanese DMARD-IR RA patients.

P1-103

Pharmacokinetics (PK) and exposure-response (E-R) relationship of sirukumab in Japanese patients with active rheumatoid arthritis (RA): Results from phase 3 studies (CNTO136ARA3001, CNTO136ARA3002, and CNTO136ARA3003 studies)

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Conflict of interest: Yes

Background/objectives: The PK and E-R relationship of sirukumab, an anti-IL-6 fully-human antibody, were analyzed using the data of phase 3 clinical trials conducted in RA patients including Japanese. Methods: Sirukumab was administrated subcutaneously at doses of 50 mg q4w or 100 mg q2w. Serum sirukumab concentrations were determined for 52 weeks, and the factors influencing the PK of sirukumab were explored. In addition, the efficacy (ACR 20/50, DAS28-CRP) of sirukumab was compared in each quartile of serum sirukumab concentrations. Results: In all population, the serum concentrations of sirukumab were lower in patients with increased body weight. The distribution of serum sirukumab concentrations was comparable between Japanese and non-Japanese; however, median concentrations were higher in Japanese. Concomitant use of MTX did not affect the PK of sirukumab. The E-R analysis demonstrated lower response rates in patients whose sirukumab concentration was in the lowest quartile in all subjects but not in Japanese subjects. Conclusion: The PK of sirukumab is comparable between Japanese and non-Japanese. Based on the similar response rate in all quartiles of serum concentration in Japanese, sirukumab 50 mg q4w was shown to provide adequate exposure for Japanese patients with RA.

P1-104

The factors of using biological DMARDs according to the T2T guideline in treatment of rheumatoid arthritis

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Conflict of interest: None

The treat to target recommendation (T2T) is an important to the conventional care of patients with rheumatoid arthritis (RA). The aim of this study was to assess the factors for the use of biological DMARDs according to T2T guideline. The patients with RA who visited our hospital since 2013 were registered and examined the factors for use of biological DMARDs. In total, 102 patients were registered. The patients who did not achieved low disease activity, were applied to the treatment with biological DMARDs. Multivariate analysis showed that the factors for using biological DMARDs was high disease activity at the first admission (Odds ratio 8.620, 95%CI 95%CI 1.96-38.0 P=0.00438), age over 80 years old (Odds ratio 0.0194, 95%CI 0.001-0.368, P=0.00827), and improvement of CDAI at 8weeks after starting therapy under 10 (Odds ratio 7.270, 95%CI 1.53-34.5, P=0.01250). The presence of erosion, high titer of rheumatoid factor, and high titer of CCP antibody did not show the significant differences. These data shows that RA patients with high disease activity, age under 80 years old should be treated with conventional DMARDs at first, and 8 weeks after CDAI should be assessed, then be considered using biological DMARD.

P1-105

Clinical features of elderly onset systemic lupus erythematosus: comparison with young or middle aged onset

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Conflict of interest: None

<Objective>To clarify clinical features of elderly onset (E-O) systemic lupus erythematosus (SLE). <Methods>We investigated consecutive patients with newly onset SLE who admitted to our department between Jan 2012 and Oct 2016. We compared 1) clinical symptoms, 2) laboratory data, 3) organ involvements, 4) induction therapy and response, and 5) adverse events, between E-O (at≧60 years old) and young or middle aged onset (YM-O, at <60 years old) groups, retrospectively. <Results> 15 E-O (67±6 years old, 9 males / 6 females) and 36 YM-O (35±13 years old, 2 males / 34 females) patients were analyzed. 1) Males were significantly dominant, malar rash and oral ulcer were significantly less common in E-O group than in YM-O group ($p<0.05$). 2) Positivity of anti-Sm antibody (Ab) was significantly lower in E-O group ($p<0.05$). 3) Interstitial pneumonia (IP) and concomitant Sjögren's syndrome (SS) were more common in E-O group ($p<0.05$), while SLEDAI at baseline was comparable. 4) Corticosteroid and immunosuppressants were similarly used and effective for induction in both groups. 5) Infections were significantly more common in E-O group ($p<0.05$). <Conclusion>Male dominancy, uncommon malar rash, oral ulcer, and anti-Sm Ab, common IP, SS, and infection were characteristic features of E-O SLE.

P1-106

Efficacy and therapeutic effect predictive factors of golimumab for Juntendo University hospital rheumatoid arthritis patients

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Conflict of interest: None

[Object] We examined the relationship of clinical effect and cytokine concentration Golimumab (GLM) effectiveness for administered rheumatoid arthritis (RA) patients. [Methods and Patients] All of 71 patients were started to receive subcutaneous injections every 4 weeks of GLM. We measured patient serum cytokine concentration of using a Beads array system and examined the relationship with disease activity before start and after the 52 weeks. [Results] DAS28 remission patients (score<2.3) at week 52 was 56.1%. The mean score of DAS28 at baseline, 52 were 4.03±1.38, 2.47±1.10. Remission group were disease duration until initiation of administration was short, the degree of progress of joint destruction was low, methotrexate (MTX) concomitant dose was high, and steroid combined dose was low. Our result suggests that GLM was effective at the early weeks, and serum IL-6 concentration was reduced. [Conclusions] GLM administration is validity from the administration early, we showed also high continuation rate after 52 weeks, also high DAS28-CRP remission achievement rate, and correlate to the decrease IL-6 concentration and decreased disease activity.

P1-107

Five-year clinical results of patients with rheumatoid arthritis -from NinJa database-

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Conflict of interest: None

Objective: To bring out the outcome of five-year treatment, 257 patients with rheumatoid arthritis (RA) were collected from NinJa databases of 2010 to 2015. They all had visited the hospital of NinJa group for the first time during 1st April 2010 to 31st March 2011. **Method:** 258 patients were divided to two groups (RL group: remission or low disease activity, ML group: moderate or high disease activity) according to their DAS-28CRP data of 2015. **Results:** Numbers of RL group was 180 patients and MH was 78. There were no significant differences between two groups concerning the age at first visit, the age of RA development, CRP or ESR data of the first year. On the other hand the duration of disease development to the first visit, stage, DAS28ESR and DAS28CRP scores of the first year had shown the significant difference. **Discussion:** Although in the decades of T2T, it is difficult to treat RA patients ideally. It seems to be important that patients with RA should visit the rheumatologist in early stages and be treated intensively.

P1-108

Evaluation of switch and continuation rate of biological DMARDs (Bio) for patients with rheumatoid arthritis in our hospital

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Conflict of interest: None

【Objective】To evaluate switch and survival rate of Bio at our hospital.【METHODS】The administration status of each Bio was examined for 420 subjects who received Bio from August 2004 to March 2016.【Results】The total number of administrations was 579 (IFX110, ETN135, TCZ112, ADA41, ABT78, GLM56, CZP16, TOF33). The number of switch was 105 (once 78, 2 times 17, 3 or more times 10), and 315 cases were administered as monotherapy (IFX58, ETN92, TCZ41, ADA25, ABT47, GLM28, CZP4, TOF20). 94% of all had less than 1 switch. Switches from IFX are 48, and 63% of them changed to TCZ. Others are ETN19, GLM9, TCZ7, ADA8, ABT11, and there were also many changes from ETN and GLM to TCZ. The Bio-naive rate was high for IFX (96%) and ETN (83%), but TCZ was 43% indicating many switch cases. The drug continuation rate, which is considered to show comprehensive usefulness, was evaluated. The IFX continuation rate is decreasing to 44% for 5 years, 27% for 10 years; ETN is 72% for 5 years, 55% for 10 years. TCZ was 63% in 2 years and maintained the same level and the continuity curves of naive and switch overlapped, indicating similar usefulness.【Conclusion】In case of TNF inhibitor failure, TCZ was often selected as second Bio and was considered to be useful showing good continuation rate.

P1-109

Changes in injection pain due to a new adalimumab (ADA) formulation and assessment of its effect on treatment eagerness

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Conflict of interest: None

The results of treatment of rheumatoid arthritis using biological formulations are currently showing dramatic improvement, resulting in marked improvements in patients' activities of daily life and quality of life. However, patients report severe injection pain with subcutaneous administration of biological formulations, which is likely to negatively affect their psychological states. A new formulation of adalimumab (ADA) has recently been developed, with a reduced injection volume from 0.8 to 0.4 mL and without citric acid. The volume of injectables and presence of excipients such as citric acid are factors that affect injection pain, and this new formulation is therefore expected to reduce injection site-related pain compared with the current formulation. Injection pain with the current and new ADA formulations was classified as generalized pain, pain at puncture, pain at injection, and pain 10 min after injection and was evaluated using a visual analog scale (VAS, taking the degree of injection pain associated with influenza vaccine injection to be 5), and the faces pain scale (FPS). The impact of a new ADA formulation on perceived pain during injection and its effect on treatment motivation with biological formulations were thus investigated.

P1-110

Challenging issues regarding instructing self-injection to elderly rheumatoid arthritis (RA) patients ~ results from questionnaire survey ~

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Conflict of interest: None

Background; We have 275 RA patients under treatment. As one of their characteristics, 68% were over 60 years old. Among all patients, 53 are self-injecting biologics. Even we instruct them introducing the injection procedure, we somehow are out of touch whether they do correct and safe procedure at home after the initial training. **Purpose** To clarify their problems from self-injection and their knowledge of drug itself. **Methods** A questionnaire survey was conducted with the consent to our 53 RA patients on self-injection of biologics (32 was≧60 yo). **Results** The questionnaire collection rate was 78%. In the 17 patients who used pen-type, 6/6 of non-elderly and 7/11 of elderly patients answered no problem with the procedure. 4 elderly patients had trouble on pushing the button through or placing pen against skin. 3/12 of non-elderly and 5/7 of elderly patients in use of syringe had no trouble, however, there are some difficulties on holding syringe or angling needle due to pain or weak grip. 5/7 of elderly were wrong to re-cap needles, and they are often forgetting to wash their hands prior to injection. **Conclusions** Based on the results of this survey, we should instruct the elderly patient repeatedly while confirming the safety of self-injection technique to avoid infection.

P1-111

Association between HTLV-1 infection and response to Tocilizumab treatment in Rheumatoid arthritis: results from the Multicenter study

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Conflict of interest: None

Purpose To investigate the association between HTLV-1 infection and response to Tocilizumab treatment in Rheumatoid arthritis patients. Methods Between July 2008 and July 2013, consecutive Bio-naïve rheumatoid arthritis patients were recruited from the Nagasaki university hospital, the Miyazaki university hospital and their affiliated hospitals retrospectively. Clinical disease activity as disease activity score (DAS) 28-ESR was examined at baseline and after introduction of the Tocilizumab therapy, and compared the differences with and without antibodies to HTLV-I. Result The study enrolled 94 RA patients with data available for DAS28-ESR evaluation. There were 8 cases of anti-HTLV-1 antibody positive, the positive rate was 8.4%. DAS28-ESR with and without anti-HTLV-1 antibody (5.77±1.73, 5.08±1.12 at baseline) were significantly decreased after 6 months of treatment (2.87±0.95, $p<0.01$, 2.61±1.20, $p<0.01$). The changes of (Δ values) DAS28-ESR was no significant difference between patients with anti-HTLV-1 antibody and patients without that. (1.82±1.20 versus 1.41±1.40, $p<0.01$). There was no case of ATLL development during the observation period. Conclusion The presence of antibodies to HTLV-I in RA patients might not be associated with the response to Tocilizumab treatment.

P1-112

Clinical evaluation of abatacept and golimumab in patients with rheumatoid arthritis in our department

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Conflict of interest: None

[Objectives] To evaluate the efficacy and the adherence of abatacept (ABT) and golimumab (GLM) in RA patients. [Patients] ABT/GLM; 24 (5 males, mean 62.5 yo, mean disease duration 9.6 y)/ 23 (2 males, 65.8 yo, 10.0 y), MTX; 16 (9.25 mg/w) / 16 (5.3), PSL; 18 (5.3mg/day) /12

(2.4). Bio-naïve: 6/11. [Methods] Efficacy of ABT and GLM was evaluated by DAS28-ESR4, CDAI and SDAI for 156 weeks. [Results] 1) Mean DAS28 at the baseline (ABT/GLM): 5.881/5.766, CDAI 25.67/24.43, SDAI 28.46/28.60. The disease activity was significantly decreased in both groups. As time went by, the ratio of LDA + remission increased significantly until 24 weeks and maintained until 104 weeks in both groups. No significant difference in both groups. 2) The adherence at 52 weeks showed more than 80% in both groups and that at 104 weeks 69.2% in ABT, 56.0% in GLM. No significant difference in both groups. 3) HAQ-DI was significantly improved after 12 weeks in ABT. 4) Both levels of CRP and MMP-3 were significantly reduced in GLM after 12 weeks, while the only CRP level in ABT after 52 weeks. 5) Drop-out reasons (ABT/GLM); inadequate response 4/5, cancer1/1, organizing pneumonia 0/1, pneumonia 1/1, EB virus reactivation 1/1 and so on. [Conclusion] The efficacy and the adherence of ABT and GLM were similar.

P1-113

Case report of 2 RA patients flared by abatacept switch therapy

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Conflict of interest: None

Abatacept (ABT) switch therapy is to examine whether the risk of infection can be reduced and remission can be maintained by switching from other bDMARD in remission RA patients. 12 cases were switched to ABT, no significant difference was found the risk of infection and remission maintenance consistent with the continuation group. This case report is 2 patients flared and returned to pre-bDMARD. Case 1 is a 69-year-old female. Golimumab (100 mg Q 4 W) was administered until 2016 / 1. After achieving DAS 28 CRP remission, when we switched to ABT (500 mg Q 4 W) from February it flared in March and DAS 28 - CRP increased to 5.38. I returned to golimumab from April and reachieved to remission in July. Case 2 is a 56-year-old female. Etanercept (50 mg Q 1 W) administered until 2016 / 3. After achieved remission, we switched to ABT (125 mg Q 1 W) from April, ABT (500 mg, 750 mg) in May and ABT (125 mg Q 1 W) again from June, it reignited in May and DAS 28 - CRP in July It increased to 4.48. I returned to etanercept in August but was still MDA in November. In both cases, ACPA was high and the effectiveness of ABT could be expected, but the RA activity was increasing tendency just before switching and it was thought that it could not be suppressed by protocol without loading.

P1-114

Usage status of biologics in Kurume University Medical Center

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Conflict of interest: None

[Objective] We report on the usage status of biological agents in Kurume University Medical Center since first biologics IFX was launched in 2003. [Methods] We analyzed the selection of biologics, the routes of administration and the prescriptions of MTX in combination with or without biologics, in 792 rheumatoid arthritis patients, treated with biologics. [Results] The 83% of the 792 patients were treated with anti-TNF drugs (IFX 11%, ETN 43%, ADA 19%, GLM 9%, CZP 1%), 12% with the anti-IL-6R antibody (TCZ), 5% with CTLA4-Ig (ABT). Subcutaneous injection was applied for 78% of the all patients. It is noteworthy that subcutaneous injection was selected for 83.7% of patients aged 60 years and older. MTX was prescribed 55.5% of patients treated with biologics. MTX was less used in patients treated with ETN and ADA. GLM, TCZ, ABT were used in combination with MTX more often compared to ETN and ADA. MTX were prescribed over 50% under the 60s, but it declined by 30% in the 70s, and 20% in the 80 years and over. [Conclusion] Subcutaneous injections are increasingly used in our hospital and used more in older patients. The prescription of MTX decreases as age increases. Recently, there was a tendency to select TCZ, ABT and GLM, which can be expected to be effective even without MTX.

P1-115

Biological therapies to treat rheumatoid arthritis in older elderly patients

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Conflict of interest: None

Object: To examine the characteristics of older elderly (OE) patients with rheumatoid arthritis (RA) and the efficacy and safety of biological therapies to treat RA. **Methods**: In total, 316 patients with RA were treated with a biological agent. Patients were stratified by age at the start of therapy, and patient characteristics and therapeutic efficacy and safety were compared among OE (age≥75 years; n=43), younger elderly (YE) (65≤age<75 years; n=73) and younger patients (age<65 years; n=200). **Results**: Methotrexate (MTX) was administered at a lower rate (30.2%) to the OE than to the other groups. At 24 weeks, the OE had a higher remission rate (62.8% in DAS and 20.9% in CDAI) and a better EULAR response (good or moderate, 90.7%) than the other groups. In the OE, the CDAI remission rate was 25.0% for anti-TNF agents (n=16), 18.8% for tocilizumab (n=16), and 18.2% for abatacept (n=11). The prednisolone dosage administered to the OE in week 24 decreased 37.1% from the baseline. Severe adverse events in the OE were an infection in 3 (6.9%) and a cardiovascular event in 3 (6.9%). These advents occurred at the higher rates than the other groups. **Conclusions**: Biological therapies in OE patients are highly efficacious, but on the other hand, should be precautions severe adverse events.

P1-116

Adalimumab can be used and effective in RA subjects with autoimmune liver disfunction as PBC

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Conflict of interest: None

A case of a 50year old female who has been treated with **Primary billary cirrhosis (PBC)** for 5 years who has been treated. The content of treatment have included administration of **PSL 5 mg / day**. Since 2 years ago, multi arthritis and swelling have been recognized repeatedly. The follow-up observation was made by administration of.NSAIDs. In this time, The symptom which multi joint pain and swelling can not improved. On data, **CRP 0.65, ESR 21** and inflammation were recognized. In addition, Anti CCP antibody and from MRI findings, we can diagnosis as rheumatoid arthritis (RA). There was also a time to recognize the growing worse of liver function data. So for half a year, there was follow-up observation with salazosulfapyridine administration. From the time when liver function stabilizationwas obtained, **Adalimumab** have started, with administration of **40 mg / 2 weeks**. The result of this treatment, the activity activity of RA has been decreased, and PBC exacerbation was not observed. From this case, **Adalimumab** administration to RA complicating autoimmune hepatitis such as PBC can show effectiveness without deteriorating hepatic dysfunction.

P1-117

A case of sulphasalazine-induced pleuritic in a patient with rheumatoid arthritis

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Conflict of interest: None

【Case】A 44 years old woman was admitted to our hospital on October 5, 2016 because of high fever, eruption, and chest pain on breathing. She had a diagnosis of rheumatoid arthritis and Sjogren's syndrome and SASP 500mg was started on September 23, 2016. On admission, she had no arthritis. The blood test showed thrombocytopenia, the increase of the hepatobiliary enzyme and CRP. On the hospitalization next day, chest computed tomography scan showed both pleural effusion, the infiltrative

shadow of both lower lobes. Bronchoscopy was revealed redness and erosion on the mucosa of epiglottis, trachea and bronchiorum. We suspected an allergy of SASP, and discontinued SASP. On the third day, her symptoms were relieved and Chest X-ray showed a decrease in pleural effusion. So we diagnosed SASP-induced pleuritis. Pleuritis is a rare side effect of SASP. Most patients were managed by drug withdrawal with prescribed corticosteroids. This case is interesting that SASP-indeced peluritis improved without steroid administration.

P1-118

Pregnancy and delivery in the patients with rheumatoid arthritis (RA) undergoing biologic therapy

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Conflict of interest: None

[Object] For young patients with RA, pregnancy and delivery are big problems. So we examined the influence of pregnancy and delivery in the pathogenesis of RA and effects of RA treatment in pregnancy and delivery in RA patients treated with biologics. [Methods] In 5 patients who became pregnant and gave birth undergoing biologic therapy, we examined disease activity before pregnancy and after delivery, steroid dose during pregnancy, infant weight and so on. [Results] Age at delivery was 27-40 years old. Etanercept was used in 3 patients and Abatacept and Tocilizumab were used for 1 each. These biologics were discontinued when the patient became pregnant. In 4 patients MTX had been administered until 2 weeks -6 months before pregnancy. In the patients with high disease activity during pregnancy, higher dose of PSL was needed. It tended to be observed low body weight in children from patients with higher usage of PSL. There was no anomaly. [Conclusion] In the patients who are not ready for the control of disease activity before pregnancy, dose of PSL tends to increase during pregnancy and problems in patients and children may occur. Sufficient control of disease activity is considered to be important for the successful pregnancy and giving birth in RA patients.

P1-119

A case of lymphoproliferative disorder developed during treatment with salazosulfapyridine against rheumatoid arthritis

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Conflict of interest: None

An 80-year-old female was diagnosed as rheumatoid arthritis (RA) for her symmetrical polyarthritis. She was initially treated with bucillamine, which was later changed to salazosulfapyridine (SASP) due to drug rush. Her arthritis improved and became low disease activity. After 5 months treatment with SASP, she noticed gradually increasing lymphadenopathies of her neck and axilla. CT scan showed multiple lymphadenopathies and soluble IL-2 receptor (sIL2-R) increase. Lymph node biopsy suggested angioimmunoblastic T-cell lymphoma with Epstein-Barr virus encoded RNA positive cells. She was diagnosed for other iatrogenic immunodeficiency-associated lymphoproliferative disorders (LPD) in WHO classification of lymphoid neoplasms. Since her general status was good, she was followed-up by discontinuation of SASP, without initiation of chemotherapy. Her lymph nodes and sIL2-R gradually decreased. LPD developing during RA treatment is reported in patients under treatment with methotrexate. Recently there have also been reports that LPD occurred during treatment with tacrolimus and biologics, but none with SASP. Because of obvious lymph nodes retraction after withdrawal of SASP in our case, LPD may have caused by SASP, which we have to take care of.

P1-120

The safety dose of oral steroid, aspecst of osteonecrosis of femoral head

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Conflict of interest: None

Background) In rheumatoid arthritis patiens, recent several guidelines recomend low dose short-term steroids. However sometime, we could see the patines with steroid induced avascular necrosis of the femoral head. There is no evidence in Japan the association steroid dose and avascular necrosis of the femoral head. Methods) In retrospective study, we have checked our medical records in patients with avascular necrosis of the femoral head who used steroid from 2006 to 2016. Result) 43 cases were steroid induced avacular necrosis. 30mg prednisolone was 24 cases, 15mg was 14, 10mg was 4, and 7.5mg was 2 respectivity ($r = 0.67$, $p < 0.01$) Discussion) Steroid dose and avascular necrosis of femoral head was correlated. However even 7.5mg prednisolone during 2 weeks had occured avascular necrosis of femoral head. Pay attention in low dose steroid short term use.

P1-121

A case of rheumatoid arthritis complicated with discoid lupus erythematosus after the administration of infliximab

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Conflict of interest: None

A 55-year-old man was diagnosed rheumatoid arthritis (RA) in 2012. He was given methotrexate (MTX), but the maximum dose of MTX was 8mg/week because of leukopenia. Therefore, we started administration of infliximab (IFX). His desease activity was improved by this treatment, and complete remission was continued. Two years later, administration of IFX was stopped. A few days later, erythema appeared at frontlet and right eyelid. On laboratory findings, anti-ds-DNA antibody were negative and C3 and C4 were almost normal range. But, findings of skin biopsy were consistent with discoid lupus erythematosus, with deposition of IgG and IgM, C3c in the basement membrane. Usually, anti-ds-DNA antibody were positive in lupus like syndrome during IFX treatment. We experienced rare case that anti-ds-DNA antibody were negative in lupus like syndrome during IFX treatment.

P1-122

Changing routes of administration of tocilizumab might enable to continue the therapy in patients with adverse reactions

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Conflict of interest: None

Tocilizumab (TCZ) is the only available agent that blocks IL-6 signals in patients with rheumatic diseases in Japan. We here report two cases of patients who developed infusion reaction or drug eruption, but could continue TCZ by changing administration routes. [Case 1] A 60-year-old woman with adult onset Still's disease received TCZ intravenously to reduce the dose of predonisolone. On the second administration of TCZ, she presented, diarrhea, vomiting and a drop in blood pressure, and the infusion was stopped. Despite the infusion reaction, the patient claimed the continuation of TCZ therapy. Under intensive watching in hospitalization, she received TCZ by subcutaneous injection and showed no adverse effects and the therapy has been continued safely. [Case 2] A 55-year-old woman with a history of rheumatoid arthritis and Crohn's disease those could not be controlled by anti-TNF agents. The patient showed highly active arthritis and intestinal bleeding and subcutaneous injection was started. The therapy improved arthritis, but developed skin rashes. Despite the drug reaction, the patient claimed the continuation of TCZ therapy. Under intensive watching in hospitalization, she received TCZ intravenously and showed no adverse effects and the therapy has been continued safely.

P1-123

A case of Bucillamine induced-Gigantomastia

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Conflict of interest: None

Case: A 40-year-old female, diagnosed as diffuse cutaneous systemic sclerosis 2 years before, started bucillamine for polyarthritis. Seven months later, subcutaneous masses developed in the bilateral axillae. Needle biopsy revealed hypertrophy of accessory breasts. Fifteen months later, her breasts, accessory breasts and nipples markedly enlarged. Hyperprolactinemia was found and treated by cabergoline. However, the masses progressively enlarged and bucillamine-induced gigantomastia was diagnosed. A breast reduction surgery was performed. The histopathology showed fibroadenoma. Clinical significance: Since Desai first reported D-penicillamine-induced gigantomastia in 1973, over 20 cases have been reported and the pathological finding is increased fibrosis. Bucillamine, an analogue of D-penicillamine, is used as a DMARD over two decades in Japan but only one case of bucillamine-induced gigantomastia was reported. Pathologically, our case demonstrated multiple fibroadenomas, which was rare but reported in cyclosporin-induced gigantomastia. The mechanism is unknown, but elevation of sexual hormone level or increased sensitivity to such hormones is among its hypotheses. Clinicians should be aware of this rare but physically and psychologically disabling adverse effect.

P1-124

Two cases of duodenal ulcer caused by Iguratimod (IGU)

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Conflict of interest: None

【Case1】73y.o female. She, who had a history of duodenal ulcer, had been treated for RA with MTX 10 mg/w and NSAIDs. One month after receiving added IGU 25mg/d, she developed duodenal ulcer. She could recover completely with oral PPI.【Case2】55y.o female. She had been treated with MTX 10 mg/w without any troubles including peptic ulcer. But seven months after receiving added IGU 25mg/d, which was very effective, she had felt upper abdominal pain. Then she took NSAIDs purchased at drug store. Because she had been suffering from severe epigastralgia after that, she visited our hospital the other day. Endoscopic examination showed a deep ulcer accompanied a microperforation in the duodenal bulb, so she was hospitalized. She could recover completely with PPI injection, and left the hospital after 5 days.【Consideration】Because IGU suppresses both COX-1 and COX-2 activities, peptic ulcer may occur if patients took NSAIDs. Patients, who have a history of peptic ulcer or take concomitant NSAIDs, should be treated with PPI.

P1-125

A case of de novo hepatitis B in rheumatoid arthritis

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Conflict of interest: None

A 80-year-old woman had been treated RA of 20 years duration. She had been treated with methotrexate (4mg/w), tacrolimus (1mg/d) and bucillamine (100mg/d) from 3 years ago. When the patient had taken methotrexate after 13 years, a blood test showed elevated aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels (131 and 151 IU/l). Methotrexate was then stopped to be administered because of suspicion that methotrexate induced liver function failure. After 2 weeks, a blood test showed elevated AST and ALT levels (220 and 230 IU/l), tacrolimus and bucillamine were stopped to be administered. After a week, a blood test showed markedly elevated AST and ALT levels (324 and 355 IU/l) and HBs-Ag (+), she was diagnosed hepatitis B. Before administration of methotrexate, a blood test showed HBs-Ag (-) but HBs-Ab and HBc-Ab were not measured. In recent years, the suggestion had done for reactivation of hepatitis B virus in rheumatoid arthritis patients treated with immunosuppressive agent. This case had long RA history and no liver function failure history, HBs-Ab and HBc-Ab were not measured. Before administration of immunosuppressive therapy, we must measure HBs-Ag, HBs-Ab, HBc-Ab.

P1-126

A case of ulcerative colitis with seronegative rheumatoid arthritis under administration of adalimumab

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Conflict of interest: None

[Object] The coexistence of rheumatoid arthritis (RA) and ulcerative colitis (UC) is rare. We report a case of developing UC under administration of adalimumab (ADA) for RA. [Case] A 75-year-old female was diagnosed with seronegative RA fulfilling EULAR/ACR 2010 criteria when she was 72 years old. At the age of 73, 40 mg per 2 weeks of ADA was started with 12 mg per week of MTX because of high disease activity. Since remission had been achieved and maintained, MTX was reduced to 8 mg per week. At the age of 75, hematochezia, abdominal pain, and diarrhea had been occurred without deterioration of joint symptom. Redness and edematous mucosa in rectum were observed with colonoscopy, and diffuse inflammatory cell infiltration, crypt abscess, and reduction of goblet cells were observed in biopsy specimens. These findings were compatible with UC. After mesalazine and Kampo prescription were started with usual prescriptions, digestive symptoms were improved. [Conclusions] This case is new onset of UC under RA because of no digestive symptom when diagnosed RA. Moreover, it occurred while ADA, therapeutic agent of UC, had been used. Similar case was reported only one case in 2016 as far as our searching. This case is an interesting case in considering pathogenesis of RA and UC.

P1-127

Malignancy related KL-6 level elevation, seen in a patient of rheumatoid arthritis treated with biological agents

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Conflict of interest: None

【Case】A 51-year-old woman of rheumatoid arthritis (StageII, Class3) had elevated level of the serum KL-6 (662U/ml), after the initiation of methotrexate (MTX) and infliximab (IFX). MTX and IFX were then changed to iguratimod and tocilizumab, and the serum KL-6 level once decreased to 528U/ml. There was no evidence of interstitial pneumonia. However, the serum KL-6 level gradually increased again up to 2,333U/ml. The symptoms of rheumatoid arthritis were under control, but the patient developed abdominal fullness. Radiological examination revealed a large intrapelvic tumor with peritoneal dissemination. Finally she was diagnosed as an ovarian cancer, which was not detected by the gynecological examination and abdominal ultrasonography performed prior to the introduction of the biological agents. We report a case of rheumatoid arthritis with elevation of the serum KL-6 level, which was related to the complicated ovarian cancer during the treatment with biological agents. It is important to investigate not only interstitial pneumonia, but also malignancy, when the elevated KL-6 level was observed during the treatment of rheumatoid arthritis.

P1-128

Epigastralgia and pretended increased IgM, proliferation of lymphoplasma like cell with sudden turn. Case report

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Conflict of interest: None

Among MTX-LPD, this disease state needed special care and quickness. A 68y female was treated with MTX 6mg /W and lowdose PSL for RA from 7 years ago.3 weeks before, she had severe wrist pain, received 20mg of PSL. 6 days before, she had dyspnea, nausea and continuous epigastric pain.3 days before, hospitalized and started antibiotics. Ttransferred to our hospital. SpO2 92%, epigastric tenderness, oral candida. WBC26600 Plt.6 atypical lymphocytes, LDH1379 CRP2 IgG286 IgA100 IgM2503, SIL2R 5417, βDglucan 80, ferritin 2145. CT presentedperipheral respiratory tract bronchitis or obstructive bronchiolitis, lymphadenopathy in supla clavicle, axilla and mediastinum, and an enlarged liver and splenomegaly. Bone mallow examination showed lymphoplasma or plasmablast like cell proliferation (66%), EBER-ISH +, κ/λ >10 She was diagnosed as MTXLPD, resulting high IgM, with bacterial pneumonia and deep mycosis. She was treated with 3litter O2, several antibiotics and stopped MTX. The 2 day after admission, after toilet, she could not stand up, went to cardiopulmonary arrest and died. CT after death showed only changes after arrest. Hyper viscosity may cause deep vein thrombosis, ischemic heart diseases. There were effects of urgent worsening of LPD and reduced PSL.

P1-129

Rheumatoid arthritis with methotrexate related lymphoproliferative disease of the lumbar vertebral body; a case report

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Conflict of interest: None

The present patient was a 74-year-old female who had been diagnosed as having Rheumatoid Arthritis (RA) in 20xx. She had been receiving Methotrexate (MTX) treatment for RA since 20xx + 8-years, with doses ranging from 6 to 12mg per week. Four-years later from medication of MTX, she developed severe low back pain with paraplegia. Magnetic resonance imaging of her lumbar showed vertebra fracture of second lumbar with abnormal intensity of fourth vertebra witch was observed as a low signal intensity on the T1-weighted image and an high intensity on the T2-weighted image. Computerized tomography (CT) demonstrated osteolytic change of fourth vertebra. Chest CT demonstrated nodular shadows in right lower lung fields. Metastatic spinal tumor was suspected from the clinical course and imaging findings, she had undergone operation of lumbar. The histological findings of fourth vertebra at this operation demonstrated a infiltration of lymphoid cells. After operation, she discontinued MTX. eight-weeks later of discontinued MTX, CT demonstrated repair of osteolytic change at fourth vertebra. MTX discontinuation with no chemotherapy followed up improved the recovery of the MTX related lymphoproliferative disease.

P1-130

The impact of chronic kidney disease (CKD) on drug survival rate in Rheumatoid arthritis (RA) patients who received Tofacitinib (TFC)

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Conflict of interest: None

[Objectives] To analyze the impact of CKD on DSR in RA patients who received TFC. [Methods] A retrospective study was performed to analyze the risk factors which affected DSR of TFC. The primary endpoint was 6 month DSR after starting TFC. DSR analyses were performed using Cox proportional hazard regression models. [Results] In 15 RA patients treated with TFC, 7 patients had CKD (stageIII 7 patients, V 2patients including 1 dialysis patients) and 8 patients had normal renal function (non CKD). There were no significant differences in 6 month DSR between CKD and non CKD groups (71.4% vs 70%:p=0.99) Other factors, Age, positive ACPA, MTX dose, PSL dose had also no effect on DSR of TFC. [Conclusion] We found that CKD was not significant risk factor of DSR of TFC in RA patients.

P1-131

Two cases who have suffered from bone marrow carcinosis during Abatacept therapy for rheumatoid arthritis

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Conflict of interest: None

[Object] Bone marrow carcinosis (BMC), which occurs metastasis into bone, that leads DIC, is the last stage of cancer with poor prognosis. We have experienced two cases with BMC during abatacept (ABT) therapy. These rare cases were reported in order to make attention for BMC in treating rheumatoid arthritis (RA). [Case1] 66-year-old lady. History; MTX started with 6mg/week in March 2008. Tocilizumab started in April 2009, switched to ABT in July 2011, later increased to 750mg in seven months. In April 2015, complained gastric pain with general fatigue and whole body pain with platelet counted 40,000/mm^3 in September. Gastric cancer (Signet-cell carcinoma) and BMC was diagnosed. DIC treatment was done, however, died on October 28, 2015. [Case2] 66-year-old lady. History; MTX started with 6mg/week in February 2010, later increased to 12mg/week in 5 months. ABT started with 750mg in October 2010. Lung cancer was diagnosed for Stage 4 with bone metastasis in October 2015. ABT discontinued. In May 2016, severe general fatigue occurred with PLT counted 31,000/mm^3. BMC was diagnosed from pathologic findings. PLT transfusion was done, and PLT increased with chemotherapy. [Conclusions] We need to pay careful attention for risk of malignancy in treating RA not only with ABT therapy.

P1-132

Clinical result with elderly rheumatoid arthritis thearpy

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Conflict of interest: None

【OBJECTIVE】The population of elderly RA (ERA) is expanding due to increasing life expectancy. While T2T therapy is recommended, no mention of established treatment goals for ERA. Regarding of ERA in our hospital, treatment contents, complications, general condition were examined.【METHODS】enrolled elderly RA randomly extracted visited our department during from June 20 2015 to June 28 2016, HAQ score and DAS28score, were assessed Changes in liver / kidney function, adverse events.【Result】The BIO group was 19 cases, 11 of NBIO. Average age 73.7 years and 74.9 years. DAS 28CRP 3.48 to 2.01 and 2.95 to 2.15 respectively. ΔHAQ improved from 1.05 to 0.82 and from 0.37 to 0.32, MTX and steroid content were dominantly reduced in the BIO group. There was no pronounced liver / kidney disease exacerbation and serious infection complication.【Conclusion】ERA needs treatment to consider steroid and MTX dose reduction, due to CKD, IP, and Frailty in order to prevent infectious diseases.

P1-133

Asymptomatic colitis induced by low dose methotrexate

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Conflict of interest: None

A 77-year-old woman with a history of rheumatoid arthritis (RA) presented with inflammatory colitis confined to her rectum, which was incidentally found by a screening colonoscopy. Histopathological examination of colonic biopsies showed nonspecific inflammatory infiltrates of lymphocytes, the cause of which was unknown. She had been diagnosed with RA 5 years before, and she was receiving methotrexate 6 mg week-

ly, to which tocilizumab had been added 4 years earlier, which achieved stable control of her disease. She had no gastrointestinal symptoms or other health problems. Tocilizumab-induced colitis was considered likely, and the drug was discontinued. Metronidazole was also prescribed because of possible *Clostridium difficile*-associated colitis. Three months later, a repeat colonoscopy showed no improvement of the colitis. The methotrexate was also discontinued, and folinic acid was prescribed daily for 2 weeks, leading to complete resolution of the colitis observed at repeat colonoscopy.

P1-134

Association between late stage elderly rheumatoid arthritis patients using biologics and adverse events : retrospective cohort study

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Conflict of interest: None

【Object】There is not the report that examined the association between late stage elderly RA patients using biologics and adverse events until now.【Methods】Participants were a retrospective cohort study from Showa University registry of Biological therapies in rheumatoid arthritis between 2005 and 2016. 309 RA patients were included. We compared under 75 years old group and 75 years or older group, and the primary outcome were the cancels due to the biologics adverse events. The statistical analysis was performed by Pearson chi-squared test and binomial logistic regression analysis.【Results】Age 57.2±15.7years old. Female 83.5%. 75 years or older 42/309 (13.6%), under 75 years 267/309 (86.4%). The cancels due to adverse events were 11/42 (26.2%) for 75 years or older group, 21/267 (7.9%) for under 75 years group. Pearson chi-squared test showed significant difference between two groups (p=0.0003). Confounding factors were sex, corticosteroid dose, csDMARDs, interstitial pneumonia, DM. On binomial logistic regression analysis adjusted for the covariates, the cancels due to the biologics adverse events were associated with age statistically (p=0.0486).【Conclusions】In a group of 75 years or older, the cancels due to the biologics adverse events were significant high.

P1-135

A case of Tocilizumab use patient masked the symptom of the severe infectious disease

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Conflict of interest: None

(Introduction) A rise of CRP is suppressed, and a diagnosis of the infection is late. Becouse Tocilizumab is IL -6 receptor antibodies. I experienced the twice case that contracted a disease for a severe infectious disease during Tocilizumab use. (CASE) 55years old, male, RA of The 1999 onset, CLASSIV STAGE3, previous history: gastrointestinal perforation medicine:Tocilizumab, Prednisolone, Methotrexate The patient uses Tocilizumab for RA from 2012. In 2013, Peritonitis developed from lower part gastrointestinal tract perforation after a traffic accident, but a symptom was poor. He did hospitalization, an emergency surgery three days later In 2016, CRP levels exceeded 20 mg/μl. After inspecting it, I accepted liquid retention to the right lung field in chest Xp, and CT. A thoracic empyema was diagnosed. (Discussion) I consider it based on documents about a risk factor, a treatment policy of Tocilizumab use and the infection. (Conclusions) I experienced one case that a thoracic empyema developed in during Tocilizumab use, I reported it.

P1-136

A case of methotrexate-associated lymphoproliferative disorders of the liver

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Conflict of interest: None

[Objectives] We report a case that was diagnosed as methotrexate (MTX)-associated lymphoproliferative disorders (LPD) of the liver. [Case] In 2000, a 69-year-old man was diagnosed with rheumatoid arthritis. He was treated with MTX from 2007. Liver disfunction and Inflammation occurred in 2015, chest and abdominal CT was enforced to clarify the cause. Abdominal CT revealed irregular hypertrophy of gall bladder wall, multiple liver tumors and hepatoduodenal lymph node swelling. He was admitted to our hospital for inspection, MTX was stopped for improvement liver disfunction before admission. Blood data were LDH 265 U/l, CRP 2.64 mg/dl, CEA 3.77 ng/ml, IL-2R 740 U/ml at the admission. Enhanced CT was performed after two weeks withdrawal of MTX. Irregular hypertrophy of gall bladder wall was improved, multiple liver tumors and hepatoduodenal lymph node swelling were reduced appalently. In this progress, he was diagnosed with MTX-associated LPD. Rheumatoid arthritis was flared up after a month, he was treated with tacrolimus and prednisolone. Clinical symptoms were improved immediately. [Conclusions] Withdrawal of MTX has led to improve multiple liver tumors and lymph node swelling in this case.

P1-137

A study of music therapy for patients with rheumatoid arthritis in terms of positive emotions

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Conflict of interest: Yes

[Objectives] We previously reported that music therapy improves general health condition, pain, and self-efficacy of patients with rheumatoid arthritis (RA) and decrease negative emotions including anxiety. In this study we investigated the effect of music therapy on positive emotions. **[Methods]** Music therapy was conducted by a music therapist, a pianist, hospital staffs, and students. Eight Japanese songs were sung with a piano accompaniment and 2 were played with chime bars by the participants. General health condition, pain, mood, and positive emotions were surveyed by self-rating questionnaire including 10cm VAS, face pain rating scale, TMS, and Positive Mood Scale (PMS). **[Results]** Nineteen female patients with RA participated. mHAQ was 0.55±0.65. GH-VAS was changed from 4.0 to 3.1, FS from 6.9 to 4.0, tension in TMS from 6.5 to 6.1, depression from 6.1 to 4.6, anger from 4.6 to 3.5, confusion from 6.5 to 4.5, fatigue from 7.4 to 4.7, vigor from 8.7 to 10.9, relaxation in PMS from 12.2 to 17.3, affinity from 11.9 to 15.1, comfort from 14.0 to 17.5, and concentration from 12.7 to 16.4. All the scales other than tension were improved significantly after music therapy. **[Conclusion]** Music therapy improves positive emotions in patients with RA.

P1-138

Investigation of rheumatoid arthritis (RA) hand/finger simulation equipment using STEF

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Conflict of interest: None

OBJECTIVE: Dysfunction of hand/finger deformity is one of the key factors for decrease of ADL in RA patients. We developed the RA hand/finger simulation equipment (RSE) which could be a vital education

material for patients. This is an open fingertip type apparatus that can be equipped to each finger accommodating various deformity. There were no significant differences in DASH (Disability of Arm, Shoulder and Hand) score between RA and RSE group (healthy volunteers (HV) equipped with RSE). Since DASH scores lack in objectivity, we investigated RSE using the Simple Test for Evaluating Hand Function (STEF). **METHODS**: The three groups were: RA, RSE and HV groups. Hand function of RA, RSE and HV groups were assessed using the STEF-scores / times. **RESULTS**: The number of cases for each group was: RA patients 5 (10 hands), HV 14 (28 hands) and RSE 14 (28 hands). Mean scores / times (seconds) of STEF were: RA 91.6 / 10.3, RSE 9.08 / 9.08 and HV 10.0 / 7.01, respectively. STEF-scores / times in RA group were significantly lower than HV group. However, no significant differences were observed in STEF scores / times between RA and RSE groups. **CONCLUSIONS**: Results indicate that there is possibility that difficulty of hand/finger function of RA patients can be simulated using RSE.

P1-139

The influence rheumatic disease activity exerts on the skeletal muscle bulk

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Conflict of interest: None

[Purpose] We investigate the influence their disease activity exerts on the skeletal muscle bulk in rheumatoid arthritis (RA) patients. [Method] 153 (25 male and 128 female) RA outpatients (average age: 68.5 years old, average disease duration: 15.7 years) were enrolled in our study. We measured their each skeletal muscle bulk (total, the upper limb, the lower limb and the trunk) with body constituent analysis equipment. We compared each skeletal muscle bulk between REM-keeping group which patients could attain DAS28-ESR remission more than half of times and REM-non-keeping group which could not attain remission more than half of times. [Result] In REM-non-keeping group, total skeletal muscle bulk, the upper limb muscle bulk, the lower limb muscle bulk and the trunk muscle bulk were significantly lower compared to those in REM-keeping group ($P < 0.001$). [Conclusion] It is important to not only control the disease activity but also keep the low disease activity from a standpoint of skeletal muscle bulk on RA treatment. Based on our study, we have to develop rehabilitation for their muscle strengthening and improvement of living function.

P1-140

The relation between the morbidity period and the upper limb function in rheumotoid arthritis

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Conflict of interest: None

[Object] The objective of this study was to consider the relation between the morbidity period and the upper limb function for rheumatoid arthritis (RA). [Methods] 246 hands of 123 cases (29men and 92women) were tested. The average age was 60.6 years, and the average morbidity period was 77.6 months. In the Steinbrocker's CLASS, All cases were classified to CLASS1:57 cases, CLASS2:47 cases, CLASS3:11 cases and CLASS4:8 cases. From Larsen grade (LG) all hands were classified to LG0:85 hands, LG1:47 hands, LG2:32 hands, LG3:30 hands, LG4:36 hands and LG5:26 hands. Simple Test for Evaluating Hand Function (STEF) was carried out in each hands for all cases. and the relation between the morbidity period of RA and STEF was considered. Statistical analysis was considered by by risk 5% using the rank correlation coefficient of Spearman. [Results] Negative correlation was admitted between the morbidity period of RA and the sum of the score of STEF of both hands. In many cases with the long morbidity period, LG were high on each right and left hands x-ray. [Conclusion] In the cases with the long morbidity period, destructive changes were observed on the hand x-ray by many cases, and the upper-limb function decreased on RA patients.

P1-141

The results of tension reduced early mobilization for reconstruction of ruptured extensor tendons in rheumatoid hands

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Conflict of interest: None

[Objective] We aimed to investigate the tension reduced early mobilization for reconstruction of ruptured extensor tendons in rheumatoid arthritis. [Methods] From 2012 to 2015, participants comprised 10 patients (1 man and 9 women) with 10 hands and 17 fingers with RA who were scheduled to undergo tendon transfer. The mean age was 62.1±12.5 years, the average implementation period for occupational therapy was 12.6±1.4 weeks and the average follow-up period was 17.4±4.4 months. Tension reduced early mobilization was performed from the third postoperative day. We evaluated range of motion of MCP joint, grip strength, pinch strength and DASH score at the time of preoperatively and the time of follow-up. [Results] Active flexion of MCP joints was 76.6˚/56.2˚/63.6˚/66.6˚/71.4˚ on ring finger, 78.8˚/53.2˚/64.0˚/70.2˚/73.4˚ on little finger preoperatively, 6, 8, 12 weeks postoperatively, and the final follow-up respectively. Active extensions of MCP joints and DASH score were improved over time. Grip and pinch strength were improved at 12 weeks postoperatively, furthermore grip strength were improved significantly at the last follow-up. [Conclusion] It is important to instruct patients how to use their hands in daily life after reconstruction of ruptured extensor tendons.

P1-142

Effectiveness of 13degree foward bending pole walking after bilateral foot artroplasties

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Conflict of interest: None

In 2012 we reported that 13 degree forward bending pole walking was useful for the rehabilitation after arthroplasty in rheumatoid arthritis patients.. 13degree forward bending pole is good for the defoemed wrist joints of rheumatoid arthritis patients and these patients felt less pain than usual. This time we reported the experiences that the rheumatoid patients undergone the forefoot artroplasties were good application of 13 degree forward bending pole rehabilitation. As we operated the both side of forefeet, we wont force them to bear their weight when the ossification of the bone gap was not mattured. We trained them to walk with poles by defensive style after their surgeries. As they wanted to continue these pole walking, after 6 months from their discharge we examined questinare about their QOL and subjective symptoms. Result: These assistance of poles were very useful for them whom undergone the both side of forefeet arthroplasties. The improvements of their subjective symptoms must be discussed consistently.

P1-143

Physical Activity of Rhematoid arthritis with accelerometer: Pilot study

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Conflict of interest: None

[Object] The aim of this study was to examine the effects of the amount and intensity of daily physical activity of rheumatoid arthritis patient. [Methods] Twenty four RA patients (2 males and 22 females) in the present study. All participants wore an accelerometer on their waist for 7 consecutive days. They also completed the PAQ: International Physical Activity Questionnaire: Short Version), mHAQ and SF-12. We extracted parameters from the acccelerometer data: min/day/Low physical activity (LPA), Moderate +Vigorous activity (MVPA). We investigate the relationship between iPAQ (MVPA score and Walking PA score) and the date of accelerometer. [Results] The Moderate+Vigorous PAscore (MVPA) and Walking PAscore (WPA) of the iPAQ was 12.43 (±36.6) and 19 (±17.4), respectively. Physical activity measured by a accelerometer "Active style Pro", min/day/LPA and MVPA was 637 (±181), 85 (±33.3), respectively. As to the relationship between the MVPA of the iPAQ and wasn't correlated with min/day/MVPA of the accelerometer. [Conclusions] The time of LPA in Rheumatoid patients is long. In order to evaluate the low activity level, we could evaluate the accuracy with higher accelerometer than the questionnaires.

P1-144

An investigation of factors contributing to QOL degradation in rheumatoid arthritis patients, including motor imagery capacity

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Conflict of interest: None

[Background] A correlation between motor imagery (MI) capacity and QOL has been demonstrated in rheumatoid arthritis (RA) patients, but it is unclear whether MI capacity remains a dominant factor in QOL degradation when disease activity and duration are taken into account. [Methods] Sixty RA patients (mean age 67.3 ± 9.7 years) were analyzed by age, DAS28CRP, disease duration, and imagined TUG (iTUG) as an index of MI capacity. QOL was assessed in terms of physical component summary (PCS) and mental component summary (MCS) with the use of SF-36v2. The statistical analysis used a stepwise multiple regression with PCS and MCS as the dependent variables, and age, DAS28CRP, disease duration, and iTUG as the explanatory variables (level of significance < 5%). [Results] The analysis extracted PCS item DAS28CRP ($b = 0.60$, $p < 0.05$) and MCS item iTUG ($b = 0.56$, $p < 0.05$). [Discussion] PCS decreased in inverse relation to DAS28CRP, reflecting declines in physical function from RA symptoms such as pain. MCS decreased in inverse relation to the number of errors in iTUG, as failure to achieve the expected result eroded self-confidence. [Conclusions] The results suggest that degradation of QOL in RA patients involves the PCS aspect of DAS28CRP and the MCS aspect of decreased iTUG.

P1-145

The use of nursing care insurance service in Rheumatoid arthritis patients

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Conflict of interest: None

Purpose: To analysis the use of nursing care insurance service in Rheumatoid arthritis (RA) patients, and offer the reference when the doctor should recommend a nursing care insurance service to RA patients. Object: RA patients who had attended our hospital April 2004- April 2016 and started to receive the nursing care insurance. Total 90 patients, male 15 and female 75, average age 79.7 year-old, RA duration average 17.7 years, nursing care level suport required 20 and needed support 70. Result: RA patients used such services as home visiting care 34, Out patient day care 9, short stay service 7, admitting to a nursing-care facility 20, rental a nursing care goods 2, home renovation 6, home visiting rehabilitation 1, home-visiting medical treatment 5, deny the service 6. Conclusion: Many RA outpatients use home visiting service but 6 patients don't use nursing care insurance after they were applied it. Once they admitted the hospital, they need not only medical service but also care service, so 20 patients used the service of admitting to a nursing-care facility after hospitalization.

P1-146

The initial combination therapy of aggressive rehabilitation and biological DMARDs leaded a bedridden elderly-onset RA patient with intense arthritis to deep remission and independence in daily life

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Conflict of interest: None

[Purpose] We tried to improve the bedridden elderly-onset RA patient with intense arthritis by the aggressive PT intervention and biological DMARDs as initial combination therapy. [Introduction of case] A 72 year old female had long-term recumbency after RA onset and exhibited remarkable disuse syndrome. August 2016, from the first treatment Certolizumab pegol was provided, at the same time, PT intervention started aiming for indoor walking independence. [Clinical course] Initial evaluation【Ability to walk】wheelchair assistance movement【ROM】Right knee joint: flexion 60° extension - 30°【ADL】BI: 80/100【disease activity】DAS28:5.28 Treatment: Introduction of passive articulation and static muscular strength reinforcement training on the right knee in which significant deterioration is observed. [Results] Evaluation after 3 months:【Ability to walk】T-shaped walking walk【ROM】right knee joint: flexion 100° extension 0°【ADL】BI: 95/100【Disease activity】DAS28:1.38 [Conclusion] From the present case, it is suggested that even in RA patients with advanced joint dysfunction, aggressive PT intervention with biological DMARDs can provide a great improvement to the physical function, resulting in independent daily life.

P1-147

Anti-ribosomal P antibodies in patients with lupus nephritis

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Conflict of interest: None

Objectives: Anti-ribosomal P (Anti-P) is frequently detected in patients with neuropsychiatric SLE (NPSLE), and lupus nephritis (LN), especially ISN-RPS ClassV. However, few reports about anti-P and LN have been investigated in Japan. The aim of this study is to identify the frequency of anti-P and the relation of anti-P and histology in patients with LN. **Methods**: Thirty-two patients (28 with LN and 4 with suspected LN) diagnosed by renal biopsy in our hospital from 2005 to 2016 were evaluated. Anti-P was analyzed by an immunoblot assay using total ribosomal proteins of brine shrimp. Clinical, laboratory and histological findings were obtained from medical records. Statistical analyses were performed using the Fisher`s test and t-test. **Results**: Six patients (18.8%) were positive for anti-P and were diagnosed with LN (3 patients, ClassIII+V; 2 patients, ClassIV and 1 patient, ClassV) and SLE. No patient was complicated with NPSLE. Comparing clinical, laboratory and histological features between patients with and without anti-P, no statistical difference was observed. Among 6 patients with anti-P, one patient

showed negative for anti-dsDNA antibody but positive for anti-Sm antibody, and the ISN-RPS Class was V. **Conclusion:** Anti-P might be involved in LN.

P1-148

Multi-target therapy with mizoribine, tacrolimus and high dose predonisolone for 43 cases of active lupus nephritis

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Conflict of interest: None

【Objectives】To evaluate efficacy of Multi-target therapy with mizoribine (MZB), tacrolimus (TAC) and prednisolone (PSL) for lupus nephritis (LN). 【Methods】We extracted all the cases with LN treated with multi-target therapy during 2008 to 2016. Retrospective chart review was done to collect following data; patient characteristics, dose of PSL, serum and urine tests, remission rates, and safety profiles. We define complete remission (CR) as urine protein < 0.5 g/gCre and normal serum creatinine. Patients were followed from the beginning of multi-target treatment to 12 months after. 【Results】43 cases (female; n=37, male; n=6, mean age; 37.4 years old) were included. Mean urine protein (g/gCr) at baseline, at 3 months, and at 6 months are 1.9, 0.4, and 0.4, respectively. Mean dose of steroid (mg/day) at baseline, at 3 months, at 6 month are 32.8, 9.8, and 8.7, respectively. 79.1% of the patients achieved CR at 3 months, and the remission rate was more than 80% at 6 months and later. As for adverse events, 14 cases had some Infection, 3 out of 14 needed antibiotics treatment. 4 cases had renal impairment after starting TAC, all of them recovered after stopping or decreasing dose of TAC. 【Conclusion】Multi-target therapy showed good remission rate, and few severe adverse events.

P1-149

The comparative effectiveness of Mizoribine and Tacrolimus versus Mycophenolate mofetil for remission induction therapy of lupus nephritis

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Conflict of interest: None

We compared the effect of treatment with the combination of Mizoribine (MZB) and Tacrolimus (TAC), or Mycophenolate mofetil (MMF) for 21 lupus nephritis patients diagnosed from April 2013 to April 2016. 13 patients were treated with MZB and TAC, and 8 patients were treated with MMF (and Hydroxychloroquine). In the 13 MZB group patients, 10 were women and mean age was 39.7 years old (19-63 years old). In the 8 MZB group patients, 7 were women and mean age was 46 years old (31-73 years old). The patient numbers for each lupus nephritis classes (II/III/IV/V) were 1/1/10/4 in MZB group and all patients were class IV in MMF group. We compared proteinuria of baseline, 3 months and 6 months later, and the amount of steroid of baseline and 6 months later. There were not significant differences between both groups. Using MZB and TAC is considered as an alternative treatment for lupus nephritis.

P1-150

A case report: Multi-target therapy and peritoneal dialysis significantly improved IVCY resistance lupus proliferative nephritis, and resulted to discontinue from dialysis

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Conflict of interest: None

37 years old man was presented to our hospital with edema and increased body weight (10kg within one month) in August 2015. Laboratory findings showed rapid progressive renal impairment, severe proteinuria and hematuria, hemolytic anemia, leukopenia, thrombopenia, positive antinuclear antibody and anti-DNA antibody, and hypocomplemetaenia. We diagnosed with rapid progressive glomerulonephritis accompanied with systemic lupus erythematosus from these findings. The renal biopsy revealed lupus nephritis ISN/RPS IV-G (A). He was treated with methylpredonisolone (mPSL) pulse therapy plus intermittent pulse intravenous cyclophosphamide (IVCY) therapy and hemodialysis. But, the renal function didn`t improved. We switched the treatment to mycophenolate mofetil plus tacrolimus, and start the peritoneal dialysis (PD). These treatment improved the renal function and disease activity. After 6 months, the renal function maintain within almost normal range, so we plan to discontinue PD. This is rare case of refractory LN inducted to remmision by using PD for many months, and finally discontinued PD.

P1-151

A case of silent lupus nephritis who was diagnosed Class III A/C (ISN/RPS) by renal biopsy

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Conflict of interest: None

She was 16-year-old who had a fever, arthritis and malar rash. She was diagnosis of as a systemic lupus erythematosus (SLE) based on her symptoms of rash and arthritis, and positive antinuclear antibody, anti DNA antibodies, hypocomplementemia and leukopenia. Although her urinalysis was normal, a renal biopsy documented the diagnosis of a ClassIII A/C (ISN/RPS). She was treated with predonisolone 50 mg per day and mycophenolate mofetil (MMF). Her fever, arthritis and malar rash gradually improved. Moreover, complement levels normalized and levels of anti DNA antibody decreased. Our experience suggest requirement of renal biopsy regardless finding of renal markers.

P1-152

Minimal change nephrotic syndrome combined with class II lupus nephritis: A case repot

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Conflict of interest: None

Case: A late 20-year-old female was admitted to our hospital because of edema at both legs, which had persistent for 1 month. She had suffered form SLE for 14 years, who had been treated with 3mg PSL for this several years, maintaining remission with normal findings of urinalysis. However, anti dsDNA Ab had gradually increased since 14 months ago, and her urinalysis showed 2+ protein since 5 months ago. On admission, her urine protein was 4.22g/day and serum albumin level was 1.6g/dl, which were fulfilled a criteria of nephrotic syndrome. Selectivity index was low (0.11) and there was no hematuria. A kidney biopsy was performed. Of the 16 glomeruli present, 1 of them was globally sclerotic, and the remaining glomeruli showed slight increased mesangial cells. On electro microscopy, there were paramesangial depositions. These findings indicated a presence of both minimal change nephrotic syndrome (MCNS) and class II lupus nephritis (LN). A dose of PSL was increased to 60mg, leading to the complete remission 7 days after and normalization of anti dsDNA Ab 21 days after. Clinical significance: There are only a few reports describing MCNS in patients with SLE, especially in patients with class II LN. In addition, this present case suggests the association of SLE and MCNS.

P1-153

Clinical features of systemic lupus erythematosus accompanied with interstitial pneumonia

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Conflict of interest: None

[Objective] Respiratory manifestations are commonly observed in systemic lupus erythematosus (SLE). However, interstitial pneumonia (IP) is reported to be accompanied in less than 10% of SLE, and its clinical features remain to be fully elucidated. [Methods] We retrospectively reviewed 78 SLE patients (male/female 14/64) who fulfilled the classification criteria and had satisfactory follow-up period between 2011 and 2015. [Results] Twenty-two (male/female 6/16; 28% in total) were accompanied with IP, and its incidence was higher in male (43%) than in female (25%). Twelve were diagnosed as having IP at the time of SLE diagnosis. The mean age of onset of SLE was 41 years old in total, but 54 years old in patients with IP. IP patterns, which were diagnosed based on chest HRCT findings, were 13 NSIP, 4 UIP, 3 OP and 2 unclassifiable. Fifteen gradually progressed chest HRCT findings, and two needed long-term oxygen therapy. One each accompanied with pulmonary hypertension and experienced acute exacerbation of IP. [Conclusion] Approximately 30% of SLE patients had IP, and a half of them were diagnosed at the first diagnosis of SLE. Patients accompanied with IP were seen dominantly in male and high age, and their prognosis was relatively good.

P1-154

A case of a SLE patient who developed pulmonary hypertension and aortitis

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Conflict of interest: None

[Case] 24-yo F [Chief complaint] dyspnea [Medical History] She had dyspnea in August 20XX, and admitted to our hospital on September 5 [Clinical course] Her CT did not identify any lung lesions, but the echocardiography identified a rise in right ventricular systolic pressure, estimated to be 71.5mmHg; thus we suspected PH. Her right heart catheterization showed a rise in her mean PA pressure, which was 43mmHg; thrombocytopenia, urinary protein, and hypocomplementemia that appeared simultaneously, so we diagnosed PH which occurred with SLE, and we started treatment with PSL and IVCY. On the 31st day of hospitalization, the patient had strong pain in both lower limbs. A dorsal artery palpation was very weak, and the contrast CT showed thickening of the wall and lumen stenosis from her abdominal aorta; thus, aortitis was suspected as a concomitant disease. Due to her continued immunosuppressive therapy, and a combination therapy of vasodilators, we were able to reduce her lower limb pain and improve CT findings. [Conclusion] It is rare for macrovascular lesions to occur in association with SLE; furthermore, we could not find other cases in which PH occurred concomitantly in the documentation. We believe this is a very notable case, and that's why we decided to report it.

P1-155

A case of acute lupus pneumonitis presented as acute respiratory distress syndrome (ARDS)

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Conflict of interest: None

[Case] A 26-year-woman was diagnosed with MCTD based on Raynaud's phenomenon, swollen fingers, pulmonary arterial hypertension, positive anti-U1-RNP antibody, and arthritis 4 years before the admission. Her manifestations improved by high-dose steroids, intravenous cyclophosphamide (IVCY), and pulmonary vasodilator. One year before the admission, she was diagnosed as SLE based on seroconversion of anti-dsDNA antibody, and hypocomplementemia. Increase of steroids ameliorated her disease again. However, she was admitted to our hospital for an emergency because of fever, dyspnea and palpitations. She had hypoxemia and bilateral patchy ground glass opacity on chest CT. There was no evidence of infection, bloody phlegm, apparent anemia, or pulmonary embolism. Her hypocomplementemia had progressed. Initially, she was diagnosed as acute lupus pneumonitis (ALP) or alveolar hemorrhage, and treated with high-dose steroids and IVCY. All the manifestations of SLE ameliorated, and she was discharged home. Because there had been no evidence of infection, bloody phlegm, or apparent anemia, her final diagnosis was ALP and adult respiratory distress syndrome (ARDS). **[Clinical Significance]** ALP is a rare complication of SLE. Prognosis was bad especially when complicated with ARDS.

P1-156

A case of SLE-PAH (systemic lupus erythematosus - pulmonary artery hypertension) which wasn't responsive to immunosuppressive therapy, was responsive to use pulmonary vasodilator together

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Conflict of interest: None

A 49-years-old woman was diagnosed with Systemic lupus erthymatosus (SLE) at 27 years old. She was diagnosed with type V lupus nephritis by kidney biopsy, and received 7.5mg of prednisolone (PSL) and 50mg of cyclosporine as treatment. She was hospitalized due to effort dyspnea in May, 2016. Her mean pulmonary arterial pressure was 51.3mmHg, NYHA/WHO pulmonary hypertension functional classification was III stage. It was highly unlikely that she had chronic thromboembolic pulmonary hypertension by testing of lung perfusion scintigraphy, so we thought her clinical condition was pulmonary artery hypertension caused by SLE. First, we prescribed her a steroid pulse, a cyclophosphamide pulse, prednisolone 1mg/kg, and 50mg of cyclosporine, then started to use pulmonary vasodilator together. Her mean pulmonary arterial pressure significantly improved after this treatment. It was reported that collagenosis PAH had good reactiveness of a steroid and an immunosuppressant, but this case wasn't responsive to the treatment, was responsive to use pulmonary vasodilator together. By case report, most of SLE-PAH cases were responsive to precociously use pulmonary vasodilator together have low SLEDAI. I thought that using pulmonary vasodilator together is necessary for SLE-PAH cases have low SLE-DAI.

P1-157

A case of systemic lupus erythematosus with shrinking lung syndrome manifesting exertional dyspnea and pleuritic pain

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Conflict of interest: None

[Case] A 63-year-old woman had developed exertional dyspnea and pleuritic pain since she was diagnosed as SLE 2 years before. The right diaphragm elevation on chest X-ray (CXR) and restrictive ventilatory impairment were pointed out. Chest CT and echocardiography findings were normal. She was admitted due to exacerbation of dyspnea and chest pain. Acute coronary syndrome was suspected but cardiac catheter examination was normal. Afterwards, dyspnea worsened and she was readmitted. Exertional dyspnea, pleuritic pain, increased heart rate and depressed SpO_2 in 6-minute walk, elevation of right diaphragm on CXR and restrictive ventilatory impairment were observed. Blood tests, echocardiography and chest CT were normal. Suspecting shrinking lung syndrome (SLS), prednisolone 40 mg/day was started, which improved the symptoms. [Discussion] SLS is a rare complication of SLE. It is important to rule out other diseases and to keep SLS in mind as one of the differential diagnoses of dyspnea in patients with SLE. Association between SLS and

pleuritic pain has been suggested. In this case dyspnea and pulmonary function tests improved in parallel with pleural pain, which supports this hypothesis.

P1-158

Successful treatment of severe mitral stenosis in systemic lupus erythematosus with immunosuppressive therapy

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Conflict of interest: None

A 44 years old Japanese woman, having thrombocytopenia for 10 years, felt exertional dyspnea in September 2014. Her symptom was gradually deteriorated. In July 2015, she was diagnosed as severe mitral stenosis (MS) with mitral valve area (MVA) of 1.05 cm^2, indicating surgical treatment. She also diagnosed as systemic lupus erythematosus (SLE) because of malar rash, positivity of anti-double-stranded DNA antibody, anti-nuclear antibody in addition to thrombocytopenia. She did not wish to have any treatment including surgery for MS. In January 2016, she suffered from shortness of breath, hemosputum and pyrexia and admitted to our hospital. She was diagnosed as congestive heart failure (CHF) and SLE with alveolar hemorrhage, hemolytic anemia, immune thrombocytopenia and nephritis. Echocardiography revealed MVA of 0.92 cm^2, suggesting that her MS was worsened. Treatment for CHF with vasopressor and diuretics, and that for SLE with immunosuppressive agent and plasma exchange were initiated. Despite of combination therapy, her nephritis and bicytopenia were still remained, however, MVA was improved to 1.88cm^2, suggesting that not only immunosuppressive therapy was effective for MS but also MS might be associated with SLE.

P1-159

A Case of Myocarditis Associated with Systemic Lupus Erythematosus Diagnosed with Endomyocardial Biopsy, with No Late Gadolium Enhancement on Cardiac Magnetic Resonance Imaging

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Conflict of interest: None

A 33-year-old woman presented with fever, exertional dyspnea and erythema on her face and arms. She had also noticed leg edema and hair loss from 4 months prior. Laboratory investigations revealed proteinuria, severe anemia, positive antinuclear antibody and low complement. Chest X-ray demonstrated cardiomegaly, and echocardiogram showed moderately decreased left ventricular systolic function with pericardial effusion. Treatment for glomerular nephritis associated with systemic lupus erythematosus (SLE) was initiated with methylprednisolone pulse 1g/day for 3 days followed by prednisolone 50mg/day for 4 weeks. Intravenous cyclophosphamide was added and prednisolone was tapered. Further workups to investigate cardiac involvement were performed. Cardiac magnetic resonance (CMR) imaging showed no late gadolium enhancement (LGE). Histopathology from endomyocardial biopsy revealed interstitial tissue fibrosis and lymphocytes infiltration, indicating myocarditis. After initiation of treatment, cardiac function improved along with anemia. Although majority of cases with myocarditis associated with SLE may show LGE on CMR, endomyocardial biopsy remains the gold standard in diagnosing these patients.

P1-160

A case of multiple aneurysms with stenosis in the coronary arteries and peripheral arteries in a patient with systemic lupus erythematosus

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Conflict of interest: None

A 34-year old woman had diagnosed with systemic lupus erythematosus (SLE) in 1997. She also had been diagnosed with antiphospholipid antibody syndrome. She had been treated with prednisolone (PSL). In December 2015, digital ulcers in her right hand appeared and anti-platelet agents were ineffective. Serology revealed high levels of anti-DNA antibodies and low complements C3 and C4. In May 2016, she admitted because of finger pain. Right radial artery couldn't palpable. The electrocardiogram on admission showed QS pattern in V1 through V3. Angiography of upper extremities revealed blood flow obstructions in the right radial artery, right ulnar artery, and the left ulnar artery with multiple aneurysms. Lower extremities also obstructed in both sides of anterior tibial arteries and peroneal arteries. Coronary angiography revealed three-vessel disease with multiple aneurysms. Coronary artery disease is common in patients with SLE, but coronary aneurysms are rarely seen. One of the cause of aneurysm in SLE patient is vasculitis and it often progresses silently. In this case, the same pathological condition as peripheral vasculitis was thought to occur in the coronary arteries. This is a valuable case to clarify the mechanism of aneurysm development in SLE.

P1-161

Systemic lupus erythematosus with initial manifestation of acute myocarditis

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Conflict of interest: None

Cardiac manifestations of systemic lupus erythematosus (SLE) include pericarditis, myocarditis, and endocarditis. We report a case of SLE with initial manifestation of severe myocarditis. A 48-year-old man developed edema of the lower extremities and shoulder joint pain. He visited an orthopedist who find a cardiomegaly and he was admitted to the cardiology department. Electrocardiogram showed atrial fibrillation and echocardiogram showed diffuse hypokinesia with decreased left ventricular ejection fraction (10 to 20%). Cardiac failure improved with diuretics, digitalis, and dobutamine, but fever refractory to antibiotics, systemic myalgia, and arthralgia continued. Blood test results showed hypocomplementemia, hypergammaglobulinemia, positive antinuclear antibody, dsDNA antibodies, and lupus anticoagulants. SLE was diagnosed and treated with corticosteroids. Systemic manifestations and cardiac function improved even after use of diuretics was stopped. Myocardial involvement in SLE is common but often asymptomatic; however, some patients have severe heart failure at SLE onset, as in our case. Lupus myocarditis is a potentially fatal complication of SLE; therefore, early diagnosis and treatment are necessary for recovery and adequate cardiac function.

P1-162

Cardiac failure due to sinus bradycardia after intravenous pulse methylprednisolone therapy in two patients with systemic lupus erythematosus

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Conflict of interest: None

Sinus bradycardia is reported as an adverse effect of high-dose glucocorticoid therapy, and it may be the cause of cardiac failure. We report two cases of systemic lupus erythematosus, who received intravenous pulse methylprednisolone. Their heart rate decreased 42% of baseline from 68 hours after the initiation of therapy and continued for 17 days in case 1, and decreased 57% from 57 hours and continued for 81 hours in case 2. In case 1, diuretics and dopamine formulation improved cardiac failure which appeared after bradycardia. In case 2, ejection fraction in

echo examination and the level of BNP got worse after bradycardia, but both improved in association with elimination of bradycardia. No other reasons were found for bradycardia, suggesting that glucocorticoid pulse therapy affected to their heart rates. SLE itself can be the cause of bradycardia, but bradycardia appeared after glucocorticoid pulse therapy in our cases. Attention to sinus bradycardia is necessary after high-dose glucocorticoid therapy.

P1-163

Analysis of risk factor of Steroid induced psychosis in Sytemic lupus erythematosus

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Conflict of interest: None

In case of treating rheumatological patients, psychiatric events after corticosteroid use are important clinical problem. The degrees of events are various, including from simple insomnia to delusion or hallucination. Steroid itself has been considered to participate in the psychiatric events, and some reports indicated that higher steroid doses would be a risk. However, there were only few studies on the incidence, background features, or its prediction and treatment. In this clinical study, We analyzed the risk factor of Corticosteroid induced psychiatric events retrospectively. Corticosteroid induced psychiatric event were significant in systemic lupus erythematosus (SLE) patients compared with non SLE patient.

P1-164

Spinal Subarachnoid Hemorrhage in a Patient with Systemic Lupus Erythematosus

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Conflict of interest: None

A 63 year-old female had fever and dizziness 2 months after stopping the treatment of rheumatoid arthritis. She was finally transported to our hospital due to suspicion of SLE. The next day of a high-dose corticosteroid (1,000mg dose of methylprednisolone) and 5,000 units of heparin were given, sudden back pain and macrohematuria appeared. She also realized lower limb paralysis and sense of paralysis down from the nipples. The region that has high signal with T2-weighted imaging in MRI was found in wide range of thoracic spinal cord. She immediately transported to another hospital for spinal surgery and spinal epidural hematoma was suspected. However, she refused operation so she turned back to our hospital. In the next day, headache and fever appeared and following MRI revealed that spinal fluid turned out bloody. Head CT scan also revealed that there was hemorrhage at cerebral sulcus and ventricle, but no aneurysm was found. Eventually, we diagnosed her as spinal subarachnoid hemorrhage. She discharged after remission of lupus nephritis by the multi target therapy. This is a rare case of spinal subarachnoid hemorrhage in a patient with SLE. We should examine carefully for this complication if a patient claims back pain, fever, and transverse myelitis.

P1-165

A case of SLE complicated with neuromyelitis optica (NMO) successfully treated with rituximab (RTX)

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Conflict of interest: None

A 30-year-old female was diagnosed with SLE in 2004. She needed intravenous methylprednisolone pulse therapy (IVMP) several times because of recurrent refractory retrobulbar optic neuritis. Although she received therapies with intravenous cyclophosphamide and intravenous immunoglobulin (IVIg), optic neuritis recurred with steroid reduction. In October 2009, visual impairment and sensory abnormalities in the lower limbs occurred. She was diagnosed as NMO by reason of positive anti-aquaporin 4 (AQP4) antibody. She was treated with IVMP and immunoadsorption, and received a combination of PSL, tacrolimus and azathioprine as maintenance therapy. In May 2014, NMO recurred and the titer of anti-AQP4 antibody markedly increased. She was treated with IVMP, immunoadsorption and IVIg again, and we added a treatment with RTX. Her symptoms improved and anti-AQP4 antibody was significantly reduced. In September 2015, NMO recurred and we repeated similar treatment including RTX as induction therapy. PSL monotherapy (15mg/day) currently maintains remission. In this case, the titer of anti-AQP4 antibody seems to be the most sensitive marker of disease activity of NMO.

P1-166

A case of systemic lupus erythematosus with posterior reversible encephalopathy syndrome developing acute visual and visual field disturbance

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Conflict of interest: None

Here we report a case of systemic lupus erythematosus (SLE) with posterior reversible encephalopathy syndrome (PRES) developing acute visual and visual field disturbance at onset of SLE. 56 years-old male noticed refractory headache since more than a half year and he was diagnosed as psychogenic headache. Then he noticed fever and he was admitted to another hospital. Blood test showed that anti-nuclear antibody was positive (ANA, x1280) and he was suspected to having connective tissue disease or acute viral infection. However, a definitive diagnosis was not established at that time and 20mg of prednisolone (PSL) was introduced consequently fever and headache were improved. During the reduction of PSL, headache, fever relapsed. Chest X-ray revealed bilateral pleural effusion. He also had high blood pressure (around 180/100 mmHg) and he was introduced to our hospital for careful evaluation and treatment. At the admission, he noticed acute visual and visual field disturbance. Head MRI showed that diffuse high intensity lesion on occipital lobe indicating possible PRES. He was diagnosed as SLE because of polyarthritis, pericarditis, nephritis and positive both ANA and anti-dsDNA antibody. Control of hypertension resulted in prompt visual and visual field disturbance and MRI findings.

P1-167

Elderly onset neuropsychiatric lupus with rheumatoid arthritis complicating anti-ARS antibody-positive polymyositis

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Conflict of interest: None

A 82-year-old female with RA developed involuntary movements. A month later she was admitted because of the right femoral neck fracture in a fall. She had a high fever, polyarthritis and chorea-like movements. Blood exam showed lymphopenia and low complement, positive for antibodies to anti-dsDNA, anti-Sm, anti-ribosomal P, and anti-CCP. Cerebrospinal fluid analysis showed mild protein increase. Enhanced brain MRI only showed chronic ischemic change. Satisfied SLICC criteria, she was diagnosed SLE and treated with high doses of glucocorticoids. 8 months after the initial treatment, she was admitted again because of a fever with elevated serum muscle enzymes. She had muscle tenderness on her limbs and aspiration pneumonia due to dysphagia. Involuntary movements had relapsed. The anti-ARS antibody was positive. The pathology of muscle

biopsy were consistent with polymyositis. Prednisolone of 1mg/kg per day got poor response. Intravenous immunoglobulin therapy was partially effective, but dysphagia and involuntary movements hardly improved. Twice Rituximab were tried but still ineffective and she died of recurrent aspiration pneumonia. We experienced a rare case of overlap syndrome with elderly onset NPSLE, RA and polymyositis.

P1-168

Systemic lupus erythematosus with aseptic meningitis

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Conflict of interest: None

Object/Methods: Systemic lupus erythematosus (SLE) is a systemic disease including pathological change of central nerve system. Aseptic meningitis is a rare manifestation of SLE, but we recently diagnosed our patient as aseptic meningitis when SLE recurred. Therefore, we conducted the study to review past literatures and consider our case from past reports. Results: Our patient was a 29-year-old woman who have diagnosed as SLE 6 years ago. She developed fever and headache. Neurological examinations were normal, and neck stiffness was not present. She was finally diagnosed as aseptic meningitis with recurrent SLE by results of lumbar puncture. 12 cases were detected from searching by PubMed. The mean age of onset was 29 years old. The most patients had fever and headache, while some patients had neurological signs alone such as muscle weakness. All patients were diagnosed by lumbar puncture and received the therapy using steroid. The symptoms of some patients including our case have improved, but one patient has died. Conclusions: We described a case of aseptic meningitis presenting as exacerbation of the disease in a patients with SLE. Although aseptic meningitis is uncommon in SLE, it is necessary to mind meningitis because it is sometimes difficult to diagnose and treat.

P1-169

A case of SLE complicate with optic neuritis associated with anti aquaporin4 anitibody

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Conflict of interest: None

The patient was 41-year-old woman. She was admitted to SLE and treated with prednisolone PSL. She had eye pain and reduced visual acuity, after her common cold in March 2016. She admitted to our hospital and was diagnosis of right optic neuritis. After twice steroid pulse therapy and administrating 30mg of PSL/day, her symptoms were improved. During tapering 6mg of PSL, visual acuity of left eye was reduced in July 2016. After same therapy, her symptom were improved. Anti aquaporin (AQP)4 antibody was positive in her serum. She was diagnosed with optic neuritis associated with anti AQP4 antibody. Optic neuritis associated with anti AQP4 antibody is one of neuromyelitis optica spectrum disorder. It is characteristic feature of optic neuritis and myelitis. Various autoantibody is positive in its patients. So it is complicated with collagen tissue disease.

P1-170

Case report: It was difficult to diagnose NPSLE because it was antibody negative in blood

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Conflict of interest: None

A 32-year-old female, She had an unknown fever and had a history of inpatients at 12 and 29 years old. At 29 years old she had relaxed fever of 40 ℃, liver injury, hepatosplenomegaly, systemic lymphadenectomy, original yellow platelet original document, inflammatory response high level for about 10 days, but it was spontaneously refreshed. She was diagnosed as ITP and started PSL 55 mg and gradually decreased at 32-year-old. 2 months before hospitalization Fever and abdominal pain were admitted, so we admitted to our department of digestive organs, CTRX and PSL administered temporarily, C1 inhibitor deficiency was suspected but did not meet the diagnostic criteria. Her gastrointestinal symptoms improved, she was discharged temporarily, but she had a strong nausea, fever abdominal pain, sore throat and consciousness disorder, and anemia was also recognized. Antinuclear antibody was speckled pattern before admission until now, but anti-ds-DNA antibody, anti-Sm antibody, anti-phospholipid antibody negative, only anti-SS-B antibody was positive. Because of low haptoglobin, high IL - 6 in cerebrospinal fluid, diagnosis of NPSLE, mPSL pulse, IVCY, HCQ administration and NPSLE improvement were confirmed. MMF was administered as a post-therapy, and the remission is currently ongoing.

P1-171

Lupus anticoagulant-hypoprothrombinemia syndrome in a patient with systemic lupus erythematosus

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Conflict of interest: None

A 19-year old woman was admitted to our hospital because of fever, arthralgia and pancytopenia. She was diagnosed as SLE, based on cutaneous lupus, hemolytic anemia, leukopenia, thrombocytopenia, positive anti-nuclear/DNA/Sm antibodies (Abs) and hypocomplementemia. Antiphospholipid Abs including lupus anticoagulant (LA), anticardiolipin and anti-β2 glycoprotein I were positive. Brain MRI revealed cerebellar infarction. Because of prolonged prothrombin time (41%), other coagulation factors were analyzed, that showed decreased activities in factor II (FII), VIII, IX, X, XI and XII. Inhibitors for factor VIII and IX were also detected by Bethesda method. Since FII activity was severely low (25%) and phosphatidylserine-dependent anti-prothrombin Abs was positive, the diagnosis of LA-hypoprothrombinemia syndrome (LA-HPS) was made. Interference by the high-titer LA might have caused broad coagulation abnormalities in this case. The patient was treated with steroid, cyclosporine, aspirin and warfarin. While patients with LA-HPS are generally at a very high risk for severe bleeding, neither hemorrhagic nor thrombotic event occurred thereafter except for silent cerebellar infarction at diagnosis. We report a rare case of SLE-associated LA-HPS, and review literature.

P1-172

A successful treatment of hydroxychloroquine for pancytopenia in a case of systemic lupus erythematosus

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Conflict of interest: None

The patient is a 60-year-old woman with the complaint of polyarthralgia. She had polyarthritis from 46 years old, and was diagnosed as Sjogren's syndrome because of hyposalivation and positive for anti-SSA and anti-SSB antibodies at 49 years old. At 59 years old, she had suffered from left knee synovial bursitis accompanied by skin ulcer, skin erythema and pancytopenia and visited to our hospital. Her laboratory findings revealed elevation of serum C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), hypocomplementemia and positive titers for antinuclear antibody, anti-DNA antibody and anti-Sm antibody. These findings were compatible with systemic lupus erythematosus (SLE). Her bone marrow examination revealed markedly decreased hematopoietic

cells. She began to receive hydroxychloroquine (HCQ) 200mg/day therapy for SLE after skin ulcer improved. CRP, ESR and anti-DNA antibody levels were normalized followed by her arthritis remission after treatment with HCQ. Also pancytopenia has been gradually ameliorated. The therapeutic efficacy of HCQ for pancytopenia in SLE is still under discussion in Japan. In the future, an increasing case number of SLE various complications, such as hematological abnormality, that was treated with HCQ may be encountered.

P1-173

Primary antiphospholipid syndrome with renal injury, involuntary movement and sensory dysfunction successfully treated via immunosuppression

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Conflict of interest: None

A 45-year-old man was admitted to our hospital with exacerbation of proteinuria, uric blood and decreased renal function. Physical examination revealed edema in his lower extremities, as well as sensory dysfunction and choreo-athetosis in his right arm. Laboratory examination revealed thrombocytopenia, prolonged activated partial thromboplastin time, elevated creatinine, and antiphospholipid antibodies (aPLs). Enhanced computed tomography showed chronic occlusion of the supramesenteric artery. The patient was diagnosed with primary antiphospholipid syndrome (PAPS) and was initially scheduled to receive only anticoagulant therapy. However, further examination revealed membranoproliferative glomerulonephritis and elevated interleukin 6 in the cerebrospinal fluid, which promoted us to add immunosuppressive therapy to his treatment plan. As a result, all of his symptoms gradually improved. Although only anticoagulation therapy is typically used for PAPS, the effectiveness of additional immunosuppressive therapy hasn't ever been established. Nevertheless, because aPLs are reported to provoke not only coagulation but also the inflammatory cascade, we believe that immunosuppressive therapy may be effective in selected patients with PAPS, as shown in our case.

P1-174

Repeated hemorrhagic events due to inhibitors against coagulation factors in a case of SLE with antiphosphplipid antibodies

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Conflict of interest: None

Antiphospholipd syndrome is characterized by recurrent arterial and venous thrombosis and intrauterine complications. In contrast, hemorrhagic manifestations occur in patients who developed autoantibodies against coagulation factors. Both conditions may be comorbidities of SLE. We report here a case of SLE with antiphospholipid antibodies presenting as repeated intracranial hemorrhage due to inhibitors against coagulation factors. A 28-year-old female who had histories of idiopathic thromcytopenic pupura and SLE was admitted to Tokai University Hospital because of intractable headache. Cranial CT showed bilateral subdural hematoma. She had histories of subdural hematoma twice and hypermenorrhea. At the time of admission, she had polyarthralgia and cytopenia, Prolongation of coagulation time, positive antinuclear antibodies, positive anticardiolipinβ2 GPI antibodies/lupus anticoagulants were observed. In addition, inhibitors against both factors XIII and IX were present. After the treatment with prednislone 30mg/day, factor VIII and IX activity returned in normal range, inhibitors against factors VIII and IX decreased and subdural hematomas reduced in size.

P1-175

Two case of hydroxychloroquine is effective for refractory thrombopenia complicated with systemic lupus erythematosus (SLE)

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Conflict of interest: None

Clinical significance:The thrombopenia occurs in about 30% of SLE. The efficacy of hydroxychloroquine (HCQ) is reported as treatment of refractory thrombopenia complicated with SLE. We report two cases that HCQ was effective for refractory thrombopenia. Case 1: 25 years old female. She had presented thrombopenia, mala rash and positive test results for anti-nuclear antibodies, anti-double stranded DNA-antibody. She was diagnosed as SLE, and was administered 30 mg prednisolone (PSL) daily. She did not improve in thrombopenia. We tried to immunosuppressive drugs (tacrolimus and mizoribine), but there was not improvement in the thrombopenia. She was administered 200mg/400mg HCQ alternatively on every other day. Her platelet counts increased from 60,000 to 130,000. Case 2: 80 years old female. She had a diagnosis of SLE with thrombocytopenia 26 years ago. She decreased 10mg PSL daily, but she decreased platelet count from 170000 to 60000. We administered 200mg HCQ daily to her, and the platelet count was improved from 60,000 to 100,000. HCQ was effective for refractory thrombopenia complicated with SLE in two of four cases in our department. HCQ is a good second-line treatment for refractory thrombopenia complicated with SLE.

P1-176

Successful treatment of puerperium deep vein thromboses with intravenous high-dose immunoglobulin in a patient with antiphospholipid syndrome

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Conflict of interest: None

We report the case of a 40-years old woman with mixed connective tissue disease and puerperium deep vein thromboses (DVTs) due to antiphospholipid syndrome (APS). Her DVTs did not respond to low dose aspirin, intravenous unfractionated heparin and warfarin. Because several reports and studies have indicated faborable results of intravenous high-dose immunoglobulin (IVIg) therapy for DVTs due to APS, IVIg was additionally given postpartum at 400 mg/kg/day×5days. The DVTs improved gradually, and there were no adverse effects. We conclude that IVIg is worth trying in such patients if they fail to respond to conventional treatment.

P1-177

Multiple primary manifestations such as bicytopenia, lupus peritonitis, pulmonary hypertension, portal vein thrombosis, lupus retinopathy in a patient with systemic lupus erythematosus

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Conflict of interest: None

【Case】A 43-year old woman presented with abdominal distension for 10 months was admitted to the Department of Rheumatology in January 2016. Based on her clinical and laboratory findings of malar rash, bicytopenia, lupus peritonitis, pulmonary hypertension, portal vein thrombosis, lupus retinopathy, anti-dsDNA antibodies, hypocomplementemia, a diagnosis of SLE was made. Pulse intravenous cyclophosphamide (0.625 g/m^2) once a month for 4 consecutive months with daily *oral* prednisolone (1mg/kg) was started, and portal vein thrombosis, serositis, pulmonary hypertension, bicytopenia improved dramatically. However, ascites and hypocomplementemia didn't improve. Further immunosuppressant therapies should be needed, and mycophenolate mofetil (2 g/day) and tacrolimus (4 mg/day) were administered additionally as maintenance therapies. After administration, ascites and hypocomplementemia were improved and she was discharged from the hospital.【Clinical Significance】

As systemic manifestations, lupus peritonitis accompanied with portal vein thrombosis are extremely rare in SLE. In our case, systemic manifestations improved dramatically with prednisolone, intravenous cyclophosphamide, mycophenolate mofetil, and tacrolimus. Previously reported patients are summarized and briefly reviewed.

P1-178

Clinical and pathohistological features of renal biopsy proven MPO-ANCA associated vasculitis

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Conflict of interest: None

[Objectives] Our goal is to assess the clinical and pathohistological features of MPO-ANCA associated vasculitis with glomerulonephritis. [METHODS] 21 patients with MPO-ANCA associated vasculitis who had been admitted to our hospital and undergone renal biopsy were enrolled. All patients met the Watt's criteria for vasculitis. We assess the correlation among clinical characteristics, laboratory data, and pathohistological findings. [RESULTS] According to Watt's algorism, EGPA, GPA and MPA patients were 4, 5, and 12, respectively. Pathohistological classification of renal biopsy were as follows; sclerotic 4, focal 12, crescentic 3, and mixed 2. Intensive therapies included mPSL pulse therapy 15, IVCY 8 and IVIG 2, following oral PSL. 16 patients had good prognosis, while 5 patients had poor. Sclerotic change of renal histology, but cellular crescent, was positively associated with renal prognosis. [CONCLUSIONS] Our data suggests that chronic lesions such as global sclerosis in kidneys could cause poor renal prognosis, while active lesions cellular crescent might have good response for therapies We considered that physicians should try to perform renal biopsy for predicting the disease activitiy, the response for therapy, and the prognosis of renal function.

P1-179

Characterization of immune cell subsets in patients with ANCA-associated vasculitis

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Conflict of interest: Yes

[Object] With recent advances in human immunology, many different kinds of subset in immune cells defined by cell surface marker expression patterns have been identified. However, the evidence of analysis for immune cell subsets with the recent definition has been scarce in ANCA-associated vasculitis (AAV). [Methods] Seven AAV patients and 32 healthy controls (HCs) were included in the study. All patients were classified into either granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) according to European medicines agency algorithm. Lymphocytes subsets in both groups were analyzed by flow cytometry, which identified 24 immunophenotypes using the same gating strategies in Human Immunology Project. We characterized immune cell subsets in the patients with AAV by comparing frequency for each subset between the two groups. [Results] The analysis revealed significant decrease in T cells, B cells, Tfh, aTreg, naïve CD8+ T cells, and mDC in the patients with AAV compared to HCs. In contrast, the frequency of Th2 and DNB were significantly elevated in AAV (p-values <0.05). [Conclusions] The study showed substantial differences in the frequency of immune cell subsets between the patients with AAV and HCs. The result implies that specific subsets may play a role in AAV.

P1-180

Neutrophil CD64 expression in systemic vasculitis

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Conflict of interest: None

Objectives. The neutrophil CD64 expression has been reported to be increased by various infections, interstitial pneumonitis and rheumatic diseases other than rheumatoid arthritis. We therefore investigated the neutrophil CD64 expression in patients with vasculitis. Methods. Thirty-four patients with active vasculitis without infection, 7 patients with vasculitis and infectious diseases were enrolled. The number of CD64 molecule on neutrophils of the peripheral blood was quantitatively assessed by using flow cytometry and 2000 molecules per cell was set to the upper normal limit. Results. The neutrophil CD64 expression in 79% of patients with active vasculitis was within the normal range (1432.2±1287.7 mol. / cell), and significantly lower than that in patients with vasculitis and infectious diseases (7629.4±5044.9 mol. /cell). The neutrophil CD64 in 3 patients with active interstitial pneumonitis of vasculitis has a tendency to be higher than those without it. Conclusions. The neutrophil CD64 was within normal range in the majority of the patients of active vasculitis without interstitial pneumonitis or infectious diseases. The results indicate that the neutrophil CD64 can be useful to distinguish infectious diseases in patients with active vasculitis.

P1-181

Interleukin-6 as a therapeutic target in patients with anti-neutrophilic cytoplasmic antibody-associated vasculitis

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Conflict of interest: None

It has been reported that inflammatory cytokines such as IL-1b, TNF, IL-6, and IL-8 may have important roles in the pathogenesis of granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA), and several studies suggested the efficacy of tocilizumab (anti-IL-6 receptor antibody) in patients with refractory or newly developed diseases. To identify possible therapeutic targets of MPA and GPA, we investigated serum levels of IL-6 in healthy controls (n=26) and patients with newly developed MPA (n=30) and GPA (n=30) who were registered to a nationwide prospective cohort study, RemIT-JAV-RPGN, and associations with clinical characteristics. Median age of the patients were 68.5 years, 32 were female, and 46 were MPO-ANCA positive and 14 were PR3-ANCA positive. The serum levels of IL-6 of the patients at baseline were significantly higher than that of healthy controls, and decreased at 6 months after the induction treatment (from 82.8 to 7.4pg/mL, $p<0.001$ by Wilcoxon test). The serum levels of IL-6 at baseline tended to be higher in patients with MPA, having BVAS renal items at baseline, or achieving remission at 6 months after the induction treatment. IL-6 is a candidate therapeutic target of MPA and GPA.

P1-182

4cases; Induction therapy with prednisolone and mycophenolate mofetil for ANCA-associated vasculitis

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Conflict of interest: None

[Objectives] We investigated the efficacy and safety of combination therapy with prednisolone and mycophenolate mofetil (MMF) for ANCA-associated vasculitis (AAV). [Methods] Four patients (3 MPA, 1 EGPA) were included. [Results] Median age was 76 years, 3 were female. Initial induction were used in 3 and recurrence in 1. In organ involvements, rapid-progressive renal damages were observed in 2, mononeuropathy multiplex in 2, interstitial pneumonia in 1, asymptomatic cerebral infarction in 1. Median PSL and MMF dose were 50 mg/day and 1500 mg/day, respectively. During 3 months course, although activities of AAV were improved dramatically in all patients, infections were complicated in all cases: bacterial pneumonia in 1, sepsis in 1, cytomegalovirus viremia in 3, and they improved by anti-bacterial agents and gancyclovir. [Conclusions] Combination therapy with PSL and MMF was effective for AAV, but complicating infections due to immunesuppressive therapy should be considered carefully.

P1-183

The Efficacy and Safety of rituximab in Granulomatosis with Polyangitis with hypertrophic pachymeningitis

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Conflict of interest: None

Background. hypertrophic pachymeningitis (HP) is a refractory lesion with ANCA associated vasculitis like Granulomatosis with Polyangitis (GPA). Rituximab (RTX) is reported to be useful agent for treatment of HP. purpose. We retrospectively analyzed the efficacy and safety of RTX in four patients with GPA who have HP. patients. Patients were 72-75 years old women. Disease duration is 32-71 months. Three of four patients were administered Intermittent pulse intravenous cyclophosphamide therapy. Additionally, all patients were received other immunosuppressant [tacrolimus (n=1), cyclosporin (n=2), azathioprine (n=1)]. In spite of these therapy, improvement in HP was not observed. Therefore they received treatment with RTX (375mg/m2/week four times), and consequently the lesion of HP was clearly improved. Although some complications [brain abscess (n=1), Pneumocystis jiroveci pneumonia (n=1), herpes zoster (n=2)] were occurred after the initiation of RTX, these were improved by appropriate therapy. result. In this report, we show that treatment with RTX is beneficial for patients with GPA who have refractory HP.

P1-184

Efficacy and safety of Rituximab for ANCA associated vasculitis

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Conflict of interest: None

Objectives: To validate the efficacy and safety of rituximab (RTX) for ANCA associated vasculitis (AAV) patients at our hospital. **Methods:** The subjects were 19 cases including 14 of first onset and 5 of recurrence. Ten were males and 9 females. All of them had MPO-ANCA positive: 16 MPA, 2 GPA and 1 unclassified. The mean age at the first induction of RTX was 74y.o. (range: 40-82). The efficacy was evaluated according to BVAS at the time of first induction and month 6. The safety was evaluated by adverse events within the 6 months. **Results:** <Efficacy> The mean BVAS decreased from 16 (range: 7-35) to 0 (0-4). Out of 10 cases, 7 cases achieved remission (BVAS=0) (remission rate 70.0%). The titer of MPO-ANCA decreased 97.9 (9.9-300) to 41.1 IU/mL (1.0-114.0). The dose of prednisolone decreased 35.0 (5-60) to 4.5mg/day (0-10). <Safety> The adverse events were as follows: 3 cases of reactivation of CMV, 1 of CMV colitis, 1 of sepsis by urinary tract infection, 1 of pneumonia. One MPA patient died of exacerbation of the original disease. **Conclusions:** Most of AAV in Japan are with elderly patients. RTX can be expected a high efficacy of treatment and it can also contribute to the decrease of dose of prednisolone. Careful monitoring of infectious diseases is required.

P1-185

Low dose rituximab therapy for ANCA-associated vasculitis

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Conflict of interest: None

Introduction: Rituximab is the agent for ANCA-associated vasculitis. There are few reports discussing about reduction regimen. Here we investigated the utility of single or twice administration of rituximab 375 mg / mm2 for MPO-ANCA positive or biopsy-proven ANCA-associated vasculitis. METHODS: Retrospective review of electric medical record was performed for all the 6 patients who received single or twice administration of rituximab 375 mg / mm 2 for ANCA-associated vasculitis. PR3 - ANCA positive cases, or cases of alveolar hemorrhage or severe renal dysfunction which requires hemodialysis were excluded. RESULTS: 6 patients were given single or twice administration of rituximab 375 mg / mm 2 for MPO-ANCA positive or biopsy-proven ANCA-associated vasculitis. The mean age was 74.5 years. 5 cases were MPO-ANCA positive, and 1 case is ANCA negative biopsy proven ANCA-associated vasculitis. All patient have lung or renal involvement. After the treatment, pulmonary lesions and renal involvement were improved in all cases at 4 weeks and no severe adverse event such as severe infections were seen. CONCLUSION: This study demonstrated the possible efficacy and safety of reduced administration of rituximab for ANCA-associated vasculitis.

P1-186

Study of remission induction therapy of microscopic polyangiitis in our hospital

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Conflict of interest: None

<Objective>Because the outcome of remission induction therapy is considered to be improved by treatment according to guidelines, we compare hospitalization treatment of MPA in our hospital. <Method>We extracted 27 patients of MPA who were first hospitalization treatment that diagnosis in our hospital from 2001 to 205 and 2011 to 2015. 15 patients from 2001 to 2005 were defined as initial groups, and 12 patients from 2011 to 2015 were defined as the late groups. We investigated and analyzed patients who diagnosed as definite MPA used MPA diagnostic criteria of Japan. <Result>7 patients in initial groups and 5 in late groups were mild, and both 7 patients were severe, only 1 patients in initial groups was most severe. Usage rate of steroid pulse therapy was 93% and 8%, more of initial groups. Among patients in which infection occurred during hospitalization, 27% and 8%. The average length of hospitalization was 84 and 43 days, and the late group was short. All patients were discharged after remission. <Result>There was a clear difference in the usage rate of steroid pulse therapy, but no difference in severity. Treatment according to the guidelines seems to affect the reduction of infectious diseases and shortening of hospitalization period.

P1-187

Strawberry gingivitis as an early manifestation of granulomatosis with polyangiitis

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Conflict of interest: None

Hyperplastic granular gingivitis, also known as “strawberry gingivitis”(SG), is a characteristic oral presentation of granulomatosis with polyangiitis (GPA). We report a case of a 38-year-old woman who complained of swollen gums, which had an over-ripe strawberry appearance. Examination revealed pulmonary involvement and a positive finding for PR3-ANCA. A gingival biopsy showed granulomatous infiltration, neovascularization, inflammatory cell infiltration, and pseudoepitheliomatous hyperplasia. These clinical features suggested a diagnosis of GPA. A moderate dose of systemic corticosteroids and methotrexate were effective. To confirm her diagnosis, we conducted a literature review of SG accompanied with GPA. Most cases were positive for PR3-ANCA/c-ANCA (14/16). Most patients were regarded as localized or being at the early systemic stage. The most common complication was ear, nose, and throat involvement (16/23), which supported the diagnoses of GPA. Some showed pathological proof of vasculitis with granulomatous formations, suggesting that SG is a typical feature of GPA. These findings suggest that SG is an early manifestation of GPA, and GPA should be considered for patients who present with swollen gums.

P1-188

A case of tumorous lesion of maxillary sinus with exophthalmos under treatment as Goodpasture syndrom

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Conflict of interest: None

A 80-year-old man, treating as Goodpasture syndrome, multiple erythemas were seen in both lower legs and diagnosed as leukocytoclastic vasculitis by biopsy in April, 2016. The erythema decreased by corticosteroid treatment. One month later, he noticed right exophthalmos. By MRI examination, tumorous lesion was seen in right maxillary sinus. Radiographically, malignant lymphoma, fungal infection or granulomatosis with polyangiti (GPA) were suspected. Immunoserologically, he showed ANCA negative. Biopsies were done twice from nasal cavity. Histopathologically, specimens showed severe inflammatory change with basophilic necrosis. We diagnosed as GPA. This case shows typical histological findings of GPA, but clinically not typical.

P1-189

Efficacy of adalimumab in ANCA-positive large vessel vasculitis with ulcerative colitis

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Conflict of interest: None

[Clinical Case] A 28-year-old Japanese female, who developed ulcerative colitis (UC) at the age of 11. When 25 years old, she was admitted with fever, cough, left neck pain and upper limb pain. Laboratory data showed elevated CRP, ESR and high titers of PR3-ANCA, MPO-ANCA. Contrast CT revealed concentric wall thickening of the left common carotid artery. HLA studies showed B52 allele. Takayasu’s arteritis (TA) was suspected, and ANCA-associated vasculitis with large vessel lesion was also considered. Prednisolone (PSL) 30mg/day was started. After remission, she repeated transient left neck pain while tapering PSL. Although azathioprine and cyclosporine were added, relapse occurred at the time of PSL 7mg/day. PSL 50mg/day was effective, but difficult to reduce because of discontinuing cyclosporine (due to legs pain so-called “calcineurin-induced pain syndrome”). After initiation of adalimumab, remission is maintained and PSL is tapered to 9mg/day without any symptoms. [Discussion] There is few reports about ANCA-positive large vessel vasculitis with UC. The clinical presentation is typical for that of TA, and HLA-B52 is positive, which is usually seen in Asian cases coexisting TA and UC. This case report suggests that adalimumab may have great efficacy in such patients.

P1-190

A case of rheumatoid arthritis (RA) complicated with microscopic polyangiitis (MPA)

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Conflict of interest: None

We report a case of RA complicated with MPA in 69-year old woman. She had a three-year history of RA. She had been treated with MTX and NSAIDs. One year after the diagnosis of RA, she presented with hematuria, proteinuria and decline in renal fanction (Cr 0.99 mg/dl). She had begun to experience numbness in both lower limbs three months earlier. She presented with purpura in her legs. Her renal function gradually decreased (Cr 1.1 mg/dl), so MTX and NSAIDs were discontinued. But her purpura and renal function were worsened (Cr 1.3 mg/dl). Laboratory evaluations were as follows:leukocytes 6000 /μl, CRP 0.34 mg/dl, and MPO-ANCA >300 IU/l. EMG showed mononeuritis multiplexus. A biopsy of skin showed necrotizing vasculitis. A renal biopsy demonstrated pauci-immune necrotizing crescentic glomerulonephritis. For these things, we diagnosed as MPA complicating RA. She was treated with mPSL 1g intravenously, followed by PSL 50 mg/day and IVCY with improvement of her purpura, numbness and renal function (Cr 0.79 mg/dl). It has been reported that MPO-ANCA associated crescectic glomerulonephritis often showed a slowly progressive deterioration of renal function. It is important to consider a diagnosis of MPA when RA patients demonstrate new-onset urinary abnormalities or renal impairment.

P1-191

Retinal and choroidal detachment in ANCA-associated scleritis and retinal vasculitis mimicking choroidal tumor

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Conflict of interest: None

<Case> One year ago, a 86-year-old woman was diagnosed with myeloperoxidase-anti-neutrophil cytoplasmic antibody (MPO-ANCA) positive microscopic polyangiitis (MPA). By steroid therapy, it was in remission and maintained by predonisolone (PSL) 10mg daily. However, the hyperemia of left eye developed and moreover rapidly progressive decrease of visual acuity for 1 month was also revealed. Retinal vasculitis was demonstrated by funduscopy. Magnetic resonance imaging (MRI) showed a protrusive tumorous lesion from juxta-retinal macular area in left eye. Optical coherence tomography showed the edematous detachment between choroid and retina in left eye. Finally she was diagnosed with choroidal and retinal edematous detachment due to ANCA-associated scleritis and retinal vasculitis. Visual acuity improved by combined therapy with increased PSL and azathioprine, and choroidal and retinal edematous detachment resolved. <Conclusion> Choroidal and retinal edematous detachment due to ANCA-associated scleritis and retinal vasculitis is very rare, however is notable to mimick choroidal tumor. This case should remind clinicians to consider choroidal and retinal edematous detachment as a rare cause of rapidly progressive decrease of visual acuity in patients with MPA.

P1-192

A case of ANCA associated vasculitis (AAV) complicated with cyclophosphamide-induced hemorrhagic cystitis (CPM-HC) and posterior reversible encephalopathy (PRES)

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Conflict of interest: None

A 72-year-old woman was admitted to our hospital because of progressive edema on legs, microhematouria, albuminuria and positive MPO-ANCA. We performed renal biopsy and it revealed the findings compatible with vasculitis (internal elastic membrane ruptures and fibrinoid necrosis in interlobular arteries), so she was diagnosed as AAV (MPA). PSL at the dose of 25mg/day was started and cyclophosphamide (CPM) 400mg (300mg/m^2) with sufficient infusion and mesna were administered intravenously (IVCY). One day after the administration her consciousness deteriorated suddenly accompanied by generalized convulsion. MRI (T2WI) showed high signals in white matter of occipital lobes, and we diagnosed her as PRES, from which she recovered with depressors and anticonvulsants. Just after the convulsion, the amount of urine decreased and apparent hematuria was noticed. We diagnosed her as CPM-HC and performed continuous saline perfusion to her bladder, which led her urine clear. There is no cases of CPM-HC with such a small amount of IVCY. We speculate that sudden increase of BP resulted in PRES and decrease of urine amount, leading to CPM-HC. When we perform IVCY, we should control high BP, which relates to the onset of PRES. We also emphasize that PRES can develop in MPS.

P1-193

Successful induction of remission with rituximab for a case of refractory granulomatosis with polyangiits complicated with pulmonary aspergillosis

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Conflict of interest: None

The patient was 71-year-old woman. She had serous otitis media for left ear 1 year ago. Because the symptom was not improved, the patient was referred to our hospital. Biopsy of nasal mucosa was performed since mucosal hypertrophy was found in nasal septum with positive result for serum MPO-ANCA. As the biopsy results, it was clinically diagnosed as granulomatosis with polyangiits (GPA). The symptom was improved by oral administration of prednisolone (PSL) (30mg/day) and methotrexate. Four months ago, headache and double vision appeared and hypertrophic pachymenigitis was detected by MRI. Steroid pulse and intravenous cyclophosphamide (IVCY) were performed and her symptom gradually disappeared. After 3 times injection of IVCY, she recognaized visual loss for left eye. Left optic neuritis was detected by MRI. Optic neuritis was improved gradually by steroid pulse and following oral administration of PSL (50mg/day). At the same time, she was complicated with pulmonary aspergillosis (PA), and it was gradually cured by oral administration of voriconazole. Later, we could maintain long-term remission of GPA by rituximab without PA flare by using maintenance therapy of voriconazole. Rituximab could be a therapeutic option for the patients complicated with fungus infection.

P1-194

2 patients with Central nerve systems involvement of ANCA associated vasculitis treated with rituximab successfully and whose C-reactive proteins increased temporaly

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Conflict of interest: None

[Background] It is difficult to diagnose and treat CNS involvement of ANCA associated vasculitis (AAV). It is common that CRP level rises after treatment with rituximab (RTX) for malignant lymphoma, but that is uncommon for AAV. We report two patients with AAV whose CNS involvement were treated successfully with RTX and showed high CRP level. [Case 1] A 70-year-old male was diagnosed AAV by otitis media and MPO-ANCA 17.4U/ml. He achieved remission after treatment with prednisolone and IV-CY. His disease relapsed with headache, hearing loss and facial nerve palsy. Cranial MRI showed a nodule at internal acoustic meatus. He was treated with prednisolone and IV-CY insufficiently. Then he was treated with RTX successfully. After treatment his CRP level increased temporal. [Case 2] A 67-year-old female was diagnosed AAV by mononeuritis multiplex and MPO-ANCA 23.7U/ml. She achieved remission after treatment with prednisolone. Her disease relapsed with headache and dysphagia. Cranial MRI showed the thickening dura mater with enhancement, revealed hypertrophic pachymeningitis. She was treated with prednisolone and RTX. While giving RTX her CRP level increased high, so it was difficult to distinguish between infectious disease and AAV, but CRP level was normalized spontaneously.

P1-195

A acute worsening case of anti-neutrophil cytoplasmic antibody (ANCA)-negative microscopic polyangiitis (MPA) with effective of early diagnosis and immediate treatment intervention

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Conflict of interest: None

We report a case of 43-year-old ANCA-negative MPA patient with effective of early diagnosis and immediate treatment intervention. He was admitted to our hospital because of sudden leg edema, ankle, and leg pain with proteinuria and hematuria. After admission, his renal function and respiratory status were rapidly worsening day by day. Chest computed tomography (CT) scan showed a new appearance of subpleural pulmonary nodular lesions, which had been undetectable at the first presentation. His nerve conduction velocity study for tibial and sural nerve was suggestive of mononeuropathy multiplex. Renal biopsy performed on the second day showed the crescentic glomerulonephritis. Though his serum tests of both MPO and PR3-ANCA were negative, he was diagnosed with MPA from renal pathological, neurological findings and pulmonary involvement. Methylprednisolone pulse therapy following daily oral prednisolone (60mg/day) was administered, resulting in improvement of his renal dysfunction and ameliorating hypoxemia. Moreover, follow-up chest CT scan showed the disappearance of pulmonary nodular lesions. This is the intriguing case of ANCA negative MPA having a rapidly progressive clinical course with effective of early diagnosis and immediate treatment intervention.

P1-196

A case of microscopic polyangiitis which relapsed with alveolar hemorrhage after a long-term remission for 12 years on maintenance hemodialysis

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Conflict of interest: None

A 58-year-old woman received a diagnosis of microscopic polyangiitis (MPA) in 2001 based on rapidly progressive glomerulonephritis and positive MPO-ANCA. Renal biopsy showed focal segmental necrotizing glomerulonephritis with crescents. Despite treatment with aggressive immunosuppressive therapies, her renal function declined and she underwent maintenance hemodialysis (HD) in Mar 2004. The immunosuppressive therapy was then totally discontinued in 1 year after introducing HD. Thereafter, no recurrence of vasculitis was observed for more than 10 years, while MPO-ANCA was persistently detected at low titers. In Jan 2016, she manifested hemoptysis, dyspnea, and progressive anemia. Chest CT revealed diffuse ground glass opacity. While MPO-ANCA was not elevated and CRP was negative, diagnosis of diffuse alveolar hemorrhage due to MPA was made, since there was no other cause for alveolar

hemorrhage such as drug or infection. She was successfully treated with a combination of steroid pulse therapy and plasma exchange. MPO-ANCA became nearly undetectable. While relapse of vasculitis is relatively rare after long-term remission periods on maintenance HD, physicians should pay attention to recurrence of vasculitis as a cause of alveolar hemorrhage.

P1-197

A case of antineutrophil cytoplasmic antibody (ANCA) related vasculitis presenting various lesions such as temporal artery involvement and hypertrophic pachymeningitis

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Conflict of interest: None

A 67-year-old-woman was diagnosed with scleritis in July, 2016. She was treated with 30mg/day of prednisolone (PSL). Although PSL was tapered off in about 2 months, the symptom was not improved. Subsequently, she was diagnosed with left ottitis media with effusion, right sensorineural hearing loss and sinusitis. She had headache at both the temporal regions and fever from October. Ultrasound sonography (US) showed thickening of right temporal artery and laboratory tests showed elevated C-reactive protein and MPO-ANCA. Her right eyesight reduced gradually. She was treated with 250mg/body of methylprednisolone (mPSL). Although, she had no lesions of skin, lung, kidney and peripheral nerve, magnetic resonance imaging showed hypertrophic pachymeningitis and US revealed beaded aneurysm and coarcraction of both temporal arteries. Fundus examination showed the right blocked central artery of retina. After mPSL therapy, she was treated with 70mg/day of PSL and intravenous pulse cyclophosphamide. We will discuss the relation between ANCA related vasculitis and these manifestations.

P1-198

A case of ANCA-associated vasculitis which relapsed with symptoms of Tolosa-Hunt syndrome and treated with rituximab

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Conflict of interest: None

A 72-year-old woman, previously diagnosed with ANCA-associated vasculitis and treated with intravenous cyclophosphamide, presented with three-month history of weight loss, worsening of numbness, and one-month history of diplopia and pain of left forehead. She had left ptosis, and her left ocular movement was limited to abduction only. Her right ankle was swollen and had tenderness. Serum CRP and ESR were high as 3.03 mg/dl and 37mm/1h. Magnetic resonance imaging (MRI) in head revealed mass in the left of sella turcica which had low signal in T2WI and highly enhanced with gadolinium. She was treated with mPSL 1g per day administrated in first three days and four course of rituximab (RTX) equivalent to 375mg/m^2, and RTX was administrated once in six months. Clinical findings improved rapidly. MRI finding resolved in two months and sustained remission in fourteen months. A few reports in past demonstrated lesions of cavernous sinus in patients with vasculitis. Our case suggested that RTX is effective in such cases. Because it is often difficult to obtain biopsy samples, therapeutic diagnosis should be considered to exclude other cause, including tumor or abscess.

P1-199

Comparsion the histological findings in temporal artery biopsies of three ANCA-positive patients with cranial symptoms

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Conflict of interest: None

【Introduction】We compared the tissues of temporal artery biopsies (TAB) from three ANCA-positive patients with systemic symptoms and cranial signs.【Case1】A 80-year-old man presents with dullness of lower limbs, jaw claudication and dysgeusia. Interstitial pneumonia was suspected on his CT and his CRPand MPO-ANCA were high. A TAB revealed occlusive vasculitis of small arteries with a spared temporal artery. Microscopic Polyangitis was diagnosed.【Case2】A 68-year-old woman presents with dry cough, difficulty in hearing, leg pain and cranial symptoms. Mass-like liesions in her lungs were seen bilatelally on CT and her CRP and MPO-ANCA were high. A TAB revealed vasculitis with fibrinoid necrosis involving small vessels adjacent to a little inflamed temporal artery. Granulomatosis with Polyangitis was diagnosed.【Case3】A 83-year-old man presents with fever, cranial symptoms and partial numbness of limbs. Although his MPO-ANCA titer were 2340IU/ml, TAB specimens revealed classic giant cell arteritis. His symptoms were improved after PSL treatment, however, he died of intestinal perforation with unknown cause.【Conclusion】TAB is a good tool to identify vasculitis pathologically, however, it would be difficult to distinguish AAV clearly from GCA by only TAB evaluation.

P1-200

A case of temporal arteritis complicated with microscopic polyangiitis

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Conflict of interest: None

[Case] The patient was 82 year-old female. She presented with fever, headache, neck pain and jaw claudication. She visited a previous hospital, and was referred to our hospital for elevated C-reactive protein (CRP), renal dysfunction, and positive MPO-ANCA. Physical examinations showed tenderness of bilateral temporal arteries, and the rest was normal. Temporal artery biopsy showed rupture of internal elastic lamina and trace lymphocytic inflammation in temporal artery, and necrotizing vasculitis of small arteries surrounding temporal artery. Temporal arteritis (TA) was diagnosed. Renal biopsy revealed crescentic glomerulonephritis, which is compatible with ANCA associated vasculitis (AAV). 3 days pulse of methylprednisolone (1 g/day) was initiated, followed by oral prednisolone (50 mg/day). After steroid therapy, renal function and symptoms of temporal arteritis quickly improved. [Discussion] TA usually involves large vessels, but sometimes involves small arteries. In previous reports, TA complicated with AAV involved only small arteries surrounding temporal artery. We report a rare case of TA complicated with AAV, which involved both the main trunk of temporal artery and small arteries surrounding the main trunk.

P1-201

A case of autoimmune pancreatitis associated with worsening of diabetes in the follow-up term for Mikulicz's disease

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Conflict of interest: None

【Case】57-year-old man【Chief complaint】Upper abdominal pain【Present illness】He had swelling of both submaxillary glands with no pain from April X-5. He was observed but he had suffered from dry mouth. He visited our department, his serum level of IgG4 was elevated. Histopathological findings of submaxillary gland revealed infiltration of IgG4-positive plasma cells, he was diagnosed with Mikulicz's disease

(MD). He was observed with no treatment and swelling of submaxillary glands repeated exacerbation and remission. In October X-1, his serum level of lipase elevated, however new lesion was not detected in pancreas with abdominal CT. His diabetes got worse, MRCP revealed irregular stenosis of main pancreatic duct and intrapancreatic bile duct. In April X, he complained slight upper abdominal pain and his serum level of pancreatic enzymes and IgG4 were elevated. He was diagnosed with autoimmune pancreatitis (AIP), and detected further lesions. He was treated with oral prednisolone 30mg/day and improved.【Clinically significance】MD with no symptoms is often observed without treatment, but there is no definite consensus of follow-up. We examined and report together with other cases in our hospital.

P1-202

A case of primary Sjögren's syndrome with tubulointerstitial nephritis treated with combination therapy of prednisolone and mycophenolate mofetil

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Conflict of interest: None

A 51-year-old woman who had diagnosed with primary Sjögren's syndrome (pSS) in 2005, had been treated symptomatically. In Oct 2016, she was admitted in our hospital with a complaint of progressive weakness and pain of her extremities for a few days. Laboratory tests showed severe hypokalemia (serum K 1.9mEq/L) with hyperchloremic metabolic acidosis and elevated levels of CRP (1.92mg/dL). Impaired urine H^+ excretion (urine pH >5.5, urine anion gap >0) and bilateral kidney stones were also shown, leading to a diagnosis of distal renal tubular acidosis (dRTA). Potassium and $NaHCO_3$ replacement therapy was initiated with clinical improvement within a week. Microscopic examination of a renal biopsy showed tubulointerstitial nephritis (TIN) underlying cause of dRTA. On 32nd day, a combination therapy of 30mg/day (0.6mg/kg/day) of prednisolone (PSL) and 1000mg/day of mycophenolate mofetil (MMF) was initiated, CRP levels were reduced to 0.03mg/dL, hypokalemia and acidosis were remarkably improved. The treatment was effective without adverse effect, subsequently PSL was tapered to 25mg/day and she was discharged on 50th day. We report a rare case of TIN secondary to pSS treated with MMF, and review the literatures.

P1-203

Final report of 10 years' SICCA project - Predictors of Progression to Sjögren's Syndrome and GWAS Analysis -

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Conflict of interest: None

Introduction: For the purpose of establishing international diagnostic criteria for Sjogren's syndrome (SS) and analyzing etiology, the Sjogren's International Collaborative Clinical Alliance (SICCA) was conducted by seven countries, USA, Denmark, Argentina, China, India, UK and Japan in 2003-2012. Result: 1. Based on the data of 3514 patients, we published SICCA-ACR criteria for SS in 2012. We published ACR-EULAR international classification for SS in 2016. 2. 771 patients were recalled and received all examination after 2 years. We evaluated pathological changes and clinical features between two years. 93% of 359 SS patients who met SICCA-ACR criteria at initial visit satisfied all items even after 2 years. 9% of cases that did not meet SICCA-ACR criteria at the first visit developed to SS with satisfied 3 items of criteria. These cases have shown hyper-gamma globulinemia and hypo-complementemia at the first visit, and the risk of developing to SS was 4 to 5 times higher. 3. GWAS analysis was performed on 1622 patients who fulfilled SICCA-ACR criteria. We found MHC, IRF5 and STAT4, in addition to KLRG1 and SH2D2 these genes reported to be associated with autoimmune diseases. Especially MHC, there was a clear difference between genetic polymorphisms of Westerners and Asians.

P1-204

IgG4-related disease resembling clinical manifestations with angioimmunoblastic T-cell lymphoma

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Conflict of interest: None

A 79-year old man was admitted due to abdominal pain. Contrast CT showed a diffuse pancreatic swelling, and axillary-abdominal lymph node enlargement. Serum IgG4 was high at 548 mg/dL. However, generalized axillary-abdominal lymph node swelling were shown by CT findings. An increased sIL-2R 1320 μg/mL and decreased CH50, positive RF and biological false positive of syphilis were seen. These clinical findings indicated having diagnosis with AIP caused by IgG4-RD. Acute pancreatitis were treated by FOY and pain disappeared. However, high fever and elevated CRP persisted. These clinical findings were required differential diagnosis of Castleman's disease or ML except IgG4-RD. The axillary lymph node biopsy specimen revealed high endothelial venule, and pathological diagnosis was achieved angioimmunoblastic T-cell lymphoma (AITL). M-PSL pulse steroid and oral administered PSL were effective and general condition was improved. Tumor cells of AITL were derived from follicular dendritic helper T cells (TFH) of germinal centers. IL-21 is thought to be induced to class switching IgG4, and overexpression of IL-21 is related with IgG4 production in IgG4-RD. This case demonstrated clinical and pathologic similarities between IgG4-RD and AITL.

P1-205

CTD like disease with IgG4 elevation

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Conflict of interest: None

IgG4RD were usually easily differentiated with SS-A positive Sjogren syndrome using (SS) value of IgG4. Because almost cases of collagen vascular disease showed low titer of IgG4 values. But some exceptional cases exist. This time we analyze CTD case with high IgG4 value. Case 1. 76-year-old female was referred to our clinic because of face edema and erution suspect of vasculitis. Labo Data revealed positive ANA, dsDNA-Ab, SS-A, and elevated IgG4 level (715). Her conditions were reactive to steroids. Case2. 53-year-old female of purpura and arthralgia had been to our hospital. Labo Data showed positive ANA, dsDNA-Ab and low complement level and high IgG4 (215). Systemic lymphadenopathy developed and thrombocytopenia, Cr level progressed. Diagnosis of SLE with ITP was made, all were well responded to steroids. <Discussion> We must pay much attention to cases overlapping of CTD and IgG4RD.

P1-206

A retrospective analysis of ESSDAI and ESSPRI of inpatients with primary Sjogren's syndrome

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Conflict of interest: None

[Objectives] To clarify the disease activity defined by ESSDAI and ESSPRI of inpatients with primary Sjogren's syndrome (pSS). [Methods] We analyzed 1) clinical background, 2) ESSDAI, and 3) ESSPRI of inpa-

tients with pSS diagnosed by 1999 Japanese criteria who were worked-up between Jan 2015 and Oct 2016, retrospectively. [Results] 1)32 patients (29 females/3 males) were included. The mean age was 56±14 years old.14 patients were glandular form (GF) and 18 were extra-glandular form (EGF). 2)The mean ESSDAI was 7.1±6.3 in all patients, 1.7±2.2 in GF, and 11.3±5.1 in EGF. ESSDAI was significantly higher in EGF than in GF. 17 patients (53%) had moderate or high activity defined by ESSDAI≧5. 15 (88%) out of these 17 patients with moderate or high activity were EGF. More than 10% of patients had any activities in glandular, articular, pulmonary, hematological, and biological domains of ESSDAI. 3) The mean ESSPRI was 3.7±2.0 in 27 patients, 3.8±1.8 in 11 with GF, and 3.7±2.2 in 16 with EGF. 21 (78%) patients achieved PASS defined by ESSPRI< 5. ESSPRI and PASS were comparable between GF and EGF. There was no significant correlation between ESSDAI and ESSPRI. [Conclusion] 53% of inpatients with pSS had ESSDAI≧5, and many cases with ESSDAI≧5 were EGF. 78% of pSS achieved PASS.

P1-207

The features of pancreatitis complicated with primary Sjogren Syndrome

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Conflict of interest: None

[Object] Sjogren's syndrome (SS) is characterized by autoantibodies to exocrine glands. SS-associated pancreatitis may fulfill the diagnostic criteria of autoimmune pancreatitis (AIP). We compare the features of two patients with SS-associated pancreatitis. [Case1] A 62-year-old woman presented with xerostomia and high titers of serum p-amylase. Antinuclear antibody (ANA), anti-SS-A/B antibodies were positive, and serum IgG4 titer wasn't elevated. Diffuse swelling of the pancreas was observed without dilation of main pancreatic duct (MPD), and the diagnostic criteria of AIP was not fulfilled. [Case2] A 61-year-old woman presented with submandibular gland swelling and xerostomia. ANA was positive, and anti-SS-A/B antibodies were negative. Reduced salivation and lymphocytic infiltration in lip biopsy lead a diagnosis as SS. Imaging studies revealed the diffuse swelling of the pancreas with irregular narrowing of MPD and para-aortic soft tissue lesions. Histological analysis of lymph nodes revealed lymphocytic infiltration and storiform fibrosis without IgG4-positive cells. As she was regarded as AIP, glucocorticoid treatment was started. [Discussion] The pathogenesis of SS-associated pancreatitis is heterogeneous, and the difference or similarity to AIP is a matter of discussion.

P1-208

Transient and migratory polyarthralgia in a patient with rheumatoid arthritis leading to a new diagnosis of comorbid Sjögren's syndrome: a case report

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Conflict of interest: None

[Background] When assessing disease activity of rheumatoid arthritis, it is important to consider the possibility that the articular symptoms can result secondarily from other diseases or inflammation from infection or malignancy. However, Treat To Target (T2T) recommendations do not emphasize this point. [Case report] The patient was a 68-year-old woman who was diagnosed with rheumatoid arthritis 4 years prior on the basis of high levels of rheumatoid factor and anti-CCP antibody, and bone erosion seen on X-rays. At her four-year follow-up, she did not present with arthritis or high serum CRP. However, transient and migratory arthralgia had developed in both shoulders, wrists, feet, and knee joints. She had been taking methotrexate but was limited to 6 mg per week because of her leukocytopenia and lymphocytopenia. Diagnosis of Sjögren's syndrome was confirmed by a positive test result for anti-SS-A antibody, low salivary flow rate, and subjective sicca symptoms (the ESSPRI score for sicca symptoms was 6). To treat her arthralgia, we increased analgesic prescriptions instead of DMARDs. [Conclusion] When patients with rheumatoid arthritis present with atypical articular symptoms, they should be re-evaluated for other possible diagnoses before deciding on a course of therapy.

P1-209

Cryoglobulinemic vasculitis and unhealed lower leg ulcers after remission of gastric MALT lymphoma secondary to Sjogren's syndrome

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Conflict of interest: None

【case】A 73 years old woman with history of gastric MALT lymphoma presented with unhealed ulcer of right lower extremity. Petechiae waxed and waned without intervention for twenty years. Gastric MALT lymphoma diagnosed 6 years ago had been in complete remission with chemotherapy (R-CHOP). The patient developed painful ulcer and numbness over right lower extremity associated with low grade fever eight month ago. Skin biopsy revealed leukocytoclastic vasculitis. Laboratory results showed low C4 level, positive for rheumatoid factor, antinuclear antibody (320x), SS-A antibody, and monoclonal gammopathy with M protein (IgM-κ). Lip biopsy showing lymphocyte infiltration of salivary gland was consistent with Sjogren syndrome. As leg ulcer following longstanding peticheae became associated with constitutional symptom and sensory impairment of right lower extremity, we diagnosed cryogloburinemic vasculitis with Sjogren's syndrome after remission of MALT lymphoma.

P1-210

A case of Sjögren's syndrome diagnosed by hypergammaglobulinemia without autoantibodies and subjective sicca symptoms

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Conflict of interest: None

Introduction. There are many patients with Sjögren's syndrome (SS) without sicca symptoms. Careful examination for autoantibodies and objective sicca symptoms is important to make a correct diagnosis of SS. Case report. The patient was a 48-year-old woman with polyclonal gammopathy and a sustainable high CRP level. A hematologist and two rheumatologists were unable to make a diagnosis. Antinuclear antibodies and anti SS-A antibodies were negative, and she denied having sicca symptoms. However, we considered SS, and performed objective diagnostic tests. Both, Saxon's test and sialography confirmed xerostomia. According to a labial salivary gland biopsy, the focus score was 1.21. We finally diagnosed her as having SS. Conclusion. According to the recommendations for early diagnosis of SS, laboratory abnormalities such as hypergammaglobulinemia suggest subclinical SS. Though the patient has negative results for the presence of autoantibodies, and no subjective sicca symptoms, if they have laboratory abnormalities typical for SS (such as hypergammaglobulinemia) or extra-glandular features, we have to consider SS.

P1-211

4 clinical courses of IgG4-related disease (IgG4-RD) observed without treatment

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Conflict of interest: None

Object: IgG4-RD is the fibro-inflammatory disorder of unknown etiology and more likely occurs in elderly men. Though basic medication for IgG4-RD is steroid, its side effects lead to a great matter for the patients who have several complications. The natural course of IgG4-RD don't be clarified sufficiently and spontaneous remission cases were reported. We have observed the natural course of IgG4-RD without important organ involvement and assess the possibility of treatment-free procedure. Method: 4 cases of IgG4-RD with mildly swelling of submandibular glands, lacrimal glands and lymph nodes have been observed with no medication. All cases were diagnosed as definite from the comprehensive diagnostic criteria for IgG4-RD. The change of the serum IgG4 concentration and involved organ size, newly appeared lesion have been examined by the blood, radiological image and ultrasonography. Result: All cases have presented the reduction of the involved organ size, the serum IgG4 concentration have decreased, and no other lesion associated with IgG4-RD have appeared. Conclusion: In the cases of IgG4-RD, a symptomatic swelling of salivary glands, lacrimal glands and lymph nodes, it can be considerable to observe carefully without medication.

P1-212

A case of IgG4-related disease preceded by the onset of membranoproliferative glomerulonephritis

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Conflict of interest: None

A 80-year-old man, who had been diagnosed as membranoproliferative glomerulonephritis (MPGN) before two years, suffered from a developing fever, arthritis, and acute renal failure (Scr 2.69 mg/dl). He has also occasionally developed cholangitis for two years. On admission, his temperature was 37.7˚C, and he had a systemic edema. His laboratory data revealed massive proteinuria, severe anemia, an increasing level of CRP, and hypoalbuminemia. In addition, his IgG4 level in sera was remarkably increasing (235 mg/dl). Renal biopsy was performed again, which showed diffuse mesangial proliferation and thickening of capillary wall in glomeruli and diffuse infiltration of inflammatory cells, which are including IgG4-positive plasma cells, in tubular interstitium. Then, he was diagnosed as IgG4-related disease. He had undergone artificial dialysis in several times, and oral admission of prednisolone was started. Gradually, renal dysfunction, massive proteiuria and arthritis were improving. This is the intriguing case of IgG4-related disease, which MPGN were preceding before two years.

P1-213

A case of IgG4-related disease with extensive granulomatous change

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Conflict of interest: None

<Case> A 61-year-old man was pointed out right submandibular tumor, dilatation of aortic root and right hydronephrosis by usual health check. Contrast-enhanced CT revealed hypertrophic periaortic root and peri-common iliac arterial lesions causing right hydronephrosis by right ureteral obstruction. The biochemical profile showed elevated levels of serum IgG4, IgG and IgE. Histological finding of submandibular tumor demonstrated storiform fibrosis with obliterative phlebitis and significant IgG4-positive lymphoplasmacytic infiltration. Notably, extensive granulomatous changes with Langhans-type giant cells extended within fibrotic lesions. Sarcoidosis and granulomatous infections were histologically and serologically denied. He was diagnosed as IgG4-related disease (IgG4-RD) with extensive granulomatous change and treated with prednisolone (PSL) 0.6 mg/kg, which dramatically reduced IgG4-RD lesions. <Discussion> IgG4-RD with extensive granulomatous change is very rare. Considering novel pathogenesis of IgG4-RD it's so significant to consider the mechanism of the development of granulomatous change on and we hopefully need to study further cases.

P1-214

A case of IgG4-related disease caused renal atrophy on lateral dominance during maintenance therapy for autoimmune pancreatitis

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Conflict of interest: None

Case Description: Six yeas prior to admission, a 73-year-old woman was diagnosed autoimmune pancreatitis. Elevated serum IgG4 level was observed and prednisolone 30mg/day was administered. After that, pancreatic mass was disappeared on images. The dose of predonisolone was tapered to a maintain dose of 5mg/day. At that time, renal function was nomal and CT showed no renal atrophy. However, renal function was decreased during one year. Enhanced CT revealed right renal dominant atrophy and multiple low-density lesions on both kidneys. We gave up performing a renal biopsy because of the right renal atrophy and malformation of the left renal vein. According to examinations, we distinguished IgG4-RKD from other vascular diseases. Finally, we clinically diagnosed IgG4-RKD and increased the dose of predonisolone to 30mg/day. One month after administration, multiple low-density lesions on both kidneys were improved slightly and renal function was improved. **Discussion**: Bilateral renal atrophy sometimes occurs in patients with IgG4-RKD. However, this patient presented with predominantly unilateral renal atrophy. Because of the specific distribution of renal parenchyma lesions in IgG4-RKD, we could explain this case that the pathologic lesions were more distributed on right side.

P1-216

The usefulness of saliva scintigraphy for the early diagnosis of Sjogren's syndrome

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Conflict of interest: None

【Introduction】In Sjogren's syndrome (SS) salivary secretion is kept early. Progression can be suppressed by immunosuppressive therapy. The previous studies reported that it reduces the therapeutic reactivity and becomes irreversible. Adaptation of biological products to SS has become practical. So we investigate the diagnostic in early SS cases with gum test normal. 【Methods】Subjects were suspected of SS in our hospital from April 1989 to June 2016, undergoing scrutiny including labial gland biopsy, with gum tests normal (SS 23 by clinical diagnosis, Non-SS 9 cases)in retrospective study. 【Results/Discussion】Significant difference ($p < 0.05$) was observed between 10 of SS and 1 of non-SS in the low accumulation rate of submaxillary glands (SUB). There was no difference between 9 of SS and 2 of non-SS in the low accumulation rate of the parotid glands. In 6 of 9 cases with decreased parotid gland accumulation rate at SS, reduction in accumulation rate of the SUB was also observed. It was suggested that SUB are often disordered earlier in the early stages of SS. 【Conclusion】For the diagnosis of early SS in which salivary secretion is maintained, it is considered that the SUB dysfunction findings in salivary gland scintigraphy may be useful for diagnosis.

P1-217

Usefulness of FDG-PET/CT Imaging for Monitoring Treatment Response in IgG4-Related Disease

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Conflict of interest: None

(Objective) To evaluate the usefulness of FDG-PET/CT imaging for monitoring treatment response in IgG4-related disease (IgG4-RD). (Method) This study included 22 patients of IgG4-RD followed up at our facility between 2008 and 2016. The diagnosis for IgG4-RD was based on comprehensive diagnostic criteria for IgG4-RD. We retrospectively studied the relation of serum biomarkers, pattern of FDG uptake, maximum standardized uptake value (SUVmax). Disease activity was measured by the IgG4-RD Responder Index (IgG4-RD RI). (Result) 11 patients who scored IgG4-RD RI≧10 points at baseline had higher serum IgG4, sIL-2R levels, a greater number of organ involvements and higher SUVmax than others who scored IgG4-RD RI<10 points at baseline. The patients who relapsed were given small dose of corticosteroid at the initial treatment. FDG-PET/CT was performed in 12 cases after initiation of treatment. There were no significant reduction of FDG uptake and poor improvement of IgG4-RD RI in 8 cases. (Conclusion) There was a connection between FDG-PET/CT imaging and IgG4-RD RI during IgG4-RD treatment. Small initial dose of corticosteroid was regarded as a risk of relapse. We investigated the usefulness of serum biomarkers and FDG-PET/CT imaging to predict prognosis in IgG4-RD.

P1-218

Clinical investigations of 26 IgG4-related diseases in our department

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Conflict of interest: None

Objective: To clarify the clinical features of IgG4 related disease (IgG4-RD) in our department. Methods: 26 patients diagnosed with IgG4-RD at our department from January 2009 to September 2016 were retrospectively reviewed. Results: All 26 patients (12 males, 14 females) had an age of 63.8 (31-75) years [mean (range)]. Mean serum concentrations of IgG was 2394 mg/dl, IgG4 691.2 mg/dl (IgG4 ≥135 mg/dl in 24patients), IgG4/IgG cells ≥ 40% proven by tissue biopsy was identified in 17 (8 in lacrimal gland/salivary gland, 2 in retroperitoneum, 2 in lips, 5 in others). In the comprehensive diagnostic criteria for IgG4-RD, there were 15 definite cases, 2 probable cases, 9 possible cases. Prednisolone (PSL) was administered in 23 patients, while 3 patients without PSL. Mean initial dose of PSL was 26.6 mg/day. In the affected organs, 9 in lacrimal gland/salivary gland, 6 parotid/submaxillary glands, 4 retroperitoneum, 3 pancreas, 2 lungs, and 7 in others. Conclusion: Unlike previous reports, IgG4-RD was more common in women than in men in our department, in part because the majority of patients with IgG4-RD in our department had head and neck lesion, as no gender difference has been reported in the head and neck lesion.

P1-219

A case of chronic progressive multiple mononrruritis associated with Sjögren's syndrome (SS)

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Conflict of interest: None

A-69-year old woman had begun to experience numbness in all of her limbs three eyars earlier. She was admitted to a hospital in 2008. She was diagnosed with SS based on the presence of both dry mouth and eyes with seropositive anti-SS-A antibody. SS-associated peripheral neuropathy was diagnosed. Prednisolone (40mg/day) and intravenous gammaglobulin (IVIG) therapy were administered. However, no marked improvement was obtained. In 2011 she was diagnosed with Rheumatoid arthritis because of swelling in multiple joints. Methotrexate was started. Since a good clinical response was not achieved, Infliximab was started and she achieved clinical remission. She had experienced numbness with gradually worsened. She presented with difficulty walking, so she was admitted to our hospital in 2015. Neurological examination revealed decreased sensation in the distal portions of all limbs. A left sural nerve biopsy showed inhomogeneous reductions in the myelinated fibers, and infiltration of inflammatory cells around small vesseles. From these findings, sensory dominant multiple mononeuritis associated with SS was diagnosed. It is important to consider a diagnosis of SS when patients present with sensory dominant multiple mononeuritis.

P1-220

A case of primary Sjögren's syndrome with Hypertrophic pachymeningitis

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Conflict of interest: None

A 32-year-old woman with a history of meningitis was admitted to our hospital complaining of fever, headache and joint pain. Although some kind of meningitis was suspected, lumber puncture showed no specific inflammatory cerebrospinal fluid findings. Brain MRI demonstrated thickening and contrast enhancement of the affected dura matter, on the other hand, the patient was diagnosed with hypertrophic pachymeningitis (HP). No symptom of cranial neuropathy appeared. Oral prednisolone (40mg/day) was started with prompt response within a day, headache and joint pain disappeared. The MRI findings of HP improved after the six days of treatment. The diagnosis of primary Sjögren's syndrome (SS) was confirmed by serologically positive SS-A and SS-B antibodies and positive Schirmer' s tear test and fluorescent dye test, although no sicca symptoms were noted. HP is a rare disease. It causes fibrosing inflammatory thickening of the dura mater and that induces headache or various neurological defects. Known causes of the disease include various infections, sarcoidosis, Wegener's granulomatosis, IgG4-related disease and carcinoma. SS is an extremely rare cause for HP. Here, we described a case of SS with HP. We suggest that SS should be considered as one of the cause of HP.

P1-221

Two cases of immunoglobulinG4-related respiratory disease (IgG4RRD) presenting with pleural lesions that needed the differentiation with pulmonary malignant tumor

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Conflict of interest: None

【Object】We report rare cases of IgG4RD presenting with Pleural lesions【Case1】A 64year-old man with a history of chronic hepatitis C presented complaining of a inappetence and a weight loss and a cough. He was referred to our hospital because of chest CT findings that showed pleural effusion and thickening of the precoridal pleura. His serum IgG and IgG4 levels elevated. Pathological findings obtained by VATS showed infiltration of abundant IgG4-positive plasma cells without malignancy lesion. We diagnosed IgG4RRD without other lesion. He was treated with 0.3mg/kg oral PSL and showed improvement【Case2】A 60year-old man with a history of COPD presented complaining of a lumbago and a weight loss. He was referred to our hospital because of chest CT findings that showed pleural effusion and nodule of the thoracic paravertebral pleura and soft tissue mass of paraabdominal aorta. His serum IgG and IgG4 levels elevated. Pathological findings obtained by VATS showed infiltration of abundant IgG4-positive plasma cells without malignancy lesion. We diagnosed IgG4RRD with retroperitoneal fibrosis. He was treated with 0.3mg/kg oral PSL and showed improvement【Conclusion】It is important to consider IgG4RRD as one of differential diagnoses when we encounter patients with pleural effusion and lesion.

P1-222

A case of IgG4related hypophysitis who was treated successfully with prednisolone for the advent of adrenal insufficiency after years of observational follow-up of IgG4-related disease (IgG4-RD) in outpatient clinic

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Conflict of interest: None

A 74-year old man was aware of swelling of both submaxillary glands in December X. The specimens obtained from his glands indicated IgG4-positive plasma cell infiltrations. His serum IgG4 was high (440 mg/dl). He was diagnosed with Küttner tumor. There were no other organ involvements, so he had been followed up without any therapy. In July X+ 3, his CT scan showed infiltrative shadow of right lung and retroperitoneal fibrosis. His pituitary MRI showed thickening of pituitary stalk and enlargement of pituitary. He presented with malaise and anorexia in September X+3. When he underwent bronchoscopy for lung lesion, his condition deteriorated and became unconscious. Laboratory data showed hyponatremia, high serum CRP level and low level of cortisol. We suspected adrenal insufficiency due to IgG4-related hypophysitis. The hormone loading test showed LH responses to LHRH were low and blunt, and the basal PRL level was high. Hydrocortisone was introduced for a week, and then he was treated with prednisolone 30 mg/day. After the treatments his condition and his pituitary MRI findings were improved. IgG4-related hypophysitis could be an important option in differential diagnosis of adrenal insufficiency and this case suggests that necessity of careful follow-up of IgG4-RD.

P1-223

Clinical evaluation of IgG4-related diseases (IgG4-RD) in our department

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Conflict of interest: None

[Aim] To evaluate the therapeutic effect of prednisolone (PSL) to IgG4-RDs. [Methods] Twenty-three patients that were enrolled in this study, who fulfilled the Comprehensive diagnostic criteria for IgG4-RD 2011. Serum IgG4 level (sIgG4) was measured in patients diagnosed with definite (DEF), probable (PRO) or possible (POS) IgG4-RD. [Results] The average age at the diagnosis was 66.4 yo. Patients were 18 males and 5 females. Numbers of DEF, PRO, and POS were 11, 1, and 11, respectively. The average sIgG4 before treatment was 528.3 mg/dl and was higher in multiple-lesion cases than in single lesion ones. During the treatment, the lesion sizes were reduced clinically in 18 cases, in whom 11 patients were DEF (100%) and 7 were PRO or POS (58%). PSL were administered in all patients and average initial dose was 21.1 mg/day. Initial dose of PSL was higher in the reduced cases than in non-reduced. sIgG4 level at two months after treatment was decreased in all 15 cases. The reduction rate of lesion size was correlated with that of sIgG4 at two months after treatment in 8 patients ($p=0.0245$). [Conclusion] PSL was effective to DEF to reduce lesion size. The reduction rate of sIgG4 level at two months after treatment may correlate to that of lesion size.

P1-224

A case report of IgG4-related desease with gastric cancer and ITP

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Conflict of interest: None

【Case】78 year old, male【Main complaint】General fatigue【Current medical history】This patient demonstrated general fatigue 2 months before hospitalization. One month before hospitalization, bairateral leg edema also appeared, and Hb 10.2 g / dL and Plt 50,000 / μL were pointed out. Tarry stool also appeared. At admission, Hb and Plt decreased to 7.3 g / dL and 4, 000 / μL respectivery. Antiplatelet antibody positive, PA-IgG high, H. pylori IgG positive, IgG 1870 mg / dL, IgG4 436 mg / dL. Patient had gastric cancer revealed by GIF. Abdominal CT showed swelling of tail pancreatic portion and fat concentration enhancement around pancreatiase, This patient demonstrated three sicknesses of gastric cancer, ITP and IgG4-related diseases. Inspite of the treatment with intravenous immunoglobulins, mPSL pulse and thrombopoietin receptor agonists, patint's platelets did not elevate significantly. His condition got worse gradually, and died at 84th day of hospitalization.【Discussion】This patient demonstrated three abnormalities of gastric cancer, ITP and IgG4-related diseases. In this case, the immunological abnormality of IgG4 generation might play mainly in production of this patient's pathophysiology.

P1-225

A case of ACPA positive IgG4-related disease with chronic monoarthritis in right shoulder

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Conflict of interest: None

IgG4-related disease (IgG4-RD) involves multiple organs, however, arthritis is uncommon and its clinical feature is not clear. Here, we report 65-year-female with chronic monoarthritis that was diagnosed with IgG4-RD. She has suffered from a right shoulder pain for 2 years. Clinical examination indicated the stiffness, swelling and tenderness of right shoulder, tonsillitis and lymphadenopathy. Laboratory test showed elevated CRP, ESR, RF, ACPA, and IgG4 (139 mg/dL). T-SPOT.TB was negative. Gd-enhanced MRI showed synovitis, erosion and bone marrow edema in the right shoulder joint. ^{18}F-FDG PET/CT revealed high uptake in right shoulder, left pharyngeal tonsil, lymph node of neck and right axillary. Arthroscopy showed severe synovial growth with partial vascular hyperplasia, the pathology revealed fibrosis, infiltration of lymphocytes and plasma cells (IgG4/IgG>40%, IgG4 positive>10/HPF) and no malignancy. Then, she was diagnosed with IgG4-RD and treated with prednisolone 40 mg per day, which immediately resolved her arthritis, lymphadenopathy and tonsillitis. IgG4-RD is one of the important diagnoses of chronic monoarthritis. It is important to distinguish this case from early rheumatoid arthritis, since she showed synovitis with strong bone destruction with RF and ACPA.

P1-226

A case of IgG4 related kidney disease, initially diagnosed as nephrosclerosis

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Conflict of interest: None

【Introduction】IgG4-RKD is mainly seen in elderly men and lacks proteinuria, making it difficult to distinguish from nephrosclerosis.【Case】An-81-year-old man attended our hospital 4 years ago. On referral day, laboratory data showed an elevation of serum IgG, mild hypocomplementemia, and antinuclear antibody positive (titers 1:320); however, the diagnosis of nephrosclerosis was made on the basis of normal urinary test and his past history of hypertension. He was admitted to our hospital with progression of anemia, and diagnosed as myelodysplastic syndrome. Elevations of serum IgG, IgG4 and anti-dsDNA antibody (3990mg/dL, 632mg/dL, 49IU/mL) developed and a progression of hypocomplemente-

mia were noted. FDG-PET/CT showed an abnormal uptake of FDG at bilateral kidneys, submandibular glands, systemic lymph nodes and prostate gland. The biopsy of kidney revealed tubulointerstitial nephritis with prominent infiltration of IgG4 positive plasma cells and storiform fibrosis; hence, the diagnosis of IgG4-RKD was made. 【Discussion】In order to improve a prognosis, it is crucial to suspect a possibility of IgG4-RKD from hypergammaglobulinemia, hypocomplementemia and characteristic uneven atrophy of the kidney.

P1-227

A case of Mikulicz's disease and retroperitoneal fibrosis complicated with bronchiolitis with IgG4-positive plasma cell infiltration

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Conflict of interest: None

[Case] A man in his 70s was visited our hospital with continuous cough, fever and swelling of submandibular gland. Blood eosinophil count was elevated and chest HRCT showed consolidation of light lung. He was diagnosed with eosinophilic pneumonia and treated with oral prednisolone (PSL) 25 mg per day. Consolidation of chest HRCT was improved and PSL was tapered by 2 years ago. 3 month before admission, he noticed general malaise, continuous cough and body weight loss. Swelling of bilateral lacrimal and submandibular gland were found, and abdominal CT showed soft tissue mass around light ureter. On immunostaining of submandibular gland, filtration of IgG4-positive plasma cell was found. And bronchial wall thickening and bronchiolitis were found in chest HRCT. TBLB was performed and infiltration of IgG4-positive plasma cell was found around the bronchioles. He was diagnosed IgG4-related disease and treated oral PSL 40 mg per day. After treatment, clinical findings and bronchiolitis on the image were improved. **[Clinical Significance]** Pulmonary lesions with IgG4-positive plasma cell infiltration are reported in many cases of inflammatory pseudotumor and interstitial pneumonia, but reports of airway lesions are rare. It is of interest to considering the pathology of this disease.

P1-228

A case of systemic sclerosis with interstitial pneumonia combined with Sjogren syndrome and pulmonary hypertension under the course of observation

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Conflict of interest: None

A 73 year old women had suffered from dry cough, dyspnea, and Raynaud's phenomenon on April 2014. She was diagnosed to systemic scleroderma because of sclerodactyly, interstitial pneumonia, and positive of anti-centromere antibody. On February 2016, her dyspnea was worsen and cystic change and diffuse ground glass appearance were progressed in CT scan. She was diagnosed to Sjogren syndrome because of positive anti-SS-A / Ro antibody and anti-SS-B / La antibody, exacerbation of hyper gammaglobulinemia, lymphocytic infiltration around the ducts by salivary gland by lip biopsy, positive of Saxon test, and apple tree appearance of MR sialography. In the echocardiographic examination, the right ventricular systolic pressure increased to 59 mmHg. In the right heart catheterization, PCWP was 12 mmHg and mean pulmonary artery pressure was 31 mmHg. She was diagnosed to pulmonary hypertension and treated with beraprost and sildenafil at first because of suspicion of lung cancer. Since interstitial pneumonia exacerbated thereafter, she was treated with prednisolone at 40 mg / day (1 mg / kg) and got improvement of respiratory symptom. Here we report this suggestive case of systemic scleroderma with interstitial pneumonia combined with Sjogren syndrome and pulmonary hypertension.

P1-229

Protein-losing gastroenteropathy in a patient with Sjogren's syndrome

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Conflict of interest: None

A 46-year-old woman presented with dry eye and facial edema in January. She was referred to A hospital because of positive for anti-SS-A and anti-SS-B antibodies. ^{99m}Tc-human serum albumin scintigraphy showed early radioisotope accumulation in the stomach and the small intestine. She was admitted to A hospital for hypoproteinemia (albumin 1.1 g/dL), leg edema, and pleural effusion in April. Her serum albumin level was decreased to 0.7 g/dL, and she was transferred to our hospital in May. Biopsy of a minor salivary gland showed mild lymphocyte infiltrates, and she was diagnosed as having protein-losing gastroenteropathy with Sjogren's syndrome. Treatment with steroid pulse therapy followed by prednisolone at a dose of 80mg/day was insufficient. She was started on mizoribine at a dose of 150mg/day in July. Her serum albumin level was gradually increased and her oral prednisolone was tapered carefully. Protein-losing gastroenteropathy with Sjogren's syndrome is rare. Most of patients with steroid-resistant protein-losing gastroenteropathy associated with connective tissue disease were treated with cyclophosphamide pulse therapy. Our case suggest that mizoribine may be successful in the treatment of steroid-resistant protein-losing gastroenteropathy with Sjogren's syndrome.

P1-230

Two patients with Sjögren syndrome showing Castleman disease-like symptoms

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Conflict of interest: None

Castleman disease (CD) is a hematological disorder characterized by swelling of lymph nodes and elevated levels of immunoglobulin and IL-6 in serum. We report 2 patients with Sjögren syndrome (SjS) who showed CD-like symptoms. [Case1] A 37-year-old woman developed polyarthralgia and purpura in lower extremities. She was diagnosed with SjS based on laboratory data. Prednisolone (PSL), azathioprine and tacrolimus failed to improve fever and interstitial lung shadows with elevated levels of immunoglobulin and IL-6. CD was considered as a possible disorder, and tocilizumab (TCZ) dramatically relieved her clinical symptoms and lung shadows. She remains remission with monthly administration of TCZ. [Case2] A 36-year-old woman diagnosed with SjS based on positive anti-SS-A/SS-B antibodies in serum. She started PSL as a treatment of fever, rash and hypergammaglobulinemia. At age 44, CT scan demonstrated swelling of intraabdominal lymph nodes, which showed obscure follicles and proliferation of plasma cells with no findings of malignancy on biopsy. Because of high inflammatory reactions persisting even after starting PSL, high-dose cyclophosphamide and rituximab were employed. [Conclusion] CD should be considered as an associated lymphoproliferative disorder in refractory cases of SjS.

P1-231

Massive periarticular calcinosis with primary Sjögren's syndrome

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Conflict of interest: None

54-year-old woman presented with a mass on her right leg. She started to feel fatigue and to have limb muscle weakness when she was 47 years old. She was diagnosed with Sjogren 's syndrome at the age of 68. She had solid and white nodules on her finger tip. The laboratory data showed intact PTH 26pg/mL, 1,25-vitaminD 74.2pg/mL, SS-A 22400U/

mL, SS-B 26.5U/mL. She didn't have electrolyte abnormality including serum calcium and phosphate. Schirmer's test was positive. She was introduced prednisolone, methotrexate and bisphosphonate, but these medicines didn't work. She was removed calcified sacral and coccygeal bone.

P1-232

A recurrent case of IgG4-related disease presented as Mikulicz disease and lung involvement after 13 years of quiescent disease

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Conflict of interest: None

[Case] thirteen years ago, a woman knew swelling and diagnosed as Mikulicz disease in biopsy. She was treated by prednisolone (PSL) and improved. After that, she stopped taking it by herself. Recently, she knew swelling again and cough happened. Lung x-ray showed bronchial wall thickening/infiltrative shadow, suspected lung lesions due to IgG4 related disease (IgG4-RD). There was High level of serum IgG 4 (2480 mg/dl), and pathological criteria was meeted. Considered to be IgG4-RD and its recurrent PSL was increased and azathioprine was added. Then, clinical symptoms and lung X-ray improved. Althought Transbronchial lung biopsy conducted, the infiltration of IgG4 positive plasma cells is not clear. But comprehensively, it was thought IgG4-related respiratory disease (IgG4-RRD). **[Clinical Significance]** Frequency of respiratory lesions was reported as 5-18% in IgG4-RD. Sensitivity of lip biopsy on IgG4-RD was reported as 56%. And, IgG4-RRD is said to be asymptomatic with a 53% possibility. I suggest in the case of IgG4-RD patients, it is possible pulmonary lesions may appear even if they are asymptomatic, and it is worthwhile to try therapeutic interventions without pathological confirmation.

P1-233

A case of IgG4-related disease with multiple ulcers in the lower legs complicated with primary aldosteronism

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Conflict of interest: None

【Chief Complaint】Skin ulcers in the lower legs【Present Illness】He has been appeared in skin ulcer of his leg from June on last year. Skin ulcers was progressive little by little. Moreover, numbness of the lower leg appeared in July. He has been introduced to our department from dermatology to serach the cause of skin ulcer in July 22. Serum IgG level was 2655 mg/dl, and IgG4 level was 318 mg/dl in biochemical data. Pathological finding in skin biopsy showed the infiltaration of plasma cells at the granuloma. The ratio of IgG4/IgG-positive cells was more than 50%, which was corresponded with IgG4-related disease (IgG4RD). A right adrenal nodule on CT scan MRI imaging revealed adrenal adenoma. In addition to high ratio of PAC/PRA, 617.5 and positive captopril loading test we diagnosed primary aldosteronism (PA). He was admitted to our hospital for treatment by prednisolone (PSL) in September 5.【Progress】Treatment was started with 40 mg PSL (0.6 mg /kg/ day). After the initiation of treatment, epithelialization at the site of ulcer progressed and IgG4 value was also decreased.【Conclusion】IgG4RD with skin ulcers was rare case, and No cases of complication with PA has been reported. We have reported a rare case of IgG4RD with both lower leg ulcers complicated with PA.

P1-234

A case of IgG4-related disease with multiorgan involvement

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Conflict of interest: None

[Case] 63-year-old female [Chief complaint] Lacrimal and submandibular gland swelling, leg edema [Past history] Chronic sinusitis, bronchial asthma, type 2 diabetes [Present illness] Three months before admission she had lacrimal and submandibular glands swelling and leg edema and purpura. After that renal, dysfunction was pointed out and she admitted to our hospital. Laboratory examination showed BUN 12.6 mg/dL, Cr 1.04 mg/dL and IgG4 2250 mg/dL. She had axon injury in right tibial and bilateral sural nerves. CT showed the paranasal sinusitis, lacrimal and submandibular glands swelling, thickened bronchial walls, periarterial inflammation and renal swelling. The lip biopsy showed IgG4/IgG positive cell ratio is 50% and the renal biopsy showed IgG4 positive plasma cell is 50/HPF. The skin biopsy showed superficial and deep perivascular dermatitis without epidermal changes. She was diagnosed as IgG4 related disease and treatment with 50mg/day of prednisolone was started, which resulted in good clinical course. We report this case with some literature review.

P1-235

Histone methylation profiling in γδT cells of Behcet's disease

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Conflict of interest: None

Object Although a line of evidence has suggested genetic contributions to Behcet's disease (BD), non-genetic factors, such as epigenetic changes, may play pivotal roles in the pathogenesis as well. We examined histone modifications of peripheral white blood cells (WBCs) in BD. **Methods** Peripheral WBCs were obtained from 28 patients with BD and 16 healthy controls (HC), and classified as below: CD4+T cells, CD8+T cells, γδT cells, neutrophils, Tregs, and B cells. All samples were analyzed with a fluorescence-activated cell sorting. **Results** The mean fluorescence intensity (MFI) levels of H3K27me3 and H3K4me3 of BD were different from HC in peripheral WBC subsets. H3K27me3 MFI of active BD were significantly lower in γδT cells than inactive BD. H3K4me3/H3K27me3 MFI ratio of active BD was significantly higher in γδT cells than inactive BD. In addition, the similar results were also observed between active and inactive phases in the same patients. Preliminary observations suggest IL-17 secretion on γδT cells in BD. **Conclusions** Differences in histone modifications could be detected in peripheral WBCs in BD. Aberrant histone methylation in γδT cells may be associated with the pathogenesis of BD. It is suggested that histone methylation could be a new candidate-biomarker for BD.

P1-236

Clinical analysis of 4 cases of childhood-onset Behcet's disease

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Conflict of interest: None

Object: Behcet's disease is an intractable disease associated with repeat episodes of acute inflammatory lesions and mainly characterized by recurrent aphthous ulcers of the oral mucosa, skin lesions, and ocular lesions. Cases of childhood-onset Behcet's disease have a lower prevalence of symptoms than in adult-onset cases. We considered clinical feature of childhood-onset Bechet's disease. Method: We investigated retrospectively the medical records of childhood-onset cases experienced in our facility. Results: A total of 4 patients (3 males, 1 female) were examined. Fever was the initial symptom in all cases with symptoms of joint pain (1), coronary aneurysm (1), blurred vision (1), and refractory recurrent oral ulcer (1) also experienced. Intestinal lesions were discovered in 2 patients during the course of treatment. A single ulcer in the ileocecal area

was identified in both of these patients. Human leukocyte antigen (HLA) was detected in all patients (HLA-B51, 3 cases; HLA-A26 1 case) by Luminex methods. Conclusion: The main symptoms that were not present at time of admission appear more often during the course in childhood-onset compared to adult onset cases. Thorough examination of intestinal tracts, blood vessels and ocular lesions is warranted regardless of disease type.

P1-237

Treatment of infliximab for Behcet's disease

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Conflict of interest: None

We examined about a long-term effect of infliximab for the Behcet's disease in this hospital. Case 1:50 years old Female Clinical history (CH):In February, 2010, she was diagnosed as uveitis. She had stomatitis and an erythema nodosum, and was diagnosed as abortive Behcet's disease. In March, 2008, she was treated in Infliximab (IFX) 200mg/8ws for uveitis. In January, 2013, she underwent vitreous surgery, but maintains eyesight to date. Case 2:28 years old. Male CH:In September, 2008, he was diagnosed as uveitis. He showed stomatitis / erythema nodosum / epididymitis / a rectal ulcer symptom, and he was diagnosed as complete and bowel Behcet's disease. Since October, 2008, he was treated in Infliximab (IFX) 400mg/8ws for uveitis to merge for Behcet's disease. Case 3:21 years old Male CH:In 2012, he was diagnosed as inferior limb cellulitis. He showed stomatitis / an erythema nodosum symptom and showed phlebothrombosis afterwards, and he was diagnosed as vascular form Behcet's disease. As for him, it is under the medical treatment with quantity of medium grade steroid. However, at every steroid loss, he repeated ill recrudescence. He was treated in Infliximab (IFX) 300mg/8ws for vascular form Behcet's disease from January, 2016. Even now he maintains remission.

P1-238

Utility of Edoxaban to Massive pulmonary thrombosis in Behçet disease: a case report

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Conflict of interest: None

<Introduction> Vascular involvement is a complication in Behçet disease. Pulmonary thrombosis is one of the complications. However, the appropriate therapy is not clear. **<Case>** A 63-year-old female was diagnosed with Behçet's disease (BD) in 2001. She took colchicine and had good clinical course. She was admitted to our hospital because of fatigue and dyspnea on exertion for 10 days. On admission, She presented shock vital signs. Enhanced computed tomography (CT) confirmed bilateral massive pulmonary thrombosis without pulmonary artery aneurysm. She had no deep vein thrombosis and intracardiac thrombus. She received edoxaban 60mg/day, then her symptoms were improved immediately. On the 8th day, most of pulmonary thrombosis disappeared by enhanced CT. On the 24th day, she left the hospital. On the 37th day, the thrombus completely disappeared by enhanced CT. Subsequently she passed without a recurrence.

P1-239

A case of vascular Behçet's disease with extensive thrombosis of the inferior vena cava

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Conflict of interest: None

A 44-year-old woman was admitted to our hospital with fever and right lower abdominal pain. She was diagnosed with Behçet's disease due to recurrent oral aphtha, uveitis and multiple intestinal ulcers. Abdominal ultrasonography on admission revealed a thrombosis extending from the bilateral femoral vein to the inferior vena cava. Laboratory evaluation showed inflammatory findings. A diagnosis of vascular Behçet's disease was made after ruling out other possible diseases. Lung scintigraphy and contrast-enhanced computed tomography didn't indicate the presence of pulmonary embolism. Therefore, rivaroxaban 30mg/day, combination therapy of prednisolone 40mg/day and azathioprine 50mg/day were administered. Clinical and laboratory findings improved soon. Ultrasonography of the abdomen and lower extremities showed a reduction of the thrombosis 2 months later. Vascular involvement in Behçet's disease is not uncommon in Japan. However, it often involves vasculitis with thrombotic lesions in the large vessels and can also cause life-threatening complications such as Budd-Chiari syndrome. The treatment of Behçet's disease with vascular lesions remains to be solved. Some case reports suggest that the efficacy of steroid and early combined immunosuppression.

P1-240

Use of infliximab in a patient with Behçet's disease complicated with cerebral venous thrombosis

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Conflict of interest: None

[Case] A 22-year-old male with history of recurrent oral ulcers for 6 years and erythema nodosum for 1 year presented with headache and fever. On admission at the prior hospital, cerebral spinal fluid analysis showed elevated leukocyte counts and enhanced MRI of the brain demonstrated thrombosis of the right sigmoid sinus. He was referred to us for further management of cerebral venous thrombosis (CVT). Physical examination showed oral ulcers, genital ulcers, folliculitis-like and erythema nodosum-like rashes in addition to significant bilateral papilledema. Colonoscopy revealed a punched-out ulcer at the ileocecal region. CVT, aseptic meningitis, and the ileocecal ulcer were considered as complications of Behçet's disease. All symptoms improved dramatically after initiation of infliximab and high dose corticosteroids. Corticosteroids were successfully tapered down without recurrence. A year later, MRI showed the regression of CVT. [Clinical significance] Use of infliximab in Behçet's disease with cerebral venous thrombosis has rarely been reported. Infliximab may be considered as one of the treatment options of vasculo-Behçet's with CVT.

P1-241

HLA-B51/A26 double positive complete Behcet's disease with bilateral ring scotoma following sudden-onset central scotoma

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Conflict of interest: None

A 44-year-old woman was referred to our clinic with complaint of severe arthritis following colitis. We found acute development of visual field defect, oral aphtha, pudendal ulcer, and erythemanodosum. She was diagnosed as Behcet's disease (BD), following diagnosis as retinocho-

roiditis at ophthalmology. We started 50mg-a-day colchicine. Although her general condition was immediately improved, her ocular symptom did not change. She got a second opinion at the department of ophthalmology of our college and fluorescein angiography identified an occlusion of capillary bed and vasculitis in macular. We started 5mg/kg infliximab on the 24th day after admission, resulting in improvement of serous retinal detachment. However, her central scotoma progressed to ring scotoma and it still remains even 18 months after her onset. «clinical implications» Generally, ocular symptoms of BD gradually exacerbate as a result of repeated attacks. Sudden onset scotoma is very rare for an initial symptom of BD. Moreover, her change from central scotoma to ring scotoma seems to have some relationship with serous retinal detachment and blood supply to the retina. We report this case, considering as a rare and severe one.

P1-242

A case of cerebral infarctions and aortic aneurysm with gastrointestinal Behçet's disease

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Conflict of interest: None

[Case] 23-year-old female [chief complaint] Right upper limb paralysis, dysphagia [Present illness] She was diagnosed as incomplete type Behçet's disease (BD) from recurrent aphthous stomatitis, pustular eruption and genital ulceration and colchicine was started in Dec 2013. She had polyarthralgia and hematochezia caused by ulcerative lesions at ileocecum and was daiagnosed as gastrointestinal BD in Feb 2015. We used PSL 5 mg/day, mesalazine 3000 mg/day and adalimumab 40 mg/2weeks. Polyarthralgia was under control but ulcerative lesions was not, so PSL was increased to 40 mg/day and ulcerative lesions were treated effectively, decreased PSL 5 mg/day gradually. She was admitted with presenting right upper limb paralysis and temporal dysphasia in Oct 2015. Brain MRI revealed multi cerebral infarctions and periaortic wall thickening and aortic aneurysm were detected by whole trunk CT. We diagnosed as vascular BD or Takayasu's arteritis and increased the dose of PSL to 40 mg/day with MTX, resulted in good clinical course. [Consideration] We report a case of gastrointestinal BD complicated with large-vessel vasculitis symptoms. On this case it is difficult to perform differential diagnosis between vascular BD or Takayasu's arteritis with gastrointestinal BD.

P1-243

A case of Vasculo-Behçet's disease complicated with multiple aneurysms and vein thrombosis

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Conflict of interest: None

A 54 year-old-man suffered for melena. Computed tomography revealed multiple aneurysms, stenosis and vein thrombosis. The patient had a history of reccurent oral aphthae, folliculitis and uveitis. We diagnosed Vasculo-Behçet's. Predonisolone, infliximab and methotrexate were initiated, and now, there is no evidence of new aneurysms. But he repeats melena because of intestinal ischemia and ileus, it is difficult to improve his condition. We report this rare case that formed aneurysms mainly in abdominal arteries.

P1-244

A case of Behçet's disease presenting with an atypical rash positive for HLA-B39/B54

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Conflict of interest: None

[Case Report] A 42 year old woman. Three weeks before coming to the hospital the patient developed a fever. One week before coming to the hospital she developed a painful rash on both legs and multiple mouth ulcers. When a skin biopsy was taken, the subcutaneous septal panniculitis was consistent with erythema nodosum, however, there was severe inflammatory cell infiltration in the dermo-epidermal junction. Neutrophil infiltration was not seen. The patient was positive for HLA-B39 and B54. Furthermore, given that the patient was presenting with an atypical rash, SLE and Sweet's disease were considered in the differential diagnosis, but based on the refractory stomatitis, genital ulceration and erythema nodosum findings the patient was diagnosed with incomplete Behçet's disease and she started treatment with colchicine. The colchicine was remarkably effective. There was no recurrence of the symptoms after discharge. [Conclusion] It is reported that HLA-B51-negative Behçet's disease has a relatively good prognosis, but even with atypical skin pathology findings the patient responded well to standard treatment. Early improvement can be expected by promptly starting treatment with colchicines, providing it is not contraindicated, without the need to use steroids.

P1-245

A case of intestinal Behçet's disease complicated with myelodysplastic syndrome

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Conflict of interest: None

[Case] Fifty-nine years old man developed fever in July 2016. He was diagnosed with intestinal Behcet's disease (BD) by aphthous stomatitis, genital ulcer, folliculitis, and ulceration at transverse and sigmoid colon. In addition, blast cells were seen on blood smear and bone marrow puncture revealed myelodysplastic syndromes (MDS). Chromosome analysis showed trisomy 8. HLA was positive for A2, B60 and B61. From September, initial treatment with prednisolone (PSL) 30 mg/day, mesalazine and colchicine was started. On October, azacytidine was added for MDS. These therapies improved his symptoms and maintained remission even after tapering PSL to 12.5 mg/day. [Discussion] Sixty-six cases with intestinal BD complicated with MDS were reported. Trisomy 8 was detected in 93.5% of the patients. Only 32.2% patients were positive for HLA-B51. Only immunosuppressive therapy was effective for 61.7%, while combination of immunosuppressant and chemotherapy and/or allogenic stem cell transplantation was effective for 88.9%. Our case showed trisomy 8, negative for HLA-B51 and improvement with PSL, mesalazine, colchicine and azacytidine. [Conclusion] The patients of intestinal BD complicated with MDS showed specific characterics.

P1-246

The usefulness of tacrolimus for ulcerative colitis like ulcer lesions of intestinal Behcet's disease

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Conflict of interest: None

Tacrolimus (TAC) is one of the immunosuppressive agents using against refractions of post-transplantation, some rheumatic diseases, ulcerative colitis (UC), etc. Intestinal Behcet's disease (BD) sometime needed to distinguish from UC; however, both therapies were almost same. Here, we succeeded to treat intestinal BD using TAC. TAC may be one of the agents for BD. Case: A 39 year-old male was diagnosed as having intestinal BD with recurrent oral aphthous ulcers, arthritis, erythema nodosum (EN), genital ulcer, and ileocecul ulcers; therefor, colchicine was started 15 years ago, and predonisolon (PSL) and 5-aminosalicylic acid were added 10 years ago. Moreover, 7 years ago, cyclosporine was

added and the dose of PSL was decreased. Now, he was admitted to our hospital with a history of 3 weeks' merena and 1 week's fever-up. The abdominal CT examination showed his colon wall thickened; his intestinal BD was recurred. In the 20th day, colonoscopy was performed and the gross findings was shown UC-like lesions. Thus, TAC was started for his UC-like lesions, his abdominal condition improved and his findings of colonoscpy showed mucosal hearing; however, the pathological findings was not UC. In conclusion, TAC may be useful to treat mucosal lesion of intestinal BD.

P1-247

A patient diagnosed as intestinal Behcet's disease in the treatment of laryngopharyngeal stenosis

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Conflict of interest: None

A female, who had been suffered from recurrent aphthae, received emergent tracheostomy for cryptogenic laryngeal stenosis in 2012. Then she received steroid, but pharyngalgia was exacerbated by steroid taper. Arthralgia and fever continued at intervals. She was admitted to our hospital in 2016. On neck CT laryngeal inflammatory change and stenosis were recognized. Upper GI endoscopy revealed no ulcerative lesion. Steroid doses increasing, and immunosuppressant adding could not control her inflammation. CT and Ga scintigraphy showed no overt abnormal findings. On lower GI endoscopy, ileocecal ulcer was founded. The biopsy samples were negative for the tuberculosis. Concerning her past history of genital herpes in 2000 we examined her medical record and confirmed a note mentioned about pudennal ulcer. She has no ocular lesion. We diagnosed her as intestinal Behcet's disease and initiated infliximab treatment. Her inflammation was improved and remission has been preserved. It is rare that recurrent refractory aphthae develops laryngeal stenosis. More than half of previously reported cases gradually developed ocular or skin symptoms, and were diagnosed as Behcet's disease. Meeting with rare laryngopharyngeal inflammation we have to consider it might be a symptom of systemic disease.

P1-248

Successful treatment with intravenous cyclophosphamide for tocilizumab-resistant adult onset Still's disease with high serum IL-18 level

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Conflict of interest: None

A 39-year-old man. He got the medical care at previous hospital because of sore throat and polyarthralgia. He was diagnosed with gout and pseudo gout. However, he additionally suffered from spiking fever and chest pain. Laboratory tests showed elevated inflammatory response and liver enzyme. So, he was admitted to our hospital. Infections, malignancies, and connective tissue diseases were excluded. Abdominal ultrasonography revealed pleural effusion. Laboratory findings showed elevated serum ferritin and IL-18 levels (respectively8673 ng/mL and >5000 pg/mL). His condition was diagnosed as AOSD complicated with pleurisy. For remission induction therapy, he was treated with MPDN pulse and CSA (CSA was stopped because of drug-induced hepatopathy). The disease activity was getting better once, but ferritin level elevated when PSL was tapered. We increased the dose of PSL and administered TCZ and TAC. However, after the dose of PSL was decreased, the disease activity took a turn for the worse. After we administered IVCY, the disease activity was completely controlled and the levels of ferritin and IL-18 decreased.

P1-249

A case of adult onset still's disease (AOSD) accompanied with pure red cell aplasia (PRCA)

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Conflict of interest: None

AOSD is a systemic inflammatory disease of unknown etiology and causes multiple manifestations. We report a case of AOSD accompanied with PRCA. A 34 year old healthy woman presented a sore throat, polyarthralgia and skin erythema. She was pointed out a high fever and high titer of C-reactive protein and liver dysfunction in the laboratory tests and visited our hospital. Blood exams showed high titers of Ferritin and CT scan reveals splenomegaly and superficial lymph node swelling. We started the NSAIDs but the symptoms and laboratory data got worse, titers of ferritin elevated 7000 to 50000 ng/dl. After the precise examination, we diagnosed as AOSD, fulfilled Yamaguchi's criteria, and accompanied with DIC. While she had an anemia of Hb9.5g/dl, reticulocyte did not increase. Bone marrow examination showed decrease of erythroblast and some hemophagocytes. Then, we diagnosed PRCA with AOSD, there were no other causes of this state like viral infection or exposure to drugs. We started the 40mg per day of prednisolone, the symptoms of both AOSD and PRCA improved. An acquired PRCA is rare condition and there are some reports representing PRCA with autoimmune disorders. But it is very rare accompanied with AOSD, we perform a review of the literature concerning with this association.

P1-250

Clinical characteristics of three cases of adult-onset Still's disease (AOSD) with atlantoaxial subluxation

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Conflict of interest: None

[Objectives] Adult-onset Still's disease (AOSD) is an acute inflammatory disorder of unknown origin. It is well known that a number of patients with AOSD have RA-like clinical courses. In the present study, we examined the clinical characteristics in patients with AOSD treated with biologics. [Methods] Ninety-nine patients with AOSD who were treated in Institute of Rheumatology, Tokyo Women's Medical University enrolled in this study. The patients group consisted of 32 men and 67 women. We classified the patients with AOSD into 2 groups; RA-subtype (n = 22) who met the revised criteria of American College of Rheumatology clinical diagnostic criteria for RA and nonRA-subtype (n = 77) who didn't met it. [Results] Nine patients developed to ankylosis with RA-subtype. Three cases showed atlantoaxial subluxation. One case complicated of organized pneumonia at onset. Three patients showed relapse with systemic symptoms at least once during the course. Disease control was poor with steroids, DMARDs, leukocytapheresis and TNF-α blockers. In both cases, joint pain and swelling improved with TCZ treatment combined with MTX. It is important to disease control with TCZ in case of treatment resistant to steroids and DMARDs.

P1-251

A case of Adult-onset still disease with IgA vasculitis

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Conflict of interest: None

A 47 year-old woman was referred to our hospital for fever of unknown origin for two weeks. The rash of limb trunk that suspects adult-onset Still's disease (AOSD), high ferritin serum was observed, and various diseases autoantibodies were measured but negative, and findings that caused the fever were attempted to observe by image examination but negative, so we diagnosed AOSD. Initially, in addition to steroid pulse therapy, treatment with prednisolone at 1 mg / kg and methotrexate combined therapy was started. Then the fever and the eruption were tended to be extinguished, but two weeks after the start of treatment, a purpura with induration appeared in the abdomen and both legs. Therefore, when skin biopsy was performed, leukocyte fragmentable vasculitis accompanied by IgA deposition was recognized and it was diagnosed as IgA vasculitis combined. At present, with the combination of tocilizumab, the disease of AOSD is being suppressed, the purpura has also extinguished without relapsing. Reports of cases of AOSD and IgA vasculitis combined are rare and we report with some literature consideration.

P1-252

A case of agranulocytosis due to adult-onset Still's disease with hemophagocytic syndrome

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Conflict of interest: None

[Case] A 59 years old woman. Due to persisting fever for three weeks, polyarthritis and erythema, she was hospitalized in December. She was diagnosed with adult-onset Still's disease (AOSD) and received steroid pulse therapy. After that, she left the hospital with 25mg of prednisolone (PSL). On January 28, PSL was tapered to 20mg. Her fever and arthritis recurred, so she was treated with intravenous-injection of dexamethasone on February 2. Because her symptoms were improved, PSL was tapered to 18mg on February 9. But at the night of the day, her symptoms recurred again. By a blood test, hyperferritinemia, agranulocytosis and anemia were revealed. On February 24, she was hospitalized again. Neutropenia due to drug, infection and autoimmunity were excluded. The findings of the bone marrow biopsy didn't suggest malignant disorder, but hemophagia. So she was diagnosed with agranulocytosis due to AOSD with hemophagocytic syndrome (HPS). She received steroid pulse therapy, then the granulocyte count was restored immediately. [Discussion] As is well known, AOSD may be complicated with a HPS. However, agranulocytosis in this condition is rare, and there are no previous reports as far as we know. So, we report details of this case with some literature review.

P1-253

A case of developing adult-onset Still disease after vaccination of 23-valent pneumococcal polysaccharide vaccine

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Conflict of interest: None

[Case] A seventy-year-old male received 23-valent pneumococcal polysaccharide vaccine (PPSV23). Two days after receiving the vaccine, he developed high spiking fever and arthritis of left hand joints, bilateral knee joints and ankle joints. He was treated with nonsteroidal anti-inflammatory drugs (NSAIDs) at a medical clinic. After taking NSAIDs, he began to experience erythematous eruption on the upper chest, back and lower extremities. After one month of treatment, his conditions were not improved. He was admitted to our hospital. Two skin biopsies were obtained from the eruption on the upper chest. Histopathologic examination showed dyskeratosis confined to the upper layers of the epidermis and mild liquefaction degeneration at the epidermal-dermal junction. The superficial dermis contained the perivascular inflammatory infiltrate with lympohcytes, histiocytes and eosinophils. These findings were persistent pruritic papules and plaques and indicating a skin lesion of adult-onset Still disease (AOSD). After clinical examination, he was diagnosed as AOSD. He was treated with prednisolone at a daily dose of 30 mg. After treatment his symptoms were improved. [Clinical meaning] We thought that a causal relationship between the vaccination of PPSV23 and onset of AOSD.

P1-254

Two cases of refractory adult onset still's disease successfuly treated with *certolizumab* pegol after changing tocilizumab

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Conflict of interest: None

[Case1] A 30-yearsold female. 4 years ago, she had fever, typical eruption, and arthritis. Blood tests showed high levels of WBC count, ferritin and CRP value. We excluded other diseases and diagnosed adult Still's disease (AOSD). High-dose glucocorticoid (GC) and methotrexate (MTX) were administered to achieve remission. After tapered GC, she relapsed and took high-dose GC. But there was no improvement, so tocilizumab 8 mg / kg was administered every 4 weeks. Clinical symptoms other than mild rash were improved. She relapsed again and had high-dose GC and tocilizumab administration again. There was no improvement, so we changed tocilizumab to certolizumab pegol. She became in remission and tapered GC. [Case 2] 29-year old female. About 6 years ago, she had typical symptom in AOSD and blood tests showed high levels of WBC, ferritin and CRP. We diagnosed AOSD. Although high-dose GC was given, we could not taper GC. So, MTX and tocilizumab were started and she was promptly remission. But one year ago she had relapse and had high-dose GC administration. Because of insufficient effect, we started certolizumab pegol. She became in remission and tapered GC. [Conclusion] Anti-TNFα agent can be a treatment option in refractory AOSD cases after changing anti-IL6 blockade.

P1-255

A case of adult onset Still's disease complicated with cytomegarovirus-associated hemophagocytic syndrome

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Conflict of interest: None

This is a case of a 75-year-old man who was diagnosed with adult onset Still's disease and initiated high-dose steroid therapy. After the treatment her fever went down. However she had a fever and her serum-ferritin levels elevated again, so she was started to treat with methylprednisolone pulse therapy. Despite high-dose steroids, her serum ferritin levels elevated again and cytomegarovirus antigenemia test turned positive. She was complicating with cytomegarovirus infection, so we administered ganciclovir. But she had a fever and her serum ferritin levels elevated after the initiation. Bone marrow aspiration revealed hemophagocytosis. We made a diagnosis of cytomegarovirus-associated hemophagocytic syndrome. Therefore we started methylprednisolone pulse therapy again and changed ganciclovir into foscarnet. Nevertheless, she didn't improved. So she required plasmapheresis for additional therapy. After treatment with plasmapheresis her symptoms significantly improved. We present A case of adult onset Still's disease complicated with cytomegarovirus-associated hemophagocytic syndrome.

P1-256

Case report: adult Still's disease complicated by diagnosis due to cytomegalovirus infection

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Conflict of interest: None

A 69-year-old woman presented on the end of December 2014 with fever and sore throat. Since January 2015 erythema and joint pain emerging in the limbs and Rheumatoid Factor was positive. The serum ferritin value increased, liver dysfunction, splenomegaly, PET-CT found numerous accumulation in the lymph nodes, malignant lymphoma or adult still's disease (AOSD) were suspected. She was treated with steroid half-pulse and plasma exchange. Unfortunately, the serum ferritin value increased again, steroid pulse was performed but no response. Cytomegalovirus (CMV)DNA quantification positive, heterozygous lymphocytes appeared, so we diagnosed hypercytokinemia due to CMV. Antibiotic and antiviral drugs were no response, there was no findings of malignant lymphoma, the serum IL-6 and IL-18 value increased, finally we diagnosed with AOSD. She was treated with Prednisolone30mg/day after steroid half-pulse. Since serum ferritin value increased again, it was considered as steroid-resistant AOSD. She was improved when tocilizumab was introduced.【Clinical Significance】CMV infection and bacterial infection were also recognized, and it was considered to be a valuable case that it was reactive to each of antiviral drugs, antibiotics, and steroid treatments, and was confused by confirmed diagnosis.

P1-257

A case of malignant lymphoma mimicking polymyalgia rheumatica

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Conflict of interest: None

PMR is an inflammatory disorder that causes muscle pain and stiffness and affects adults over the age of 50. PMR is a condition in which the diagnosis most relies upon the exclusion of other probabilities. We report a case of malignant lymphoma mimicking PMR. A-56-year female was admitted to our hospital with complaints of pain in her shoulders and pelvis girdle. Given that the patient was older than 50, had an ESR of > 40 mm/h, a morning stiffness lasting for more than one hour and an episode of abrupt onset of symptoms and that ACPA and RF tests were negative, the patient was diagnosed with PMR. The response to a low-dose of prednisone was dramatic. 3 week later the patient visited our hospital with complaints of hoarseness. CRP level and ESR were slightly elevated. Hoarseness was persistent without improvement. Further examination of pharynx made the diagnosis of malignant lymphoma. In this case the clinical course was atypical. 1, The patient experienced younger onset of symptoms. 2, The soluble IL-2 receptor level was elevated as high as 2000 IU / mL. 3, Elevation of CRP level and ESR was persistent. This case suggests that further studies are needed to confirm the diagnosis of PMR in case it takes atypical clinical course.

P1-258

A difficult case of polymyalgia rheumatica with preceding unilateral cystic lesion of the iliac muscle

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Conflict of interest: None

[Introduction] Polymyalgia rheumatica (PMR) often presents a diagnostic difficulty. We report a difficult case of PMR with preceding cystic lesion of the iliac muscle. [Case report] A 69-year-old man presented with right coxalgia. MRI examination showed a unilateral cystic lesion of iliac muscle with perimyositis of the thigh. Lab tests presented elevated ESR and CRP. These findings led us to suspect an infectious disease. Antibiotic therapy was started, but the patient developed bilateral lower and upper extremity swelling, pain in the neck and shoulders, bilateral hand and foot pitting edema. MRI re-examination showed an inflammatory change around the opposite hip joint. US examination demonstrated not only proximal bursitis but also distal synovitis. The patient achieved a complete response after treatment with 15mg/day of prednisolone. [Conclusions] Based on 2012 EULAR/ACR provisional classification criteria for PMR, US findings of mainly proximal bursitis led to a diagnosis of PMR. These results suggest that the preceding unilateral cystic lesion reflected iliopectineal bursitis. [Clinical significance] US is an useful method in diagnosis of PMR. Primary care orthopedist should know about the disease that requires careful clinical observation and diagnosis of exclusion.

P1-259

Successful treatment of refractory remitting seronegative symmetrical synovitis with pitting edema (RS3PE) syndrome with tocilizumab

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Conflict of interest: None

[Case] 79-year-old woman developed fever, symmetrical swelling and tenderness of finger joints, and pitting edema of dorsum of both hands and both feet. Antibiotics was not effective. She was admitted our hospital. Serum CRP was 11.3 mg/dl, and rheumatoid factor, anti-CCP antibody and antinuclear antibody were negative. Bone erosion was not found by hands and feet X-ray. Based on these findings, the patient was diagnosed with RS3PE syndrome. Treatment with 15 mg/day prednisolone (PSL) was started, but the symptoms was not improved completely. After the dosage of PSL was increased to 20 mg/day, the symptoms were improved. However, after the dosage of PSL reduced to 11 mg/day, joint pain was appeared again. Consequently, subcutaneous injection of tocilizumab (162 mg per every two weeks) was added. The symptoms were disappeared, and CRP was decreased to normal range. PSL was tapered to 5 mg/day without recurrence of the disease. [Discussion] In this case, treatment with tocilizumab improved the symptoms of RS3PE syndrome and is enable to reduce the dosage of PSL. A through search of database, only one case of RS3PE syndrome treated with tocilizumab was reported. [Conclusion] Tocilizumab is a potential alternative therapy for refractory RS3PE syndrome.

P1-260

Clinical experience of RS3PE syndrome presenting in a unilateral pattern :A report of two cases

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Conflict of interest: None

Objectives: To review our two cases suspected remitting seronegative symmetrical synovitis with pitting edema (RS3PE) presenting in a unilateral manner. Case: Case1: A 67-year-old man was presented with left painful swollen hand. Blood exam test showed raised inflammatory markers (CRP7.35). Autoantibody screen and rheumatoid factor were negative. X-rays showed the fragmentation of the lunate. He underwent the removal of the lunate and synovectomy. His symptoms were getting better but inflammatory markers were still high. A low dose of prednisolone at 5mg daily dosage worked well for this patient. But 5 months later it was discovered that he had a gastric cancer. Case2 A 79-year-old man was presented with right painful swollen hand. Blood exam test showed raised inflammatory markers (CRP1.86). Autoantibody screen and rheumatoid factor were negative. He responded extremely well to low dose prednisolone at 5mg daily dosage. Discussion: Patients with RS3PE will be expected an excellent response to low corticosteroids. While RS3PE is almost always a symmetric disease of the upper extremities, it may rarely present in a unilateral fashion. And clinicians need to be aware of the RS3PE in aging population and initiate appropriate investigations to exclude any occult malignancy.

P1-261

Examination of patients with polymyalgia rheumatica in the Ogawa Red Cross Hospital

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Conflict of interest: None

Objective;To analyze polymyalgia rheumatia (PMR) under treatment in my hospital. Patients;Seven males and 6 females, with a mean age of 75.4 years, were studied. Mean serum CRP; 7.71 mg/dl. Mean Steroid dose at start of therapy; 11.9 mg/day. Methods;The desease activity of PMR and efficacy were evaluated by tha level of CRP. The symptom and the laboratory findings were surveyed by tha medical record for 24 weeks. Results;The levels of serum CRP concentration became normal in seven patients after the treatment for weeks. Additional immune suppressive agents were needed in five patients. A rheumatoid factor is positive in 3 patients. We distinguished rheumatoid arthritis (RA) from PMR by peripheral joint findings. We have not corrected them to RA for 24 weeks. Conclusion; We report patients with polymyalgia rheumatica under the treatment in our hospital.

P1-262

The first case of autoimmune neutropenia associated with psoriatic arthritis successfully treated with cyclosporine A

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Conflict of interest: None

An eighty-year-old woman was diagnosed as plaque psoriasis in 2012, and psoriatic arthritis (PsA) in 2014. She developed chronic neutropenia in 2013 and was treated with G-CSF on demand. In 2015, she received successful treatment of Golimumab (GLM) for active PsA. However, the neutropenia was not improved. In 2016, she was hospitalized for skin infection and severe neutropenia. The anti-neutrophil antibody was detected and she was finally diagnosed as autoimmune neutropenia (AIN). She received IVIg therapy, and switched the treatment from GLM to cyclosporine A (CsA). Following the CsA therapy, neutropenia was improved without G-CSF administration, and CsA was also effective for psoriatic eruption and arthritis. Adult-onset AIN is mainly seen in patients with autoimmune diseases, such as RA, SLE, and SS. However, there are no previous case reports of AIN with psoriasis. Although glucocorticoid and G-CSF supportive therapy are applied for treatment of neutropenia, risk of long-term glucocorticoid therapy and worsening psoriasis by G-CSF administration have been reported. Our case was the first case of PsA with neutropenia, which the CsA therapy was effective for improvement of both PsA and AIN. We also discuss the pathology and underlying mechanisms of the present case.

P1-263

Three cases of SAPHO (synovitis-acne-pustulosis-hyperostosis-osteitis) syndrome with malignancy

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Conflict of interest: None

Sixteen patients seen from April 2009 to March 2016 were diagnosed with SAPHO syndrome. We report three cases with malignancy within 2 years of diagnosis.【Case1】A 60-year-old man having palmoplantar pustulosis for 30 years was diagnosed with prostate adenocarcinoma 4 months prior. CT and bone scintigraphy revealed osteoblastic changes and increased accumulation in the sternoclavicular joint and 10th thoracic vertebra. We initially suspected bone metastasis but diagnosed him with SAPHO syndrome.【Case2】A 51-year-old woman diagnosed with extranodal NK/T-cell lymphoma 1 year prior who achieved remission after chemotherapy noted pain in her finger/knee/hip joints. MRI and FDG/CT showed sternoclavicular/ileosacral arthritis. She was diagnosed with SAPHO syndrome.【Case3】A 56-year-old man diagnosed with carcinoma in situ of the bladder 5 years prior who received Bacillus Calmette-Guerin therapy noted pain in his right knee and upper back. MRI revealed an occupational lesion in the 5th/6th thoracic vertebra. Osteitis was found in a sternal biopsy. Cancer recurrence was found by urine cytology 1 year later. Thus far, an association between SAPHO syndrome and malignancy has not been indicated. We report these cases with a literature review.

P1-264

Airway lesion of relapsing polychondritis is a key factor to determine the response of medical treatment: Four case reports in our department

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Conflict of interest: None

Relapsing polychondritis (RP), which is a rare multisystem autoimmune disorder causes recurrent inflammation to systemic cartilage tissues. Patients with airway lesions have the risk of life-threatening events. Here we describe four cases with RP. **[Case 1]** In 2012, a 13 y.o. man got suddenly developed hearing loss, vertigo and dyspnea, and CT scan revealed subglottic thickening and stenosis. He was operated tracheostomy. The treatment immunomodulators (IMs) and adalimumab failed. However, treatment with tocilizumab was effective. **[Case 2]** A 65 y.o. man was suffering from trachyphonia in 2008. He was revealed glottic and subglottic edema, and serum antibody to typeII collagen was positive (78.1 EU/ml). He was treated with IMs and PSL. **[Case 3]** A 49 y.o. man developed hyperemia of eyes, epistaxis and headache in 2004. Subsequently, He had redness, swelling of his pinna and was revealed the thickness of bronchial wall by CT scan. He was treated with PSL + IMs. **[Case 4]** A 46 y.o man developed ear redness, swelling and hyperemia of eyes. The pinna biopsy revealed lymphoplasmacytic infiltration around the cartilage, and the treatment with PSL was effective. **[Conclusion]** The patients having airway lesions are resistant to steroid therapy and need to treat with IMs or biologics.

P1-265

Update for relapsing polychondritis

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Conflict of interest: None

【Object】Relapsing polychondritis (RP) is rare disease. Because it occur 2 or 3 patient per 1 million person, its treatment depend on doctors experience.【Method】We have 4 RP patient for 2004 to 2016. We study this disease retrospectively.【Results】2men patient,2women patient. Women patient is bad disease activity, treatment is very difficult.【Conclusion】we experience RP, report its disease.

P1-266

Elderly onset multicentric reticulohistiocytosis mimicking osteoarthritis: a case report

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Conflict of interest: None

Case: A 69-year-old woman, who had left distal interphalangeal joints swelling together with nodular lesions on her fingers, was diagnosed as multicentric reticulohistiocytosis (MRH). Although her initial diagnosis was osteoarthritis (OA), biopsy from the nodule demonstrated infiltration of multinucleated giant cells and histiocytes, suggesting typi-

cal histology of MRH. However, immunosuppressive therapies had been suspended because of her hepatitis B virus (HBV) carrier. At admission to our hospital, polyarthritis and tenosynovitis were demonstrated as well as multiple papulo-nodular lesions on her ears and face. Laboratory examination showed neither elevation of C-reactive protein nor positivity for autoantibodies. No malignancy was detected on systemic assessment. She was concomitantly administered methotrexate and prednisolone, which was effective for achieving favorable outcome in both skin lesions and arthritis, together with entecavir for HBV regulation. Conclusion: MRH is an inflammatory disease characterized by multiple skin nodular lesions and erosive arthritis. According to our report, histological diagnosis is necessary for the definitive diagnosis even in an early phase of MRH, because it is concerned that OA could be a different diagnosis in elderly patient.

P1-267

A case report of multicentric reticulohistiocytosis complicated with breast cancer and ovarian cancer

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Conflict of interest: None

A 37 year old woman who suffered from breast cancer two years ago and received an operation and radiation therapy, chemotherapy visited our hospital on June 27, 2016. Her family career had many breast cancer, ovarian cancer and connective tissue diseases. In May 2016, she had papule on PIP and DIP joint, erythema on lower limbs. And she experienced many arthralgia. Rheumatoid factor and anti-CCP antibody were positive, and she was diagnosed as rheumatoid arthritis. A diagnosis of multicentric reticulohistiocytosis was done by skin biopsy which may cause arthritis, too. The abdominal tumor and ascites were detected by computed tomography and positron emission tomography scan. Some kind of cancers and peritoneum dissemination were doubted. She was operated and ovarian cancer became clear. Multicentric reticulohistiocytosis is often complicated with malignancy or autoimmune diseases. When multicentric reticulohistiocytosis is detected, it is necessary to search for these diseases.

P1-268

Early recovery of complete atrioventricular block in cardiac sarcoidosis (CS)

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Conflict of interest: None

39 years-old man. 4 years before admission, he was pointed out bilateral hilar lymphonode enlargement. CT and bronchoscopy were performed, but sarcoidosis was not confirmed. 4 months before admission, electrocardiogram showed no abnormality. On January 2015, he felt shortness of breath at the time of exertion, and a complete atrioventricular block was observed. It is thought to come from Sarcoidosis, he admitted to the hospital to evaluate it. Lymphonode biopsy revealed noncaseating epithelioid granuloma; It confirmed the diagnosis of sarcoidosis. FDG accumulation was observed at interventricular septum on PETCT, and late gadolinium enhancement was observed at the same site on MRI. There was no morphological change such as thinning of the interventricular septum on echocardiogram. Firstly, pacemaker was inserted, and after that prednisolone 40 mg / day was administered. On the 19 th treatment day, the sinus rhythm recovered. There has been no relapse for seven months. [Discussion] It is said that an atrioventricular block associated with CS can respond to treatment, however, the predicting factor is still not clear. In our case, no morphological change and FDG accumulation showed he was at early and active stage of disease. We reconfirmed the importance of early treatment in CS.

P1-269

A Case of Multiple Organ Sarcoidosis with Unilateral Pleural effusion

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Conflict of interest: None

A 69-year-old man with nonalcoholic steatohepatitis, hepatocellular carcinoma complained dizziness with gait disorder. Multiple cerebral infarction was found and he was hospitalized. Bilateral hilar, mediastinal lymphadenopathy, right pleural effusion, parietal dural hypertrophic lesion, and bilateral renal masses were observed. Renal biopsy revealed noncaseating granulomas. He was transferred to our hospital. High serum calcium (11.0 mg / dL), ACE increase (56.0 U / L), sIL2R increase (2330 U / mL) were consistent with sarcoidosis. TTE and myocardial fatty acid SPECT suggested lower wall motor decline. Autonomic nerve disorder was suspected with the Schelling test and 0.65% CVRR in ECG. Pleural effusion increased and drainage was performed. The fluid was exudative, CD4/8 ratio was 8.5. In the FDG-PET/CT, accumulation of forehead, right pleura, both kidneys, muscle was observed. Based on those findings, diagnosis of sarcoidosis in multiple organs (pleura, heart, kidney, nerve and muscle) was made. 40 mg/day of prednisolone improved his condition. (Clinical Significance)Having both cardiac sarcoidosis and hepatic disorder, differential diagnosis for pleural effusion was important. Pleural sarcoidosis was considered according to property of pleural effusion and results in FDG-PET/CT.

P1-270

Successful treatment of severe flexion contracture associated with eosinophilic fasciitis

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Conflict of interest: None

A 21-year-old man was presented with progressive stiffness of limbs since he had exercised at the gym for 2 months, persistent fatigue and worsening limitation in range of joint motion in extremities. Physical examination revealed symmetrical swelling with induration and thickening of skin on distal extremities, which caused severe flexion contracture in fingers. Cutaneous symptoms in extremities were consistent with Groove signs and Orange peel signs. Laboratory findings showed hypereosinophilia and negative result of all of autoantibodies. MRI of extremities demonstrated diffuse thickened fascia with hyperintensities on STIR. A skin and muscle biopsy showed inflammatory cell infiltration of the thickened fascia with scarce eosinophil, suggestive of eosinophilic fasciitis (EF). Since severe flexion contracture progressed with 0.5mg/kg/day of prednisolone (PSL) treatment, we re-started methylprednisolone pulse therapy (1000mg/day × 3 days) followed by 1mg/kg/day of PSL and 16mg/week of MTX. Seven months after treatment, the hardening of subcutaneous tissue was partially improved. [Clinical significance] In case with severe flexion contracture associated with EF, early and intensive intervention with high dose PSL and MTX treatment might be effective.

P1-271

Calcineurin inhibitors are effective and safety to corticosteroid-resitant TAFRO syndrome. (37 case reviews include two cases of successful treatment with Tacrolimus.)

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Conflict of interest: None

We reviewed 37 cases include two cases of successful treatment with Tacrolimus to investigate clinical entity and response to treatment. PubMed search of human cases of TAFRO syndrome was performed by

combining the terms (TAFRO Syndrome) or (Multicentric Castleman disease, thrombocytopenia), and the cases which didn't fulfill the criteria of TAFRO syndrome were excluded. case1: 68-year-old woman, who had multiple lymphadenopathy, myelofibrosis, thrombocytopenia, hepatosplenomegaly, and massive anasarca, was diagnosed as TAFRO syndrome after lymph node biopsy. Corticosteroid did not improve her symptoms. She got septic shock caused by empyema after Tocilizumab (TCZ) therapy, but switched TCZ to tacrolimus produced clinical remission. case2: 17-year-old man, who had renal dysfunction, thrombocytopenia, lymphadenopathy, hepatosplenomegaly, myelofibrosis, and congestive heart failure with acute myocardial damage, was diagnosed as TAFRO syndrome after lymph node biopsy. Corticosteroid and Tacrolimus therapy was started in concurrence with treatment for congestive heart failure, and this combination therapy improved his symptoms dramatically. conclusion: calcineurin inhibitors have equivalent efficacy to TCZ, and safety to use for corticosteroid-resistant TAFRO syndrome.

P1-272

A case of Sweet's syndrome with pulmonary involvement resolved with steroid pulse therapy

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Conflict of interest: None

[Case] A 47-year-old man was referred to our hospital with a 3-week history of fever and arthralgia. He had cough and hypoxemia requiring oxygen. Physical examination revealed polyarthritis and many painful erythematous plaque with overlying bulla over his face, forearm, dorsal hands, lower legs and feet. His WBC count was 27000/μL with 97% neutrophils; CRP, 23 mg/dL. CT demonstrated bilateral pulmonary infiltrates with air-bronchogram. BAL fluid contained increased neutrophils (88%). Skin biopsy specimens showed a diffuse neutrophilic infiltration in the dermis. The diagnosis of Sweet's syndrome with pulmonary involvement was made. Treatment with intravenous methylprednisolone (mPSL) 125 mg for 3 days, followed by oral prednisolone (PSL) 1mg/kg, resolved his symptoms, However, 4 days after the start of steroid therapy, his fever, cough and pulmonary infiltrates relapsed. Intravenous PSL 2mg/kg and colchicine were temporarily effective, but his pulmonary symptoms relapsed again. Finally, He had a good response to steroid pulse therapy (mPSL 1g for 3 days), and then was able to taper steroid therapy without relapse. [Clinical significance] Sweet's syndrome with pulmonary involvement can be refractory to high-dose steroid therapy and require steroid pulse therapy.

P1-273

A case of lupus profundus which developed hemophagocytosis

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Conflict of interest: None

【Case Report】A 41-year-old female who was diagnosed lupus panniculitis 12 years ago was treated with systemic and topical corticosteroid therapy. But she presented with large non-healing erythema and scar on face, trunk and limbs. In Mrach 201X, She had high fever over 38 degrees for 3 weeks though she was treated with antibiotics. The blood test showed pancytopenia, high level of LDH and ferritin. Examination of bone marrow showed hemophagocyte. Heophagocytosis (HPS) was considered on clinical and histopathological grounds. She responded well to systemic corticosteroid, PSL 1mg/kg. There were no evidence that she suffered from infection or malignancy. She had no manifestations of systemic lupus erythematosus (SLE). When corticosteroid was reduced to PSL10mg/day, her skin lesion turned worse. After starting therapy with hydroxychloroquine, her skin lesion was improved and she needed less PSL.【Discussion】In this case, we think the cause of HPS was lupus profundus. SLE is well known as the cause of HPS, but there is no report of lupus profundus was a cause of HPS. The legion of lupus erythematosus is limited to skin, but this is a valuable case to suggest that patients of lupus profundus may have immune abnormality which causes HPS.

P1-274

Association of a Single Nucleotide Polymorphism in *TNIP1* with Type 1 Autoimmune Hepatitis in the Japanese Population

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Conflict of interest: None

Objectives: Several studies reported that autoimmune diseases share a number of susceptibility genes. Of these genes, a SNP in *TNIP1* was reported to be associated with systemic lupus erythematosus (SLE). Autoimmune hepatitis (AIH), a very rare chronic progressive liver disease, shares some clinical features with SLE. Therefore, we investigated whether the SNP is associated with Japanese AIH. Methods: An association study of rs7708392 in *TNIP1* was conducted in 343 Japanese AIH patients and 828 controls. Results: We found that rs7708392 is associated with AIH (P=0.0236, odds ratio (OR) 1.26, 95% confidence interval (CI) 1.03-1.54), under the allele model for C allele. With respect to AIH clinical subsets, rs7708392 was associated with AIH with platelet number higher than $18.8X10^4$/μl (P=0.0038, Q=0.0416, OR 1.51, 95%CI 1.14-1.99). There was a tendency of rs7708392C to be associated positively with AIH with AST level higher than 463.8 IU/L (P=0.0092, Q=0.0508, OR 1.52, 95% CI 1.11-2.09). Of interest, association with TNIP1 was stronger in AIH without *HLA-DRB1*04:05* allele (P=0.0075, OR 1.47, 95%CI 1.11-1.95). Conclusions: The C allele of rs7708392 was associated with AIH, especially AIH without *DRB*04:05*, an already established risk factor.

P1-275

A case of colchicine myopathy during the course of Behcet's disease and secondary amyloidosis

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Conflict of interest: None

A 71 year- old woman had refractory oral aphthae for over 30 years. Six years ago, multiple colon ulcers was detected by colonoscopy and Behcet's disease was diagnosed. Colchicine 1mg/day and PSL 5mg/day was started. Four years ago, colchicine dosage was increased to 1.5 mg/day. Six months before the admission, progressive proteinuria had been detected. A kidney biopsy was performed, which revealed deposition of amyloid mainly on the mesangial matrix, and renal amyloidosis was diagnosed. Her serum creatine kinase level on initial examination had elevated (CK 1465 U/L), after discharge she presented muscle weakness, and she was hospitalized again. A muscle biopsy revealed colchicine myopathy. After colchicine was discontinued, elevation of CK and muscle weakness improved. In this case, because of renal amyloidosis renal function was getting worse (Cr 1.27 mg/dL), and renal dysfunction may have led the elevation of plasma colchicine levels and myotoxicity. Colchicine myopathy generally occurs weeks after initial administration of colchicine. Even if it's used by the same amount for several years like this case, it's progressive, when admitting kidney dysfunction, a patient develops myopathy. Therefore attentive observation is needed.

P1-276

A case study which Castleman disease was well effected by tocilizumab who has Chronic type B hepatitis virus and hepatocellular carcinoma

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Conflict of interest: None

Object: We experienced a pacient who has Chronic type B hepatitis virus and hepatocellular carcinoma with arthritis, unknown fever and lymphocytes, which tocilizumab was well effected. Present Illness: 57 years old man. In 2007, He was diagnosed with Chronic type B hepatitis virus. In 2016 January, he was diagnosed with lymphocytes occurred by cancer in another hospital and administered PSL30mg, but not well effected. He was invited to our hospital in 2016 April. Clinical progress: We administered with steroid pulse therapy and PSL40mg, but not well effected. So we administered tocilizumab, arthritis and fever changed for the better. Also IL-6 and lymphocytes changed for the better. Cosideration: This case was well effected by administered tocilizumab. We report this case with literature about Chronic type B hepatitis and Castleman disease.

P1-277

Efficacy of tocopherol N for perimenopausal arthralgia

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Conflict of interest: None

[Object] Peri-menopausal women complaining of MS/ joint pain and irregular menses visited the clinic. Most cases showed no evidence of abnormality in blood test and joint swelling except for joint pain. We present clinical practice for these patients. [Methods] 43 peri-menopausal women visiting the clinic from 2013 to 2015 were enrolled. Blood exam included serum CRP, RA, ANA, anti-SS-A, E2 and FSH. Assessment of joint pain recorded by patient VAS, E2 and FSH were obtained on the first visit, 2, 6 month. These patients received Tocopherol N without NSAID. [Results] E2:107.0±144.0 pg/ml after treatment is higher than E2:76.5±78.7pg/ml before treatment (p=0.0588). FHS:32.6±31.7 mIU/ml after is significantly lower than FSH: 75.9 ±29.6 before (p=0.0016). P-VAS: 31±33 after is lower than P-VAS:100 before (p<0.0001). MS and joint pains were significantly reduced within 2~6 months in 16 out of 43 (37.2%). [Conclusions] Tocopherol N was used for the patients with irregular menses. Tocopherol N is one of the method to treat the perimenopausal women complaining of MS and joint pains

P1-278

A case of pulmonary arterial hypertension associated with systemic lupus erythematosus, systemic sclerosis, and pulmonary langerhans cell histiocytosis

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Conflict of interest: None

A 36 year-old-female was diagnosed as pulmonary langerhans cell histiocytosis (PLCH) at 28 years of age. Around 29 years old, she began noticing puffy finger, Raynaud's phenomenon, and the presence of anti–Scl-70 antibody was detected. Then she also noticed a oral ulcers, polyarthralgia, and the laboratory tests revealed lymphocytopenia, presence of anti-dsDNA antibodies, and urinary protein. Based on these findings, she was diagnosed with overlapping syndrome with systemic sclerosis (SSc) and systemic lupus erythematosus (SLE). She was treated using pulse therapy of intravenous cyclophosphamide and prednisolone and these therapies effectively reduced the disease activity. However, she noticed dyspnea on exertion at 35 years of age. Her right heart catheterization (RHC) revealed mean pulmonary artery pressures (mPAP) at 28mmHg. On the other hand, echocardiography and chest computed tomography scan showed no evidence of left ventricular dysfunction and interstitial lung disease. From the results of these investigations, she was diagnosed with pulmonary hypertension (PH) due to SLE, SSc, and PLCH (WHO group 1 and 5). Beraprost and riosiguat were started and she experienced a great improvement of exercise capacity and a follow-up RHC revealed decreased mPAP (23 mmHg).

P1-279

A case of systemic lupus erythematosus (SLE) developed allergic reaction and hepatopathy by readministration of trimethoprim-sulfamethoxazole (TMP/SMX) and review of the literature

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Conflict of interest: None

A 17-year-old-woman was diagnosed having SLE because of positive anti-nuclear antibody, positive anti-ds-DNA antibody, central nervous system lesion, arthritis, and lymphopenia in April, 2016. She was treated with 60mg/day of prednisolone, intravenous pulse cyclophosphamide and tacrolimus. On May 24, We started upfront graded administration of TMP/SMX for prophylaxis against many infections. On July 2, 1T/day of Daiphen was initiated. On July 10, she developed headache, sore throat, joint pain, fever and hepatopathy. Antibiotic was administered and Daiphen was discontinued with clinical improvement. When Daiphen was readministered from July 16, she developed fever, headache, conjunctival hyperemia, coughing, joint pain, and muscle pain one hour after readministration. Severe hepatopathy (AST 1524U/l, ALT 1596U/l, LDH 1534U/l) was observed. Daiphen was discontinued again and there was a striking improvement. This paper presents a case of allergic reaction and hepatopathy by TMP/SMX, during the therapeutic course of SLE, followed by review of the literature.

P1-280

Investigation on requests of RA patients to promote the cooperation in rheumatism professional facilities and home doctors in RA patients

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Conflict of interest: Yes

[Purpose] Cooperation in rheumatism professional facilities and home doctors is necessary. For cooperation promotion, reality and request of patients were investigated. [Methods] It was investigated by questionnaire survey of no signature for 508 RA patients in out patients service and a citizen open class. [Results] It was investigated from 508 patients (female 435) of the 64.4 years old of average and disease period for 11.4 years. Between rheumatism professional facilities and family doctors, "cooperation +.", were 38%, "lack of cooperation" were 39% and a problem has occurred in 4.3%. 43% of patients thought that ideal system of RA treatment was the system with "A RA medical specialist always treats" and 48% of patients thought "cooperation of a RA specialist and a family doctor". Patients who would like to be always treated by a RA medical specialist have not home doctors and needs steroid treatment. [Conclusion] Many patients haven't enough cooperation between RA medical specialist and home doctors. The RA patients have different hopes and requests, and the cooperation building for each patients should be considered.

P1-281

The Effect of Disease Activity Control on Nutritional Condition in Rheumatoid Arthritis Patients

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Conflict of interest: None

Background: With recent advances in the treatment of rheumatoid arthritis (RA), life expectancy has improved in many patients. However,

the reason is not clear. *Purpose*: To study the effect of biological disease modifying anti-rheumatic drug (bDMARD) on nutritional condition in RA patients. *Methods*: We analyzed the data for 76 RA patients who were treated with the first bDMARD intravenously. The patients' data were obtained retrospectively from their medical records. *Results;* The patient age was 59.5±14.2 years old, and the duration of RA was 10.4±10.3 years. Clinical disease assessment score (CDAI), body mass index (BMI), hemoglobin (Hb), total lymphocyte count (TLC), and serum albumin (Alb) showed significant improvements 6 months after bDMARD administration (CDAI: 20.9 11.8 vs 8.02±6.01, $p<0.001$, BMI: 23.3±4.61 vs 23.8±4.39 kg/m^2, $p<0.001$, Hb: 11.9±1.65 vs 13.0±1.63 g/mm^3, $p<0.001$, TLC: 1.38±0.489 vs 1.73±0.705 / 10^3 mm^3, $p<0.001$, Alb: 3.64±0.430 vs 4.12±0.412 g/dL, $p<0.001$). These trends were reconfirmed in the patients who took constant dose of prednisolone and methotrexate. *Conclusion:* Control of RA disease activity may improve the nutritional condition and contribute to the extension of life expectancy.

P1-282

A case of anti CADM-140 antibody positive dermatomyositis complicated with idiopathic portal hypertension with refractory massive pleural effusion

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Conflict of interest: None

<Introduction> Anti-CADM-140 antibody (CADM-140) positive dermatomyositis (DM) is famous for complicated rapid progressive interstitial pneumonia (IP), However rarely complicates hepatobiliary disease. <Case> A 51-year-old woman developed DM and IP in 2012. Although it was positive for CADM-140, she improved with prednisolone (PSL) and tacrolimus. In 2014, abdominal distension progressed in 2 months, Mild hepatic atrophy, intrahepatic AV shunt and massive ascites were seen by contrast CT. Due to unknown cause, trans-jugular vein liver biopsy was performed. However, there was no pathological abnormality. In 2015, dyspnea rapidly emerged in a week. Images showed right pleural effusion and we diagnosed as chylothorax by analysis of pleural effusion. Lymph leakage was not observed in lymphangiography. 2nd liver biopsy was performed but showed no pathological abnormality. It became difficult to eat due to refractory pleural effusion and ascites and finally died due to sepsis caused by central venous catheter infection. At necropsy, pathological findings consistent with portal hypertension were seen. <Discussion> Autoimmune abnormality is suspected as the etiology of idiopathic portal hypertention (IPH). We report the first case of combination with DM and IPH with literature reviews.

P1-283

A Case of large B-cell lymphoma which was diagnosed not by lymph node biopsy nor by bone marrow biopsy, but by pathologic anatomy

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Conflict of interest: None

[Case] An 84 years old woman. Nine month ago, she had fever with multiple lymphadenopathy. In another hospital, intensive examination including lymph node biopsy and bone marrow aspiration and biopsy (BMA&B) was performed because intravascular lymphoma was suspected, but she was not diagnosed. The fever was alleviated with anticancer chemotherapy and prednisolone (PSL). The fever recurred at 3 months ago. After random skin biopsy and the second BMA&B was performed, acute renal failure, multiple cerebral infarction and macrophage activation syndrome developed. These symptoms weren't controlled by the steroid pulse therapy either, so she was transferred to our hospital. Although the second intensive examination was performed, she was not diagnosed, The symptoms weren't controlled with combination therapry cyclosporine and PSL. She died of bacterial infection 2 months after administration. Eventually a diagnosis of large B-cell lymphoma was confirmed by pathologic anatomy. [Discussion] BMA&B is powerful diagnostic method in the examination of fever with unknown origin. But, in our case, although hematopoietic malignant disorders were suspected, diagnosis was not obtained by repeat BMA&B. We report the detail of this case with some literature review about diagnosis power of BMA&B.

P1-284

A case of polyarthritis whose secondary adrenal insufficiency is found during treatment as rheumatoid arthritis

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Conflict of interest: None

[Case] 73-year-old male [CC] Polyarthralgia, polymyalgia and edema [FH] No rheumatic disease [PH] left intraorbital tumor surgery in 2009, followed by the administration of betamethasone (BM). [PI] When temporary BM was discontinued, left PIP-joints pain and left knee pain appeared. Polyarthralgia, Lower back pain, myalgia and mild edema appeared from September 2014. He visited our hospital on September 28, 2015 due to worsening of symptoms. CRP0.03mg/dl, RF 18.0IU/ml, anti-CCP antibody0.6U/ml, MMP-3 43.4ng/ml. No joint narrowing and erosion was observed in X-ray examination, whereas bone scintigraphy showed peripheral polyarthritis. Salazosulfapyridine was started as RA, but it was not effective. On the other hand, by interview, it was revealed that BM was gradually decreased and canceled in mid September 2015. As clinical examination showed an increase in ACTH (81.0pg/mL) and a decrease in cortisol (3.0μg/dL), a diagnosis of secondary adrenal insufficiency was made. Prednisolone was started and increased gradually from 3.5 mg to 10 mg and his symptoms relieved. [Discussion] This may be the case of rheumatoid symptom caused or worsened by secondary adrenal insufficiency. A detailed interview of medical history of steroid administration is necessary in such a case.

P1-285

A case of Cushing's syndrome who manifested arthritis after adrenal surgery

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Conflict of interest: None

[Purpose] Diagnosis of joint pain associated with endocrine disorders may be differentiated from seronegative RA. We here report a female case of adrenal Cushing's syndrome who developed arthritis after adrenal surgery. [Method] Case: a middle-aged female, Chief complaints: Swelling, stiffness and pain of bilateral hands. The patient has been pointed out regarding her feature of central obesity for six years. Screening CT for secondary hypertension detected a right adrenal tumor. Based on the endocrine workup, she was diagnosed as Cushing's syndrome due to the right adrenal tumor. Replacement therapy with hydrocortisone commenced after adrenal surgery; however, she had suffered arthritis symptoms of the bilateral finger joints since 2 months after the surgery. Serological results were as follows: CRP 1.22, RF (-), anti-CCP antibody (-), and MMP-3 14.4. [Result] Early RA was suspected but increasing the dose of steroid was effective to ameliorate her arthritis. [Conclusion] Following the surgery of Cushing's syndrome, occurrence of muscle pain and joint pain has been reported to be 6-13%. In such cases, the possibility of relative adrenal insufficiency, namely "painful hypoadrenalism", should also be considered.

P1-286

Successful treatment of refractory malar rash and alopecia by hydroxychloroquine in a patient with Systemic lupus erythematosus

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Conflict of interest: None

A 28-years-old woman was admitted because of fever, thrombocytopenia, and alopecia. At age of 24, the patient developed malar rash, pleurisy, and arthralgia. She was diagnosed as having Systemic lupus erythematosus (SLE) and treated with prednisolone (PSL) successfully. At the age of 28, because of ultraviolet exposure, she developed fever, thrombocytopenia, and alopecia. She was diagnosed as having flare of SLE and treated PSL 30mg/day and tacrolimus (TAC) 2mg/day. However, as dose of PSL was reduced, her cutaneous symptoms worsened. Therefore, we decided to treat them with hydroxychloroquine (HCQ). The symptoms became better and we could reduce the dose of PSL and tapered off the dose of TAC. Our case indicated that HCQ may have a favorable effect on patients with refractory lupus cutaneous symptoms.

P1-287

Comparison of clinical features of patients with rheumatoid arthritis and pseudo-rheumatoid arthritis

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Conflict of interest: None

OBJECTIVE: To clarify the clinical features of patients with rheumatoid arthritis (RA) and pseudo-rheumatoid arthritis (pseudo-RA) for differential diagnosis. METHODS: 50 RA patients and 20 pseudo-RA patients, whose diagnoses were made in my Hospital between April 2012 and March 2013, were examined with laboratory data, X-ray and ultrasonogram. The diagnosis of each disease was established when the diagnosis was maintained without an alternative diagnosis for at least three years follow-up. RESULTS: The average age in each group was 63.0 years (median 69.5 years) in the RA group, and 71.3 years (median 73.5 years) in the pseudo-RA group (P<0.05). The sex ratio of each group was 35:15 female/male in the RA group, and 17:3 female/male in the pseudo-RA group. The number of patients who fulfilled the RA classification criteria of ACR / EULAR (2010) was 44/50 (88%) in the RA group and 7/20 (35%) in the pseudo-RA group. The sensitivity of RF and ACPA was significantly higher in the RA group, however, all patients with pseudo-RA with RF or ACPA were misdiagnosed as RA at other medical institutes. Detection of chondrocalcinosis by ultrasonogram raised the possibility of pseudo-RA. CONCLUSION: This study highlighted usefulness of ultrasonography for diagnosis of pseudo-RA.

P1-288

Prescription and Prognosis of RA with CKD

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Conflict of interest: None

[Object] We investiged retrospectively the prescription and prognosis of RA patient with CKD under Stage 3a. [Methods] 19 RA patients with CKD under stage3 at the end of 2010 (total 191 RA patient), were investiageted the prescripiton, 5years' CKD & RA condition. [Results] Stage3a;11, Stage3b;5, Stage4;3. MTX;11, PSL;15, csDMARDs14, bDMARDs;2. All 3 with stage4 were treated with PSL and other csDMARD. During 5 yrs. 2 were dead (due to pancreatitis, and leukemia) and other 2 were transferd to general hospital because of RA worsening and pneumonia. [Conclusions] We need device to manage the RA patients with CKD, but it is possible to control with slowly progression of CKD.

P1-289

Association of leptin and leptin receptor gene polymorphisms with systemic lupus erythematosus in a Chinese population

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Conflict of interest: None

Objectives Recent studies demonstrated that leptin (*LEP*) is associated with multiple autoimmune diseases and abnormally elevated in patients with systemic lupus erythematosus (SLE). In this study, we aimed to explore the association of *LEP* and leptin receptor gene (*LEPR*) single nucleotide polymorphisms (SNPs) with susceptibility to SLE in a Chinese population. **Methods** Four *LEP* SNPs (rs11761556, rs12706832, rs2071045, rs2167270) and nine *LEPR* SNPs (rs10749754, rs1137100, rs1137101, rs13306519, rs8179183, rs1805096, rs3790434, rs3806318, rs7518632) were genotyped in a cohort of 633 SLE patients and 559 health controls. The selected SNPs were genotyped in both cases and controls using improved multiple ligase detection reaction (iMLDR) genotyping assays. **Results** No significant differences were detected for the distribution of allele and genotype frequencies of all 13 SNPs between SLE patients and controls. The genotype effects of recessive, dominant and additive models were also analyzed, but no significant evidence for association was detected. However, further analysis in SLE patients showed that the TT genotype and T allele frequencies of the rs2071045 polymorphism were significantly higher in patients with pericarditis (P=0.012, P=0.011 respectively). In *LEPR*, the GA/AA genotype and A allele frequencies of the rs1137100 polymorphism achieved the significant difference in patients with photosensitivity (P=0.043, P=0.018 respectively). Moreover, we found that the genotype and allele distribution of rs3806318 was also significantly associated with photosensitivity in the SLE patients (P=0.013, P=0.008 respectively). **Conclusion** In summary, *LEP* and *LEPR* SNPs are not associated with genetic susceptibility to SLE, but may contribute to some specific clinical phenotype of this disease, further studies are necessary to elucidate the exact role of *LEP* and *LEPR* gene in the pathogenesis of SLE.

P1-290

Stage-specific differences in secretory profile of mesenchymal stromal cells (MSCs) subjected to early- vs. late-stage OA synovial fluid

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Conflict of interest: None

Objective: Although, mesenchymal stromal cells (MSCs) are being clinically investigated for their use in osteoarthritis (OA), it is unclear whether their postulated therapeutic properties are equally effective in the early- and late-stages of OA. In this study we investigated MSC cytokine secretion post-exposure to synovial fluid (SF), obtained from early- vs. late-stage knee OA patients to justify a potential patient stratification strategy to maximize MSC-mediated treatment effects. **Method:** Subjects were recruited and categorized into early- [Kellgren-Lawrence (KL) grade I/II, n=12] and late-stage (KL III/IV, n=12) knee OA groups. SF samples were obtained, and their proteome was tested using multiplex assays, after three-days culture, with and without MSCs. SFs cultured without MSCs were used as a baseline to identify MSC-secreted factors into

SFs cultured with MSCs. Non-parametric tests were used to identify alterations in the MSC secretome during exposure to OA SF (three-days). MSCs cultured for three-days in 0.5% fetal bovine serum-supplemented medium were used to compare SF results with culture medium. **Results:** Following exposure to OA SF, the MSC secretome contained proteins that are involved in tissue repair, angiogenesis, chemotaxis, matrix remodeling and the clotting process. However, significant MSC donor-independent differences after OA SF exposure were only noted for CXCL8 (chemokine (C-X-C motif) ligand-8; chemoattractant), which was significantly elevated in response to early- compared to late-stage OA SF. **Conclusion:** Early- vs. late-stage OA SF samples elicit a differential MSC response arguing for stratification of OA patients to maximize MSC-mediated therapeutic effects.

P1-291

Expression of podoplanin in synovial tissue of rheumatoid arthritis

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Conflict of interest: None

Introduction: Podoplanin, known as platelet aggregation-inducing factor in the haematogenous metastasis of tumor cells and mucin-type transmembrane glycoprotein and possible potent molecule of inflammation. The aim of this study was to investigate its tissue and cellular distribution in the rheumatoid synovium. **Methods:** The synovial tissue samples were obtained surgically from the patients with rheumatoid arthritis (RA) treated with biologic disease-modifying anti-rheumatic drug (DMARD) (BIO, n=30) or conventional DMARD (cDMARD, n=30) and osteoarthritis (OA, n=5). Serial 5-μm-thick frozen tissue sections were stained by rat monoclonal anti-human podoplanin (NZ-1). The sections were incubated with anti-CD68, anti-fibroblast 5B5, anti-IL17 and anti-lymphatic endothelia LYVE-1 with anti-human podoplanin for immunofluorescence and immunohistochemical staining. Podoplanin+ cells were scored (3+; >50%/ area, 2+; 20%>50%, 1+; 5%>20%, 0: <5%) in the rheumatoid synoial tissues with analyses of inflammatory grading (0-3) and cell-typing. Mann–Whitney U test and Spearman's rank correlation coefficient analysis were performed ($p<0.05$). **Results:** Inflammatory grading score was 1.6 in both BIO and cDMARD, and 0.2 in OA. Podoplanin+ cells were expressed in the lining layer (BIO 1.6, cDMARD 1.3, OA 0.2) and lymphoid aggregation (BIO 0.7, cDMRD 0.7, OA 0.2), which correlated with grading of RA synovium in both BIO and cDMARD ($r=0.7/0.9$, $p<0.05$), not OA ($r=0.2$). Podoplanin was markedly expressed in CD68+ type A macrophages-like and 5B5+ type B fibroblast-like cells in the lining layer and partially IL-17+ cells in lymphoid aggregations of RA, slightly in LYVE-1+ lymphatic vessels. **Conclusions:** Podoplanin was markedly expressed in the immunologically inflamed synovium and correlated to inflammatory, which was surgically treated due to progressive arthritis against both BIO and cDMARD. It indicates that podoplanin will be a possible new therapeutic target in the treatment of RA.

P1-292

Platelet rich plasma with Chinese medicine in hyaluronic acid gel for articular cartilage retrieval and immunoregulatory effect on rodent osteoarthritis model

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Conflict of interest: Yes

Objective: Aim to address platelet rich plasma (PRP) with Chinese medicine formulas Ling-Zhi (LZ) and San-Miao-San (SMS) or Magnoflorine to promote chondrocyte proliferation and synergistic immunoregulatory effects for the articular cartilage retrieval at rodent model of osteoarthritis (OA). **Methods:** Patients undergoing total knee arthroplasty (TKA) were recruited and Oxford knee scores were recorded. The radiographs of OA knee were evaluated by Kellegren-Lawrence system. The biochemical parameters from blood and synovial fluid samples were measured. In vivo, the traumatic OA model was made by transection of the anterior cruciate ligament (ACLT) in rats. All ACLT treated rats were administrated with PRP, PRP hyaluronic acid (HA) gel, and PRP with LZ-SMS or Magnoflorine in HA gel, respectively, twice a week for 3 consecutive months, following which the animals were performed micro-CT scan, biochemical parameters detection and histological staining. **Results:** We obtained an average PRP concentration of around 1×10^7 platelets/ ml and tagged platelets with the cell tracker indium-111 radioisotope to view the platelet distributed throughout in the HA gel. The proliferation of human endothelial cells cultured with thrombin activated PRP increased relatively compared to control, which demonstrated the potential benefit of PRP to induce cartilage proliferation. In vivo study, the female Dukin Hartley guinea pigs treated with 100 μl of PRP HA gel were not found any significant worsening in morphology of cartilage, when compared to the control limb. Furthermore, the treated limb had an increased content of glycosaminoglycan compared to the control limb. **Conclusion:** Our study elucidated the *in vivo* immunoregulatory effect of the refined PRP with LZ-SMS and magnoflorine in HA gels on articular cartilage retrieval in a rodent model of traumatic OA and promotes chondrocyte proliferation *in vitro,* as well as characterizing the clinical features of OA patients.

P1-293

COX-2 inhibitor contributes autophagic cell death in rheumatoid arthritis fibroblast-like synoviocytes via PI3K/Akt signaling pathway triggered by oxidative stress

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Conflict of interest: Yes

Objectives: Recently, the possibilities that autophagy regulates apoptosis resistance and hyperplasia of fibroblast-like synoviocytes (FLS) were also presented. The aim of this study is to investigate the influence of COX-2 inhibitor on viability of rheumatoid arthritis (RA) FLS and to reveal how COX-2 inhibitor affects the viability of RAFLS. **Methods**: RA synovial tissue was obtained from patients during total knee replacement surgery or arthroscopy. FLS was cultured with COX-2 inhibitor, caspase inhibitor (z-VAD-fmk), autophagy inhibitor (3-methyladenine; 3-MA), knockdown of si-autophagy protein 5 (Atg5) or si-Beclin1. Cell viability was measured by MTS assay and by cell count using trypan blue staining. The expression of autophagy flux was analyzed by western blot and apoptosis activation was measured caspase3/7 activity assay. **Results**: A kind of COX-2 inhibitor dose-dependently decreased cell viability (mean IC50 of 120 μM) of RAFLS. Combination treatment with caspase inhibitor and COX-2 inhibitor increased cell viability than a single treatment with COX-2 inhibitor. COX-2 inhibitor also increased the expression of conversion of LC3-I to LC3-II, Atg5, Beclin1, p62 and decreased expression of lysosomal associated membrane protein 1 (LAMP1) in RAFLS. Inhibition of autophagy by 3-MA, si-Atg5 or si-Beclin1 restored viability of RAFLS by COX-2 inhibitor. COX-2 inhibitor decreased expression of phosphorylation-Akt signaling pathway. And, COX-2 inhibitor-induced autophagic cell death via ROS-dependent effect in RAFLS. **Conclusion**: Taken together, this study indicated that autophagy contributed RAFLS from COX-2 inhibitor-induced apoptosis, and the combined use of COX-2 inhibitor and an autophagic inhibitor in RA patients may be an effective therapeutic strategy.

P1-294

Expression of IL-37, IL-18BPa and IL-18 in primary Sjogren's Syndrome

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Conflict of interest: None

Objective: To investigate the expression of the IL-37/IL-18/IL-18BP/IL-18Ra axis in patients with primary Sjögren's syndrome (pSS). **Methods:** Serum concentrations of IL-37, IL-18 and IL-18BPa were measured in 36 pSS patients, 13 sicca patients and 14 healthy controls by sandwich ELISA. The serum concentrations of IL-37, IL-18 and IL-18BPa were correlated with various clinical and biological parameters. The expression of IL-37, IL-18, IL-18BP and IL-18Ra was investigated in salivary glands (SG) by immunohistochemistry. **Results:** Serum levels of IL-18 and IL-18BPa were statistically significantly increased in pSS relative to healthy controls ($p < 0.0001$) and correlated with each other. There was no significant difference in serum levels of IL-37 among SSp, sicca and healthy controls ($p = 0.1695$). IL-37 overexpression is present in excretory ducts and inflammatory infiltrates in pSS patients, compared to Sicca patients. Immunohistochemistry also revealed an increase in expression of IL-18, IL-18BPa and IL-18Rα in the salivary glands of pSS patients. **Conclusions -** Our study demonstrates an overexpression of IL-37, IL-18, IL-18BPa and IL-18Ra in minor salivary glands by immunohistochemistry and increased serum levels of IL-18 and IL-18BPa in pSS patients. Thoses finding suggest the implication of IL-18 axis in pSS pathophysiology.

P1-295

The effect of myostatin inhibition on bone loss in murine osteoporosis models

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Conflict of interest: Yes

[Objectives] Myostatin, a secreted member of TGF-β family, negatively regulates skeletal muscle mass. Recent study reported that myostatin regulates bone as well as muscle, by showing that myostatin deficiency directly suppresses osteoclastogenesis and ameliorates articular bone destruction in murine arthritis models (B. Dankbar, et al. Nat Med 2015). However, it is not clarified whether myostatin inhibition prevents systemic bone loss. In this study, we investigated the effect of myostatin inhibition in murine osteoporosis models. [Methods] We used C313Y mutant myostatin transgenic mice, in which myostatin prodomain is excessively expressed and subsequently inhibits myostatin activity. For RANKL-induced bone loss model, 1 mg/kg of RANKL was injected intraperitoneally at day 0 and 1, and the sera and bones were collected at day 2. For tail-suspension unloading model, the tails of the mice were suspended for 2 weeks. At the end of the period, the sera, bones, and muscles were collected. Serum TRAP5b levels were measured by ELISA. Bone properties of vertebra and tibia were determined by micro-CT. [Results] At baseline, the myostatin mutant mice exhibited increased muscle mass similarly to myostatin null mice. RANKL injection induced severe bone loss in wild-type mice, and the myostatin mutant mice also exhibited bone loss to a similar extent. Serum TRAP5b levels are also comparable between RANKL-treated wild-type and myostatin mutant mice. In the unloading model, myostatin mutation did not prevent bone loss and also muscle atrophy. In murine primary bone marrow macrophage culture, myostatin stimulation had only minor effect on the RANKL-induced osteoclastogenesis. [Conclusion] Myostatin inhibition did not exhibit the protective effect on bone loss in the osteoporosis models we tested. The role of myostatin inhibition might vary in different pathologic conditions. Therefore, further research will be required to clarify the clinical implications of myostatin inhibition.

P1-296

Fucosylation mediates rheumatoid arthritis angiogenesis

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Conflict of interest: None

【Object】Glycosylation is a common post-translational modification of proteins in eukaryotes. We previously showed the expression of fucosylated proteins in rheumatoid arthritis (RA). Here, we have shown the role of fucosylated proteins in RA angiogenesis.【Methods】Total glycans were determined in serum from normal (NL) subjects and RA patients using mass spectrometry. To determine whether fcosylated proteins involved with RA inflammation, the correlation with DAS28 (ESR) was measured. To block the expression of fucosylated protein, human umbilical vein endothelial cells (HUVECs) were treated with 2-deoxy-D-galactose (2-d Gal). In order to confirm the role of fucosylation in RA angiogenesis, we performed 2-d Gal treated HUVEC tube formed assay was performed towards RA synovial fluids. Finally, we examined that cytokines in 2-d Gal treated HUVEC were measured by ELISA.【Results】Total glycans in RA serum were significantly higher than in NL serum. Total glycans in RA serum were also correlated with DAS28 (ESR). Percent of fucosylated proteins in total glycans were decreased with treatment. 2-d Gal treated HUVEC tube formed towards RA synovial fluids were decreased compared with nontreated HUVEC tube formed. Fractalkine/CX-3CL1, CXCL16, or interleukine (IL)-8/CXCL8 in 2-d Gal treated HUVEC conditioned medium were decreased compared with in non-treated HUVEC conditioned medium.【Conclusions】These results indicate that glycosyration is involved with RA inflammation, and suggesting that fucosylation may play a role in RA angiogenesis.

P1-297

Rho activation plays an important role in the additive effect between methotrexate and anti-TNF agents in TNF-producing cells

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Conflict of interest: None

Objectives To understand the mechanism (s) of additive effect of MTX and anti-TNF agents in the treatment of rheumatoid arthritis (RA). 1) Additive effect of MTX and anti-TNF agents on the inhibition of transmembrane TNF-producing (tmTNF) cells was studied. 2) The mechanism (s) of this additive effect were examined. Methods: 1) A human Jurkat T cell line stably expressing transmembrane TNF was treated with 0.1uM MTX, 0.01uM anti-TNF (Infliximab, Etanercept, Certolizumab Pegol) alone or 0.1uM MTX plus 0.01uM anti-TNF agents. The apoptotic cells were detected by a flow cytometry. 2) Y-27632 (Rho kinase inhibitor) and folic acid were used to inhibit intracellular events. 3) Cell lysates from the tmTNF cells that treated with Infliximab were studied for Rho activation by western blot. Results 1) Apoptosis of tmTNF cells was significantly increased by the co-stimulation of MTX and anti-TNF agents compared to the treatment with MTX or anti-TNF agents alone. 2) A Rho kinase inhibitor, Y-27632, significantly inhibited IFX-mediated apoptosis of tmTNF cells, but not in MTX-treated cells. Rho GTPase was activated in the IFX-treated tmTNF cells. 3) Folic acid inhibited MTX-mediated apoptosis of tmTNF cells, while it did not show any effects on the IFX-mediated apoptosis of tmTNF cells. Conclusions Additive effect by MTX and anti-TNF agents was shown in the induction of apoptosis of our tmTNF cells. This result may explain in part the additive effect of MTX and anti-TNF agents in RA patients. Apoptosis mediated by anti-TNF agents is mediated through activation of the Rho-signaling pathway.

P2-001

The causes of death in deceased patients with RA by NinJa 2015 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 2015 [Methods] 119 Japanese deceased patients with RA, who were registered in the large cohort database (NinJa: National Database of Rheumatic Diseases by iR-net in Japan). We investigated the age at death, the causes of death of all patients. [Results] The mean age at death was 76.9years old. The major cause of death in deceased patients was malignancy in 36 patients. Next was infection in 20patients involving in pneumonia in 16patients., respiratory dysfunction involving intestinal pneumonia in 19 patients, cardiovascular disease in 11 patients. [Conclusion] The life expectancy of Japanese patients with RA was getting better. But the average of RA onset is recently older, the duration from RA onset to death is shorter. The major causes of death were changed from infection to malignancy.

P2-002

Course of Death and Risk Factors of Death in Patients of Rheumatoid Arthritis

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Conflict of interest: None

[Object] To determine whether cardiovascular events are important courses of death among Japanese patients with rheumatoid arthritis (RA). [Methods] We reviewed the data of the two years prospective cohort study of the patients with RA. The data of dead patients at baseline were compared with those of other patients. [Results] The number of the dead patients was 18 in 161 of all patients. They were significantly older, and had higher prevalence of male, coronary disease, and diabetes mellitus than the survival patients. The dead patients had significantly higher levels of hemoglobin A1c, C-reactive protein, and erythrocyte sedimentation rate, brachial-ankle pulse wave velocity, and mean intima-media thickness, and lower levels of estimated glomerular filtration rate compared with the survival patients. The direct courses of death were 5 cases (27.8%) of heart disease, 3 cases (16.7%) of stroke, 4 cases (22.2%) of malignancy, and 8 cases (44.4%) of pneumonia. [Conclusions] Cardiovascular events were the important course of death among Japanese RA patients. The disease activity of RA, atherosclerotic changes, and chronic renal disease were seemed to be associated with the poor prognosis.

P2-003

Incidence and risk factors for herpes zoster in patients with rheumatoid arthritis registered in NinJa 2015

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Conflict of interest: Yes

[Object] To investigate the incidence and the risk factors for herpes zoster (HZ) in Japanese patients with rheumatoid arthritis (RA) in daily clinical practice. [Methods] Using data of NinJa (National database of rheumatic diseases in Japan) in 2015, crude incidence rate (April 2015 to March 2016) and standardized incidence ratio (SIR) of HZ in RA patients were calculated. Logistic regression analyses were performed to evaluate the risk factors for development of HZ. [Results] A total of 13,368 patients were analyzed. The median age of total patients was 67 years and 80.3% were female. HZ developed in 192 patients, crude incidence rate of HZ was 14.6 per 1000 patients-years, and SIR of HZ was 3.31 (95% confidence interval [CI], 2.84-3.78). Multivariate analysis showed that age (adjusted odds ratio [OR] for 10-year increase: 1.16, 95% CI:1.02-1.33), corticosteroid use (prednisolone≧5mg/day) (OR:1.51, 1.00-2.29), TAC use (OR:1.74, 1.16-2.60), and TOF use (OR:8.31, 4.31-16.0) were significant risks for HZ. [Conclusions] As reported in the results of clinical trial, this study showed that TOF use related to the increased risk of HZ in daily clinical practice. We need to pay attention for development of HZ in RA patients treated with TOF.

P2-004

Prodromal symptoms of serious infections in RA patients treated with tocilizumab - Retrospective analysis using a Post-Marketing Safety Database -

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Conflict of interest: Yes

Objective: To identify initial symptoms prior to serious infection (SI) in tocilizumab (TCZ) treated patients (pts) using clinical narratives from post-marketing safety database. **Methods:** A post-marketing safety database maintained by Chugai Pharmaceutical Co. Ltd. was used, obtaining case reports with structured (age, event, etc) and unstructured data (clinical narratives). Reports had to meet 4 criteria: reported Apr 2008-Apr 2015/ TCZ treated Japanese RA pts/ SIs/ causality with TCZ reported by healthcare professionals. Descriptive statistics was used to summarize pt characteristics and text-mining method for clinical narratives. **Results:** 7653 RA pts were retrieved with 1732 SIs in 1221 pts; pneumonia (15.9%), cellulitis (9.9%), and sepsis (5.0%). Within the 782 pts with diagnosis date of SI, 475 (60.7%) pts had symptoms within 28 days of SI. Prodromal symptoms extracted were pyrexia (14.2%), pain (14.2%), and cough (13.7%). Lab abnormalities within 7 days from SI were seen in 56.5% for CRP ≥1.0 mg/dL, 48.9% for BT ≥37ºC, and 42.8% for WBC ≥10,000/μL. **Conclusion:** The presence of prodromal symptoms in those who developed SIs after TCZ administration was described in most cases. Therefore, data mining of clinical narratives may have additional value in characterizing SIs.

P2-005

Recent change in prevalence of rheumatoid arthritis-related surgery. Comparison of patients whose disease onset was 1995-1999 and 2000-2004 using NinJa cohort

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Conflict of interest: None

Purpose: Thanks to introduction of methotrexate and biolgics, treatment strategy of rheumatoid arthritis (RA) has changed after 2000 in Japan. The purpose of this study was to clarify the effect of this change on prevalence of RA-related surgeries. Methods: We extracted and compared the data of patients whose disease onset was between 1995 and 1999 and disease duration was 5-14 years (group A) and patients whose disease onset was between 2000 and 2004 and disease duration was 5-14 years (group B) from data of NinJa between 2003 and 2015. The number of patients included in group A and B was 9,813 and 18,120, respectively. Results: The number of patients who underwent RA-related surgery per year was significantly large in group A than group B, and its ratio was approximately 1:0.7. Prevalence of TKA, THA, and TEA has decreased, but prevalence of toe surgeries and finger surgeries has not decreased. The difference of prevalence of RA-related surgery was much larger in the young patient group than in the old patient group. Conclusion: Just 5 year difference of disease onset affected the prevalence of surgery as much as 30%. The decrease of surgeries was prominent in young patients, possibly because agressive treatment strategy has mainly introduced in young patients.

P2-006

Orthopedic surgery for RA in NinJa report 2015

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Conflict of interest: None

Aim Analyze/report RA-related orthopedic surgeries performed in '15 using NinJa. **Method** Presence or absence, type, frequency, etc. of surgeries examined in 15100 patients registered in '15 (12105 women, 2995 men) & compared with '03 to '15. **Results/Discussion** Of 15100 patients in '15, 382 patients/494events (2.5%/3.3%) underwent RA surgeries. The number of RA surgery cases decreased from 8.5% in '03 to 3.3% in '15. In '15, RA surgeries to total patient number ratios were (per type) 1.44%(TJA), 0.15%(synovectomy), 0.61%(arthroplasty), 0.31%(arthrodesis), 0.15%(tendon repair) & 0.21%(revision TJA). Medication: 63.1%, 27.5% and 0.99% of patients received total MTXs, total biologicals & total JAK inhibitors, respectively: an increase. In the main-Bio group, the rate of RA surgery peaked at 15% in '06 and decreased thereafter to 4.7% in '15. In the main-MTX group, the rate of surgery also decreased from 9.5% in '03 to 2.9% in '15. Among patients receiving JAK inhibitors, three surgeries had been performed. Although the number of surgeries decreased with increasing use of drugs in the Bio and MTX groups, the rate of decrease was decreasing. We plan to continue to follow up on changes in surgery rates with the emergence of new drugs such as JAK. Follow up planned.

P2-007

The risk of femoral neck fracture after sacral fracture is higher in rheumatoid arthritis patients than in non-rheumatoid arthritis patients

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Conflict of interest: None

As the span of life become longer, the number of sacral insufficiency fracture or femoral neck fracture is increasing. We report the number of patients suffer from femoral neck fracture after sacral fracture with or without the rheumatoid arthritis. We retrospectively counted the number of femoral neck fracture patients with or without rheumatoid arthritis, and the number of sacral fracture patients before femoral neck fracture. We also counted the number of male and female. In the rheumatoid arthritis patients, the risk of femoral neck fracture after sacral fracture was twice as high as that of non-rheumatoid arthritis patients.

P2-008

Nutritional assessment of patients with rheumatoid arthritis

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Conflict of interest: None

Background Cachexia in rheumatoid arthritis (RA) is characterized by loss of muscle mass and concomitant increase in fat mass. Recognition of cachexia is necessary not only to design appropriate treatment program but to improve the long-term outcome. **Objectives** To investigate nutritional status and body composition in RA. **Methods** Cross sectional study. In 163 RA out-patients (75% women), Mini Nutritional Assessment (MNA), body composition determined by bioelectrical impedance analysis, and blood chemistry were assessed. Nutrition managers assessed individual nutrient intake using food frequency questionnaire and diet records. **Results** The percentage of patients either malnourished or those at nutritional risk by MNA was 39%. Low serum albumin, weight loss, low BMI, were seen in 3.7%, 0%, 8.5% of the patients, respectively. In 6/13 cases, total energy intake was lower than estimated energy requirement. Lower muscle mass than those of age-matched previously reported control (<-1SD) were seen in 34%(male), and 22%(female) of the patients. **Conclusion** Comprehensive assessment revealed undernutrition and muscle wasting were prevalent in our RA patients. Combination of nutritional treatment and physical training may be effective to improve nutritional states and body composition in RA.

P2-009

Determinants of discrepancies between physician's and patient's global assessment (GA) of disease activity in rheumatoid arthritis (RA) - three dimension joint index vector (Vji) analysis based on NinJa 2015 database

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Conflict of interest: None

[Object] Vji is a novel method to measure RA disease activity containing affected joint distribution components (Nishiyama S. Rheumatol Int 2012). The discrepancies between RA patient's and physician's GA may be a hindrance in clinical practice. The aim of the present study is to explore the determinants for this discrepancy in further detail based on NinJa 2015 by including Vji assessment. [Methods] We analyzed 12084 RA patients whose VAS data were available. Patient's GA minus physician's GA was calculated as ΔGA, and ΔGA of > 2.5 was categorized as positive discordance (n=2146), and ΔGA of -2.5 to 2.5 as no discordance (n=9766). [Results] Multivariate logistic regression analysis revealed that age, pain VAS and mHAQ, as parameters with Odds ratio (OR) higher than 1, while CRP, class, x (upper joint component), Vz (large joint dominant component) and |Vxy| as those with OR less than 1. [Conclusions] The physicians should pay attention to the pain, ADL and small joint involvement to share the recognition of disease activity with their patients.

P2-010

Disease activity of rheumatoid arthritis (RA) is influenced by seasonal change - Nishiyama's three dimension joint index vector (Vji) analysis based on NinJa 2015 database

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Conflict of interest: None

[Objective] Vji is a novel method to measure RA disease activity containing affected joint distribution information. Previous studies have suggested that environmental factors, such as weather and seasonal change may affect RA (Iikuni N et al. Rheumatology 2007). We thus aimed to explore the influence of seasonal change on RA disease activity including Vji based assessment using NinJa2015. [Methods] RA patients registered in NinJa are evaluated at any point during the indicated year. RA disease activities in spring (March to May, n=3111), including Vji components, were compared with those in fall (September to November, n=1038) using NinJa2015 in the present study. [Results] TJC, SJC, physicain's global assessment (GA), mHAQ, DAS-28, x (upper joint component), y (lower joint component) and |Vxy| were significantly higher in spring than those in fall, indicating that RA disease activities are higher in spring than in fall. Larger joint index was significantly higher in spring than in fall. [Conclusions] Seasonal changes can affect RA disease activities and affected jpint distribution. Influence of season on RA manifesta-

tions should be considered when seeing RA patients to better understand their symptoms.

P2-011

Characteristics of rheumatoid arthritis patients who achieved clinical remission with help of steroids treatment

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Conflict of interest: None

[Object] To elucidate the characteristics of patients who achieved clinical remission with help of steroid treatment. [Methods] We extracted 3147 patients from National Database of Rheumatic Diseases by iR-net in Japan (NinJa) 2012, who had achieved clinical remission (DAS28-ESR<2.6). They were allocated to two groups: group 1 composed with patients who were always prescribed steroids (933 patients), group 2 composed with patients treated without steroids (2168 patients). We compared these patients' backgrounds such as age, disease duration, disease activities (DAS28, SDAI, CDAI), stage, class, mHAQ, usage rate of NSAIDs, usage rate and dose of methotrexate, usage rate of biologics, admission rate and remission retention rate within a year between the two groups. [Results] Daily dose of steroid was 3.83±2.97 mg (mean ± SD) prednisolone in group 1. Age, disease duration, the rate of stage 3 or 4, the rate of class 3 or 4, the dose of methotrexate, the usage rate of NSAIDs, admission rate, and disease activities were significantly higher in group 1 than group 2. The remission retention rate within a year was significantly lower in group 1. [Conclusions] The patients who needed steroids to achieve clinical remission were at higher risk of exacerbation and admission.

P2-012

Profiles of the elderly patients (aged 75 years or more) with higher rheumatoid arthritis disease activity from the AORA registry

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Conflict of interest: None

[Objectives] Elderly patients with RA have shown higher disease activity compared with young patients. We investigated the data of elderly patients with RA from the Akita Orthopedic Group on Rheumatoid Arthritis (AORA) registry. [Methods] Of 2116 patients with RA (mean age, 67 years) in the AORA registry, we examined 271 (46 men and 225 women) aged ≥75 years (mean age, 81 years, DAS28ESR ≥3.2). [Results] The mean disease period was 14 years. MTX and PSL were administered to 116 patients (mean, 5.4mg/week, 43%), and 158 patients (mean, 4.0 mg/day, 58%). bDMARDs were administered to 58 patients (ETN to 29, IFX to 11, and ABT to 7, other drugs to 11). Compared with the group showing remission and low disease activity, the higher disease activity group had similar age, duration of disease, anamnesis, and drug use (MTX, PSL and bDMARDs). However, the number of swollen and tender joints, according to PtGA, PrGA, CRP, RF, MMP-3, or HAQ assessments, was significantly higher in the high disease activity group. A significant positive correlation was found between ACPA and DAS28ESR. [Conclusion] Regarding the control of disease activity, aggressive treatment should be considered for elderly patients when ACPA is high.

P2-013

Influence of anti-CCP antibody (Ab) on large joint predominance in elderly onset RA (EORA) - Nishiyama's three dimension joint index vector (Vji) analysis based on NinJa 2015 database

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Conflict of interest: None

[Objective] Vji is a novel method to measure RA disease activity containing affected joint distribution information. We previously demonstrated that lower positivity and higher titers of anti-CCP antibodies were associated with increasing age at RA onset. The aim of the present study is to investigate the influence of anti-CCP Ab on large joint predominance using joint index vector (Vji) analysis based on NinJa 2015. [Methods] We compared large joint predominance index (Vz) in RA patients registered in NinJa2015 whose affected joint information and anti-CCP ab data were available. [Results] Vz were significantly higher in EORA (n=382) than YORA (n=421). When we categorized RA patients based on anti-CCP positivity and the age at RA onset, Vz was highest in anti-CCP positive YORA, and lowest in anti-CCP negative EORA. When we focused on anti-CCP positive RA, Vz was significantly higher in EORA than in YORA. [Conclusions] Degree of large joint predominance was different between anti-CCP positive YORA and EORA, suggesting that distinct pathogenic factors might be involved in the two subtypes.

P2-014

Clock genes regulate the cell cycle in RA-FLS

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Conflict of interest: None

OBJECTIVE: Mural regulations between clock genes and cell-cycle regulators, including Cyclin/Cdk and p21, were recently reported. In this study, we examined the mechanism of those in primary cultured rheumatoid fibroblast-like synovial cells (RA-FLSs). METHODS: RA-FLS was

cultured with DMEM containing 50% horse serum for 2hr to synchronize clock genes (serum shock). Total RNA was extracted periodically until 32hr after serum shock to measure expressions of *Bmal1/p16/p21/p27/Rorα/Rev-erb/CyclinE1/CyclinE2* by qPCR. Results were evaluated on a periodic regression analysis. RESULTS: 24hr cycle of the rhythmic expressions were determined in *Bmal1* and *Rev-erb*, with 65% and 93% of multiple coefficient of determination, respectively. Expressions of *p21* and *Cyclin E* were also rhythmic throughout 24hr period, though they acted antagonistically, with 71% and 83% of multiple coefficient of determination, respectively. CONCLUSION: The 24hr cycle of expressions were detected in the transcriptional regulator of clock gene *Rev-erb*, and the cell-cycle regulators *p21* and *CyclinE1.* In the transcriptional regions of *p21,* ROR response element (RORE) is present where REV-ERB binds to inhibit gene transcriptions. Results suggested a direct effect of REV-ERV on the regulation of *p21* and *Cyclin E* in RA-FLS.

P2-015

IL-6 and TNF-α modulate expressions of Cell Cycle regulators of Rheumatoid Arthritis Fibroblast-Like Synoviocytes

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Conflict of interest: None

Object: To investigate the growth mechanism of Rheumatoid Arthritis Fibroblast-Like Synoviocyte (RA-FLS), the involvement of inflammatory cytokines (IL-6 / TNF-α) on cell cycle regulation was analyzed in conjunction with cell proliferation activities. **Methods:** RA-FLSs were cultured for 0~32h, 3days, 5days in serum free medium with or without IL-6 (100ng/ml)/sIL-6R (100ng/ml) or TNF-α(10ng/ml). Total RNA was extracted to analyze the expressions of CDKIs and *CyclinE2* by Real-time PCR, respectively. In addition, total Protein was extracted to analyze the expression of CYCLIN D1 and CYCLIN E by Western Blot, respectively. After 5days' stimulation, the cell viability was measured by WST-8 assay. **Results:** IL-6 decreased the expression of $p16^{INK4a}$, and increased the expressions of CYCLIN D and *Cyclin E2*. TNF-α increased the expressions of $p27^{Kip1}$, CYCLIN D, *Cyclin E2* and CYCLIN E. The cell viabilities was increased by TNF-α, but not changed by IL-6. **Conclusion:** This presenting results suggested that IL-6 and TNF-α cooperatively induced CYCLIN D1 to promote G1 phase progression, whereas TNF-α dominantly induced CYCLIN E to lead S phase for cell proliferation of RA-FLS.

P2-016

N-acetylcysteine (NAC) demonstrates anti-inflammatory effects through JNC/SAPK path way in rheumatoid fibroblast-like synovial cells (MH7A)

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Conflict of interest: None

[Objective]The aim of this study was to investigate about how change to cytokine's and matrix-metalloproteinase's proteins expressions, mRNA expressions and MAP kinase pathway of N-acetylcysteine (NAC) using immortalized and overexpressed inflammatory cytokines rheumatoid fibroblast-like synovial cells (MH7A) in vitro. **[Material and Method]**MH7A cell's dishes were incubated for 3h and 24h with NAC (1μM, 10μM, 100μM). Expression of mRNA for IL6, TNF and MMP3 mRNA were assayed by performing Real time PCR. In addition, Expression of IL6, Phospho-JNK/SAPK, Phospho-P38MAPK protein were assayed by Western blotting procedure. **[Result]**Dose dependently of NAC supressed expression of IL6 mRNA after 3h treatment. These tendency was preserved even after 24 h treatment. IL6 protein expression was also suppressed in dose-dependently of NAC by Western blotting procedure. In addition, although phospho-JNK/SAPK protein had been promoted all expression after 3h and 24h, phospho-JNK/SAPK protein that NAC treated was suppressed completely expression after 3h and 24h. In contrast, phospho-P38 MAPK protein that NAC treated was promoted all expression after 3h and 24h. **[Conclusion]**This study was suggested that anti-inflammatory signaling of NAC was involvedJNK/SAPK pathway mainly.

P2-017

The efficacy of HDAC inhibitors specific for its subclasses on IL-6 production from RA synoviocytes

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Conflict of interest: None

Plasma IL-6 concentration is known to be elevated in patients with rheumatoid arthritis (RA) as compared from healthy individuals. Previous reports have demonstrated the aberrant epigenetic regulation of gene expression from RA synoviocytes, including IL-6. We previously reported the reactivation of latent HIV by histone deacetylase (HDAC) inhibitors. We demonstrated that pan-HDAC inhibitors could effectively inhibit IL-6 gene expression at both mRNA and protein levels. In contrast, we found the inhibitory effects of specific for classes HDAC inhibitors on IL-6 production from RA synoviocytes and presented the data at the 60th JCR meeting. In this meeting, moreover, we examined the efficacy of newly developed HDAC inhibitors specific for its subclasses on IL-6 gene expression using quantitative mRNA detection by real time PCR. These data will be presented at the present meeting.

P2-018

Comprehensive analysis of functions of layilin in human synovial fibroblasts

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Conflict of interest: None

[Objective] We previously reported that TNF-α up-regulated expression of layilin (LAYN) in chondrocytes and that LAYN signaling enhanced secretion of a complement factor from the cells. Therefore, speculating that LAYN was involved in pathophysiology of arthritis, we here comprehensively investigated functions of LAYN in human synovial fibroblasts (HSFs). [Methods] Immortalized HSFs were transfected with siRNA for human LAYN (siLAYN) or control siRNA (siCont). The cells were further treated with or without human TNF-α for 24 hours. Then, we compared protein profiles of the cells using 2-dimensional differential gel electrophoresis. Further, we identified differently expressed proteins by mass spectrometry. [Result] Out of 1092 detected protein spots, TNF-α stimulation increased intensity of 50 spots more than 1.3-fold and decreased intensity of 14 spots less than 1/1.3-fold with statistical significance in the siCont-treated cells. In the siLAYN-treated cells, the TNF-α-induced intensity alteration was found suppressed in 10 out of the 64 protein spots. Five out of the 10 proteins spots were identified. [Conclusion] A part of TNF-α-induced protein alteration in HSFs would occur via LAYN.

P2-019

TNFα modulates expression of the circadian clock gene *Bmal1* via histone acetyltransferase in rheumatoid synovial cells

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Conflict of interest: None

Objective: Expression of the clock gene *Bmal1* is regulated by the transcriptional activator *Rorα* and the repressor *Reverbα*. We previously showed that TNFα up-regulated *Rorα* and down-regulated *Reverbα* to induce the expression of *Bmal1,* and these effects were cancelled by inhibition of intracellular [Ca^{2+}] influx. Since a histone acetyltransferases, p300 and CREB binding protein (CBP), have been reported to be associated with calcium signaling, in this study, we tried to reveal the role of these histone acetyltransferases in TNFα-induced *Bmal1* overexpression. Methods: After incubation with p300/CBP inhibitor C646 (10, 25 μM) for 1h, synovial cells were stimulated with TNFα(10ng/ml) for every 8h for 32h. Then, *Bmal1, Rorα, Reverbα, p300* and *CBP* mRNA expression were analyzed by qPCR. Results: The mRNA expression of *p300* was significantly increased by TNFα, but that of *CBP* was not affected in synovial cells. In addition, TNFα-induced overexpression of *Bmal1* and *Rorα* and suppression of *Reverbα* was cancelled by pretreatment with C646. Conclusion: TNFα modulates the expression of *Bmal1* via p300/CBP in synovial cells, suggesting p300/CBP as a novel therapeutic target of RA.

P2-020

Effects of omega-3 lipid mediator on synovial inflammation and RANKL expression in human rheumatoid synovial fibroblasts

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Conflict of interest: None

[Objectives] Rheumatoid arthritis (RA) is a chronic progressive inflammatory disease as the proliferative synovitis and bone destruction. The production of specialized pro-resolving mediators as resolvin E1 (RvE1) and Maresin 1 (MaR1) were derived from the omega-3 polyunsaturated fatty acids (ω-3 PUFAs), such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). We investigated the effects of these lipid mediators on synovial inflammation and RANKL production in RA synovial fibroblasts (RASF). [Methods] Human RASF (MH7A) were cultured and treated with pro-resolving mediators such as RvE1 or MaR1, followed by interleukin (IL) -1β or tumor necrosis factor alpha (TNF-α) or IL-17 stimulation. COX2 mRNA and protein expression were analyzed by real-time PCR and Western blotting. IL-6 was analyzed by real-time PCR and ELISA. MMP-3 was analyzed by real-time PCR, and RANKL analyzed by real-time PCR and western blotting. [Results] The expression of COX2, IL-6, and MMP-3, and RANKL were reduced by pro-resolving mediators compared to vehicle control. [Conclusion] The pro-resolving mediators derived from ω-3 PUFAs might inhibit synovial inflammation and RANKL expression.

P2-021

ADAM-17 is correlated with monocyte migration and adhesion to RA synovial fibroblasts in rheumatoid arthritis

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Conflict of interest: None

Objective: A disintegrin and metalloproteinase 17 (ADAM-17) have been reported to be involved in a number of inflammatory conditions. We examined the expression of ADAM-17 in rheumatoid arthritis (RA) biological fluids and the role it plays in RA. **Methods**: ADAM-17 expression was measured by enzyme-linked immunosorbent assay and immunofluorescence in serum and synovial fluids from normal (NL) subjects, osteoarthritis (OA) and RA. We also analyzed relativity with ADAM-17 and disease activity score (DAS28) in RA. RA synovial fibroblasts and THP-1 (human acute monocytic leukemia cell line) were transfected with siRNA against of ADAM-17. THP-1 adhesion to RA synovial fibroblasts was measured. THP-1 chemotaxis assay was performed towards RA synovial fluids and monocyte chemotactic protein-1 (MCP-1)/CCL2. **Results**: The expression of ADAM-17 in RA serum and synovial fluids were significantly higher compared with control fluids. RA serum was correlated with DAS28. ADAM-17 siRNA treated THP-1 cells had decreased adhesion compared with control THP-1 cells. ADAM-17 siRNA treated THP-1 cells also had decreased migration compared with control THP-1 cells towards RA synovial fluids and MCP-1/CCL2. **Conclusion**: These date indicate that ADAM-17 may play a role in RA inflammation.

P2-022

Inhibitory monoclonal antibody against citrullination catalytic cleft of PAD4 reduces inflammatory polyarthritis in rheumatoid arthritis model, D1CC mouse

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Conflict of interest: None

[Objectives] Peptidylarginine deiminase 4 (PAD4) that catalyzes the conversion of protein arginine residues to citrulline residues in the presence of Ca^{2+} is likely to be involved in rheumatoid arthritis (RA), because anti cyclic citrullinated protein antibodies against its catalytic modified peptides are associated with onset of RA disease progression. However, it is still not clear whether PAD4, in particular, its catalytic activity directly affects onset of RA symptoms. [Methods] To reveal this, we created that anti PAD4 monoclonal antibodies recognized catalytic cleft of PAD4. Antibodies were obtained by phage display technique to be combined with immunization in chick. [Results] Anti PAD4 antibodies that were selected from chick immune system were improved in terms of affinity constant and inhibition of PAD4 activity in vitro rather than by mouse antibodies currently being obtained. They were introduced by intraperitoneal administration in RA model mouse, called D1CC mouse, resulted in reduction of onset of inflammatory arthritis. [Conclusion] Anti PAD4 antibody reduces inflammatory arthritis in D1CC mouse. We therefore concluded that PAD4 played critical role in the pathogenesis of initial phase of RA.

P2-023

Expression of podoplanin in lipopolysaccharide-induced rabbit arthritis model

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Conflict of interest: None

[Object] Podoplanin (PDPN) is widely used as a specific lymphatic marker. Expression of PDPN has been reported in various inflammatory lesions and neoplastic lesions, and PDPN is drawing attention as a biomarker and a molecular target. However, the relevance of synovitis and expression of PDPN has not been clear. In this study, expression of PDPN in knee synovitis of lipopolysaccharide (LPS)-induced rabbit arthritis model was analyzed by using anti-rabbit PDPN monoclonal antibody, PMab-32. [Methods] Model preparation: Experimental group; LPS

was injected into the right knee joint of 9 Japanese white rabbits every 3 days, a total of 3 times. After 3, 6 and 12 weeks, bilateral knee synovial tissues of 3 rabbits were collected. Control group; Normal saline was injected into the right knee joint. Immunohistochemistry: Histologic sections were stained by Hematoxylin and Eosin, and PMab-32. [Results] In H-E staining, synovitis was the strongest in the synovium collected at 3rd week, and gradually subsided at 6th week and 12th week. PMab-32 strongly recognized PDPN in synovitis tissues of 3rd week in accordance with inflammatory response, and its reactivity was declined gradually. [Conclusions] In the LPS-induced rabbit synovitis model, PMab-32 was useful for evaluating the inflammatory condition.

P2-024

The involvement of C5a in the progression of *P.ginigivalis*-infected rheumatoid arthritis in SKG mice

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Conflict of interest: None

[Object] There is accumulating epidemiologic evidences suggesting that periodontal disease (PD) is involved in rheumatoid arthritis (RA). Complement system plays a critical role in immune response. It was hypothesized that Pg infection was involved in the progression of RA via C5a elevation. [Methods] Analysis of patients' serum: The correlation between C5a levels and antibody titers to periodontopathogenic bacteria were examined by ELISA. Animal experiments: RA model mice (SKG mice) were established by injection of laminarin (LA). Pg W83 was orally inoculated every 3 days. Mice were divided into 4 groups (PBS-inoculation; Ctrl, LA-injection; LA, Pg-administration; Pg, Pg-administration+LA-injection; Pg/LA), and analyzed after 6 weeks. Arthritis were evaluated by histological observation of joint, serum levels of C5a. The effect of C5a in serum was determined by osteoclast differentiation (OCD). [Results] C5a levels in patients' serum were correlated with antibody titers to Pg. The increase of inflammatory cell infiltration, bone loss of joint, and C5a in serum were observed in Pg/LA mice. The serum of Pg/LA mice promoted OCD and neutralization antibody against C5a suppressed OCD. [Conclusion] These results suggest that Pg infection might affect the progression of RA via C5a.

P2-025

Analysis of arthritis inhibitory long chain ω-3 fatty acid derived lipid mediators

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Conflict of interest: None

Purpose: Previously, we demonstrated that dietary supplementation with long chain ω-3 fatty acid (FA) reduce arthritis, and modulate local and systemic lipid mediators (LM) profiles. Some study showed specialized proresolving LM decrease inflammatory responses. However, it is unclear how these LM play in RA joints and systemic immune cells. The purpose of this study is to determine these LM control in inflammatory joints and immune cells, and identify the mechanisms contribute to inflammatory regulations by LM. **Method:** We used *in vitro* and *ex vivo* RA model experiments. Cells were treated by a long chain ω-3 FA derived LM and inflammatory cytokines, and then cells were collected and subjected to RT-qPCR analysis and Western blot analysis. **Result:** We showed long chain ω-3 FA derived LM were able to suppress inflammatory changes in joint regional cells. In addition, the inflammatory response were also depressed in immune cells by long chain ω-3 FA derived LM. **Conclusion:** Increase of dietary long chain ω-3 FA derived LM in arthritis joints suggested critical role in suppression/recovery of inflammation. Likewise, the suppression of immune cells by LM could lead the recovery of systemic inflammation in arthritis mice.

P2-026

Inhibition of IGF-1R tyrosine kinase is a potential therapy for rheumatoid arthritis

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Conflict of interest: None

【Introduction】Insulin like growth factor-1 (IGF-1) stimulates cell proliferation and differentiation. We focused on the effects of IGF-1 for RA, and inhibitory effects of NVP-AEW541, a selective IGF-1R tyrosine kinase inhibitor (TKI), *in vitro* models.【methods】We assessed MH7A, synovial fibroblast cells to determine the inhibitory effect of cell proliferation and phosphorylation of ERK, Akt, downstream signalings of IGF-1R for TKI. We differentiated mice bone marrow cells into osteoclasts, extracted mRNA and quantified IGF-1 and IGF-1R levels by RT-PCR. HUVEC was assayed to analyze the relation with IGF-1 and angiogenesis.【Result】NVP-AEW541 suppressed MH7A cell proliferation and phosphorylation of ERK and Akt. IGF-1 and IGF-1R expression levels were upregulated during osteoclast formation. The differentiation was suppressed by the TKI. IGF-1 enhanced HUVEC angiogenesis and NVP-AEW541 suppressed this function.【Conclusion】IGF-1 strikingly interacts with cell proliferation and differentiation regarding synovial proliferation, osteoclastogenesis and angiogenesis and the TKI suppressed these effects. These data indicate IGF-1 affects with the pathogenesis of RA and the TKI serve as a potential therapeutic agent in the treatment of RA.

P2-027

The regulation of Th-17 cells via the suppression of aryl hydrocarbon receptor (AHR) expression by T-bet overexpression

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Conflict of interest: None

Purpose: To clarify the effect on Th-17 differentiation by T-bet overexpression. **Methods:** 1) $CD4^+$ T cells from B6, T-bet transgenic (Tg), and Tg/IFN$\gamma^{-/-}$ mice were cultured for Th-17 differentiation. The IL-17 production was analyzed by Flowcytometry, and the mRNA expression of transcription factors relevant to Th-17 cells were analyzed by quantitative PCR (qPCR). 2) Naïve $CD4^+$ T cells from B6 and IFN$\gamma^{-/-}$ mice were transduced T-bet gene, then the cells were cultured for Th-17 differentiation, and examined in the same way as 1). 3) The effect of IL-17 production by AHR stimulation was analyzed by Flowcytometry under the condition of 1) and 2). 4) The lymph node cells from B6 and Tg mice after the collagen type II (CII) immunization were cultured with CII, and the *ahr* expression was analyzed by qPCR. **Results:** 1) IL-17 production was suppressed, and *rorc* and *ahr* expression were reduced in Tg and Tg/IFN$\gamma^{-/-}$ mice. 2) IL-17 production and *rorc* and *ahr* expression were inhibited by T-bet transduction. 3) The facilitation of IL-17 production by AHR stimulation was canceled by T-bet overexpression. 4) The *ahr* expression was reduced in CIA model of Tg mice. **Conclusion:** T-bet overexpression negatively regulates the expression of RORγt and AHR, resulting in the suppression of -17 differentiation.

P2-028

IL-29 is expressed in rheumatoid arthritis, and play peripheral blood mononuclear cell migration

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Conflict of interest: None

Objective: Interleukine (IL)-29 is one of IFN-λ, induced by viral infection and has effect simirar to IFNα/β. it is distantly related to IL-10, and is elevated in rheumatoid arthritis (RA) patients. In this study, we demonstrate the role of IL-29 induced peripheral blood mononuclear cells (PBMC) migration. Methods: In order to confirm that the IL-29 is expressed in RA, IL-29 was measured in synovial fluids from RA (n=16), normal (NL, n=7) and osteoarthritis (OA, n=12) using ELISA. To determine the expression of IL-29 on RA synovial tissues, immunohistochemistry was performed. To examine the role of IL-29 in inflammation, we used PBMC chemotaxis. Finally, to determine PBMC IL-29 associated signaling mechanism, western blotting was performed. Results: IL-29 in RA synovial fluid was significantly higher than in OA synovial fluids. We found that IL-29 is expressed on RA synovial tissues. We also found that number of migrated PBMC toward IL-29 was increased compared with control. Finally, we showed that phosphorylated STAT3 signaling in IL-29 stimulated PBMC was increased at 10 minutes. Conclusion: IL-29 is expressed in RA synovial fluid, and mediates PBMC migration.

P2-029

IL-1 is clucial for the development of coronary arteritis induced by *candida albicans* water soluble fraction

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Conflict of interest: None

[Objectives] We investigated a role of IL-1 receptor in pathogenesis of Kawasaki disease. [Methods] We used coronary arteritis model mice induced by *candida albicans* water soluble fractions (CAWS). CAWS (2mg/day) were administered intraperitoneally to IL-1 receptor knockout mice (IL-1R KO) and C57BL/6 mice for 5 days. Mice were sacrificed at 28 days after administration of CAWS. The severity of arteritis were evaluated in four grade points (0-3) pathologically in five segments: right coronary caps, left coronary caps, non-coronary caps, right coronary artery and left coronary artery. The average of the number of involved segments and severity of arteritis were calculated. [Results] Each 11 mice were administered CAWS in the two groups. One (9%) in IL-1R-KO and 9 (82%) in C57BL/6 had panvasculitis ($p<0.01$). The average of the number of involved segments were 0.18 ± 0.12 /mouse in IL-1R-KO and 2.55 ± 0.55 /mouse in C57BL/6 ($p<0.001$). The average of severity of arteritis were 0.072 ± 0.056 in IL-1R KO and 1.44 ± 0.32 in C57BL/6 ($p<0.001$). Coronary arteritis induced by CAWS were significantly suppressed in IL-1R KO mice. [Conclusions] It was shown that IL-1R played an important role in development of coronary arteritis induced by CAWS.

P2-030

The effect of long-term antibiotics treatment on the course of arthritis developed in IL-1 receptor antagonist deficient mice

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Conflict of interest: None

[Background] Intestinal microbiota can influence systemic immune response, in turn the development of RA. [Purpose] To investigate the effect of long-term antibiotic (ABX) use on the intestinal microbiota and arthritis in IL-1 receptor antagonist (ra) KO mice. [Methods] 3 or 10 weeks old IL-1ra KO mice were treated with or without ABX-containing water (doripenem 0.25g/L and vancomycin 0.5g/L) until 24 weeks of age. Time kinetics of bacterial DNA in the cecum, arthritis score, pathology, bone mineral density (BMD), and concentration of cytokines in joints was evaluated. [Result] After ABX treatment at 3 weeks of age, bacterial DNA decreased to 8% after 4 weeks of age. Arthritis and BMD improved from 8 to 15 weeks of age. Infiltration of neutrophils, dendritic cells, and macrophages decreased with reduction of CXCL1, MCP-1, MIP1-β, and RANTES. On the other hand, IL-17A level did not show significant change. After 16 weeks of age, these parameters were comparable between mice treated with or without ABX. Starting ABX after 10 weeks of age did not improve arthritis. [Conclusion] ABX use just after weaning brought temporary improvement of the arthritis. The timing of administration of ABX and long-term course is important to apply modification of microbiota for the treatment of RA.

P2-031

Analysis of a novel anti-podoplanin monoclonal antibody LpMab-3

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Conflict of interest: None

Podoplanin (PDPN), a platelet aggregation-inducing factor, is a selective marker of lymphatic endothelium and also involved in tumor metastasis and invasion. Expression of PDPN has been reported in many tumors including osteosarcoma, malignant brain tumor, lung cancer, esophagus cancer, mesotheliomas, and osteosarcoma. PDPN expression has also reported in synovial tissue of rheumatoid arthritis (RA) patients. In this study, we had established and characterized a novel monoclonal antibody against human PDPN. Methods: We first established a novel anti-PDPN mAb, LpMab-3, by immunizing mice with LN229/hPDPN. To determine the epitope of LpMab-3 ELISA, Western blotting and flow cytometry analyses were performed. Several glycan-deficient cell lines (Lec1, Lec2, Lec8) were used in flow cytometry analyses. Results: Reaction of LpMab-3 was lost in point mutations of 76-81 animo acid by Western-blot and flow cytometry analyses. Furthermore LpMab-3 did not react with Lec2 (sialic acid deficient) cell lines. Discussion: The epitope of LpMab-3 was identified as Thr76-Glu81 of human PDPN, which is a sialylated glycopeptide. Because LpMab-3 detects sialylated podoplanin, it could be useful for uncovering the physiological function of sialylated human podoplanin.

P2-032

A method for detection of proteins released from the cell surface by shedding

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Conflict of interest: None

【Objective】It has been reported that cell surface proteins digested at their extracellular domains and released from the surface (shedding) is associated with pathophysiology of rheumatoid arthritis. However, there has been no method to comprehensively investigate the mechanism. Previously, we reported a method for isolation of shedded proteins. In the current study, we improved the method to be combined with 2-dimension polyacrylamide gel electrophoresis (2D-PAGE). 【Methods】We used a human synovial sarcoma cell line of SW982. Cell surface proteins of living cells were labeled and then the cells were cultured. We isolated proteins released from the cells into media, and separated the proteins by 2D-PAGE. Released cell surface proteins were detected by fluorescence. 【Results】Many protein spots were visualized on 2D-PAGE. There were multiple protein spots whose intensity were increased by treatment with a calcium ionophore of a shedding accelerator or were decreased by treatment with a sheddase inhibitor. 【Conclusions】We established a method to comprehensively observe proteins released by shedding.

P2-033

Stromal cell derived factor 1 induces integrin activation through direct binding to a newly identified binding-site (site 2) in integrins

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Conflict of interest: None

Object: Integrins are activated by stromal cell derived factor 1 (SDF1). However, the mechanism is unclear. We studied how SDF1 activates integrins and we developed new inhibitors for SDF1-integrin interaction. **Methods:** We performed docking simulation of SDF1-integrin interaction. As docking simulation predicted that SDF1 binds to site 2 in the closed-headpiece of integrin, we generated a peptide from site 2 of integrins. And we studied if the peptide binds to SDF1 and suppresses SDF1-induced integrin activation. **Results:** SDF1 induced integrin activation through direct binding to a newly identified binding-site (site 2) in integrins. A peptide from site 2 that bind to SDF1 suppressed the integrin activation. **Conclusions**: Integrin activation through site 2 may be a potential therapeutic target in inflammation.

P2-034

Role of GM-CSF-producing effector B cells in systemic sclerosis

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Conflict of interest: None

【Objective】B-cell depletion therapy highlights an Ab-independent effector function of B cells, particularly cytokine production, in autoimmune diseases. GM-CSF exerts effects mainly on myeloid cells, and B cells can be another cellular source of GM-CSF that is induced by IL-4 and TGF-b. Given a pathological relevance of these cytokines in systemic sclerosis (SSc), we here have investigated a role of GM-CSF-producing effector B cells in this disease.【Methods】B cell subsets in peripheral blood from healthy donors and patients with SSc were subject to the analysis of GM-CSF mRNA and protein. The relationship between GM-CSF-producing B cells and the clinical features of SSc was also evaluated.【Results】Among $CD4^+$ T cell-derived cytokines, IL-4 most significantly induced B cells to produce GM-CSF, a phenomenon observed at a specific stage of their differentiation. GM-CSF production in B cells from patients with SSc was more pronounced than that from healthy donors. This trend was observed in both naïve and memory B cell subsets. The patients with SSc of the diffuse type and concomitant IP represented enhanced GM-CSF production in memory B cells.【Conclusions】These findings suggest that GM-CSF-producing effector B cells play a pivotal role in the pathogenesis of SSc.

P2-035

ADAM-15 is expressed in rheumatoid arthritis synovial tissues

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Conflict of interest: None

【Background】A disintegrin and metalloprotease (ADAM)-15 expression is reported in several malignancies. However, the role of ADAM-15 in rheumatoid arthritis (RA) is unclear. We have shown the role of ADAM-15 in RA.【Methods】ADAM-15 expression was determined in serum and synovial fluid from RA and normal (NL) using ELISA. We also measured ADAM-15 in RA serum after treatment with tocilizumab (12, 24 and 54 weeks). To determine ADAM-15 expression in RA synovial tissues, immunohistochemistry was performed. Finally, to determine the role of ADAM-15 in RA, cytokines in ADAM-15 siRNA treated human umbilical vein endothelial cell (HUVEC) was measured.【Results】ADAM-15 in RA serum was significantly higher compared with NL. After treatment with tocilizumab, ADAM-15 in serum was significantly decreased between pre and 24 weeks, pre and 54weeks. ADAM-15 is expressed in RA synovial tissues. Fractalkine/CX3CL, in ADAM-15 siRNA treated HUVECs was decreased compared with control siRNA treated HUVECs【Conclusion】These date show ADAM-15 is expressed in RA synovial tissues and may play a role in RA angiogenesis.

P2-036

Analysis of glomerular chemokine expression in lupus nephritis

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Conflict of interest: None

[Object] The objective of the current study is to explore the profiles of chemokine gene expression in glomeruli from lupus-prone mice and human lupus nephritis. [Methods] Glomerular expressions of chemokines were examined with real-time PCR using isolated glomeruli by the magnetic microbead method from lupus-prone MRL-lpr mice and control MRL-+/+ mice. Infiltrating T-cells and monocytes in glomeruli were detected by immunohistochemistry. Histologic glomerular damages were scored semi-quantitatively. Regarding human glomeruli, the expression profile of the intraglomerular genes of 32 patients with lupus nephritis (GSE 32591) were used. Expression of Ki-67 was used as an indicator of glomerular damage. [Results] The numbers of infiltrating T cells and monocytes and chemokine expressions in glomeruli of MRL-lpr mice significantly increased with age. Among the parameters examined, glomerular damage scores were significantly correlated with numbers of monocytes, T-cells and the expression chemokines. Correlation analysis with expression of Ki-67 in human lupus nephritis showed similar tendency. [Conclusions] Our data suggest that glomerular chemokine expressions and infiltrating T cells and monocytes may have a potential role in glomerular damage of lupus nephritis.

P2-037

Involvement of mucosal-associated invariant T cells in the pathogenesis of ankylosing spondylitis

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Conflict of interest: None

[Object] Ankylosing spondylitis (AS) is characterized by chronic inflammation of the axial and peripheral joints and ligamentous attachments. Gut immunity is thought to play a role in AS, because a prominent coexistence of gut and joint inflammation has been observed in AS patients. We previously reported that mucosal associated invariant T (MAIT) cells contribute to the arthritic inflammation by using murine models of arthritis. In this study, we investigated whether MAIT cells are involved in the pathogenesis of AS. **[Methods]** Peripheral blood mononuclear cells (PBMCs) were separated from AS patients and healthy controls. We analyzed the frequency of innate lymphocytes. The expression of MAIT cell activation marker (CD69) and the frequency of active caspase-3 postive MAIT cell were analyzed. PBMCs were stimulated with phorbol-myristate-acetate and ionomycin, and the cytokine production by MAIT cells was examined by intracellular cytokine staining. **[Results]** MAIT cells were activated in AS patients and enhanced the production of IL-17. CD69 expression on MAIT cells correlated with the Ankylosing Spondylitis Disease Activity Score (ASDAS) in AS patients. **[Conclusions]** These findings suggested the involvement of MAIT cells in the pathogenesis of AS.

P2-038

Inhibitory effect of Resolvin E1 on IL-17 induced PGE_2 production in osteoblasts

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Conflict of interest: None

【Object】Resolvin E1 displays beneficial effects in many chronic inflammation diseases including rheumatoid arthritis as a resolving inflammation agent. IL-17 is secreted from Th17 cells, and then induces PGE_2, and RANKL expression in osteoblasts. The RANKL plays a role in a bridge and induces osteoclasts differentiation. Thus, IL-17 indirectly induces osteoclastogenesis via osteoblast. We investigated the mechanism of PGE_2 production stimulated by IL-17, and the effect of Resolvin E1 on PGE_2 production in osteoblasts.【Methods】MC3T3-E1 cells were cultured in the presence or absence of recombinant mouse IL-17 (30 ng/mL) with or without Resolvin E1. The production of PGE_2 in the culture medium was determined by ELISA kit. The protein and gene expression of COX2 and mPGES-1 were measured by western blotting and real-time PCR.【Results】IL-17 induced PGE_2, COX2 and mPGES-1 production in dose dependent manner. Resolvin E1 significantly reduced IL-17 induced PGE_2 production in the supernatant compared to vehicle control. And also, Resolvin E1 significantly reduced IL-17 induced COX2 and mPGES-1 gene expression compared to vehicle control.【Conclusions】These results suggested that Resolvin E1 might suppress PGE_2 production via inhibition of COX2 and mPGES-1 production in osteoblasts.

P2-039

Comparison of the induction of c-*fos*-eGFP and Fos protein in the rat spinal cord and hypothalamus resulting from subcutaneous capsaicin or formalin injection

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Conflict of interest: None

We generated c-*fos*-enhanced green fluorescent protein (eGFP) transgenic (TG) rats expressing the c-*fos* and eGFP fusion gene. Capsaicin (15 μg/100 μL) or 5% formalin were subcutaneously injected into bilateral hind paws (100 μL per each paw) in the adult male TG and Wistar rats. Control rats were injected with ethanol or saline respectively. The rats were perfused at 1.5-24 h after treatments. eGFP and Fos-Like-Immunoreactivity (LI) cells in lamina I-III of the fifth lumbar spinal cord and hypothalamus were compared. Immunohistochemistry for oxytocin (OXT) in the hypothalamus was examined to evaluate the activation of OXT neurons. After capsaicin and formalin treatment, peak time points of the number of eGFP cells were at 1.5 h in lamina I; at 6 h in laminae II-III; and at 3 h in the hypothalamus, whereas, those of Fos-LI cells were at 1.5 h in all regions. The number of Fos-LI cells in the hypothalamus after capsaicin treatment tended to increase, however, the value did not reach significance. In capsaicin groups, using the TG rats, we could detect the activation of OXT neurons, which could not be detected in Wistar rats. These results suggest that the induction of eGFP appeared later and was more sensitive in comparison with Fos after exposure to acute nociceptive stimuli.

P2-040

Expression of mRNA for response gene to complement 32 in CD34+ cells of the bone marrow in rheumatoid arthritis

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Conflict of interest: None

[Object] Previous studies showed the accelerated generation of monocyte-lineage cells from bone marrow (BM) progenitor cells in rheumatoid arthritis (RA). Recent studies have demonstrated that response gene to complement 32 (RGC32) is a novel membrane regulator for macrophage phagocytosis. The current study examined the mRNA expression of RGC32 in BM CD34+ cells from RA patients. [Methods] CD34+ cells were purified from BM samples from 47 RA patients and 31 osteoarthritis (OA) patients during joint operations via aspiration from iliac crest. The expression of mRNA for RGC32 was examined by quantitative RT-PCR. [Results] The expression of mRNA for RGC32 was significantly higher in RA BM CD34+ cells than OA BM CD34+ cells ($p=0.0366$). The RGC32 mRNA expression level was not correlated with medication or serum CRP. The RGC32 mRNA expression was significantly correlated with nuclear factor-kappa B1 (NFκB1) gene expression in RA BM CD34+ cells ($p<0.0001$, $r=0.5550$). [Conclusion] These results indicate that the enhanced expression of RGC32 mRNA in BM CD34+ cells plays a pivotal role in the pathogenesis of RA. Moreover, the data also suggest that the enhanced RGC32 mRNA expression might be closely associated with mRNA expression of NFκB1.

P2-041

Monocyte-derived microparticles in circulation of patients with rheumatoid arthritis: A novel biomarker for the disease activity

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Conflict of interest: None

[Object] To clarify the pathogenesis and identify novel biomarkers of rheumatoid arthritis (RA) through examination of the source of microparticles (MP) in circulation. [Methods] Twenty patients with RA, 5 SLE, and 13 healthy controls were involved. Using gradient centrifugation, plasma was isolated from whole blood and applied to flow cytometry. Megamix was used to detect vesicles under 1mm in diameter (identical to MP). Sources of MP were identified by expression of cell-specific markers using fluorescence-conjugated antibodies. In patients with RA, correlation between clinical information and proportion of MP subsets were also analyzed. [Results] Platelet-derived MP covered the largest proportion in all diseases and controls. Interestingly, proportion of immune-cell-derived $CD45^+CD41^-$MP was higher ($P < 0.006$) in patients with RA compared to controls. Proportion of immune-cell-derived MP was positively correlated with inflammatory markers such as CRP and composite disease markers such as DAS28-ESR. Furthermore, proportion of monocyte-derived MP showed a same trend with the results of immune cell-derived MP in RA, but that of non-monocyte MP did not. [Conclusions] Circulating monocyte-derived MP is involved in the pathogenesis and can be utilized as a novel biomarker for RA.

P2-042

Sequential Effect of Abatacept on lymphocyte subsets in Rheumatoid Arthritis

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Conflict of interest: None

【Introduction】The pathogenesis of rheumatoid arthritis (RA) is characterized by immune dysregulation, inflammation and joint destruction. Since biologics may exert different impacts on immune dysregulation, we here have sought to determine the sequential effects of abatacept (ABA) on lymphocyte subsets in RA. 【Methods】Twenty-five of bio-naive patients with RA were treated with ABA and subject to the sequential analysis (0, 3, 6, 12 month) of lymphocyte subsets and the titers of autoantibodies, along with the assessment of disease activity. 【Results】After the treatment with ABA, amelioration of disease activity was paralleled with sequential reduction in the number of activated Th subsets and the ratio of Th17, Tfh and Treg cells. In addition, the proportion of central and effector memory $CD4^+$ T cells was sequentially decreased, while that of naïve T cells was increased. Changes in $CD8^+$ T cells were modest. Moreover, changes in B cell subsets and the titers of autoantibodies (ACPA, RF) were not remarkable. However, a correlation between RF titers and Tfh numbers was noted and the good responders to ABA appeared to have high titers of RF prior to treatment. 【Conclusions】Along with inhibition of disease activity, ABA could correct immune dysregulation in RA.

P2-043

A role of the a disintegrin and metalloprotease (ADAM)-10 in rheumatoid arthritis monocyte migration

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Conflict of interest: None

【Background】We examined the expression of a disintegrin and metalloprotease (ADAM)-10 in rheumatoid arthritis (RA) and the role it plays inflammation. 【Methods】ADAM-10 expression was determined in serum and synovial fluids from normal (NL) subjects, osteoarthritis (OA) patients and RA patients. To determine whether ADAM-10 involved with RA inflammation, the correlation with DAS28 (ESR) was measured. In order to confirm the role of ADAM-10 in RA synovium, THP-1 and monocyte chemotaxisis was performed. 【Results】ADAM-10 in RA serum was significantly higher than NL serum. ADAM-10 in RA synovial fluids was also significantly higher than OA synovial fluids. Hence, ADAM-10 in RA serum was correlated with DAS28 (ESR). Finally, number of migrated THP-1 towards ADAM-10 depleted RA synovial fluids were decreased compared with sham depleted RA synovial fluids. Number of migrated monocytes towards ADAM-10 depleted RA synovial fluids were decreased compared with sham depleted RA synovial fluids. 【Conclusion】These data show that ADAM-10 is expressed in RA, and this study suggests that ADAM-10 may play a role in RA inflammation.

P2-044

The status of regulatory T cells in rheumatoid arthritis by a meta-analysis

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Conflict of interest: None

[Background] Regulatory T cells (Tregs) suppress the activation of auto-reactive T cells. Lower function of Tregs may cause autoimmune diseases such as rheumatoid arthritis (RA). But the status of Tregs in the pathology of RA has not been elucidated sufficiently. To clarify the status of Tregs in RA, we investigated the proportion of Tregs in RA patients by a meta-analysis. **[Methods]** We identified the studies reporting the proportion of Tregs in RA patients using 2 search web sites. We performed a meta-analysis to evaluate the proportion of Tregs among $CD4^+$ T cells in peripheral blood (PB) and synovial fluid (SF) of RA patients and control subjects. **[Results]** A total 31 studies were selected. The definition of Tregs was remarkably varied in each study. Then we performed sub-analyses based on individual definitions. The proportion of Tregs defined by either $FOXP3^+CD25^+$ or CD25-high was lower in PB of RA patients than that of control subjects. The proportion of Tregs defined by $FOXP3^+CD25^+$ was higher in SF than that in PB among RA patients. **[Conclusion]** The status of Tregs varied according to the definition system. If the proportion of Tregs differs in RA, accurate and functionally relevant definitions of Tregs are necessary to elucidate their status in RA.

P2-045

Analysis of peripheral blood regulatory T cell subsets in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To clarify the effect of the alternation in regulatory T cell (Treg) subsets on the pathogenesis of rheumatoid arthritis (RA). [Methods] We collected $CD4^+$ T cells isolated from peripheral blood mononuclear cells of healthy control (HC) and treatment naïve RA patients, and examined the cells using multi-color flow cytometry. We analyzed as follows; 1) We made comparisons of subsets in $CD25^{hi}CD127^{low}$Treg subclassified from the cell surface antigens (CD45RA, CXCR3, CCR6) and their expression of transcription factor (TF) Foxp3 between HC and RA. 2) We checked the expression of TFs in Treg cell subsets. 3) Relationships between Treg cell subsets and clinical parameter of RA were assessed. [Results] 1) Significant reduction was observed in the rate of $CD45RA^-Foxp3^{hi}$ effecter Treg, especially in T helper 17 (Th17) cell specific cell surface antigen $CCR6^+$ effecter Treg in RA compared with HC. 2) The expression of Th17 specific TF RORγt was significantly increased in $CCR6^+$ effecter Treg and $CCR6^+CD45RA^-Foxp3^{low}$ non Treg in RA compared with HC. 3) The rate of $CCR6^+$ effecter Treg and $CCR6^+$ non Treg was positively correlated with serum CRP level in RA patients. [Conclusions] Our data suggested the possibility that $ROR\gamma t^+CCR6^+$Treg might be related with the pathogenesis of RA.

P2-046

Analysis for the gene expression profiles in rheumatoid synovial fibroblasts regulated by FasL

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Conflict of interest: None

Objectives: FasL is a member of TNF superfamily and the activation of Fas by binding to FasL induces apoptosis. The FasL-Fas signaling pathway is essential for the regulation of the immune system. In contrast, decoy receptor 3 (DcR3) competitively binds soluble FasL and inhibits the signaling of FasL via Fas. In this study, we investigated the genes expression profiles regulated by FasL in RA-FLS by comprehensive genetic analysis using microarrays. Methods: RA-FLS were incubated with 1.0 μg/ml FasL for 12 h. Gene expressions were detected by microarray assay, and the relative gene expression profiles in FasL-stimulated cells and unstimulated controls were analyzed. The relative expression levels of mRNA of the top-5 genes upregulated and those downregulated were

compared using RealTime-PCR system. Results: The microarray analysis revealed that 1039 genes were upregulated and 1518 genes were downregulated more than twice of controls by the stimulation with FasL. The RealTime-PCR analysis confirmed that mRNA expression of the top-5 genes upregulated and those downregulated was actually regulated by FasL. Discussion: In this study, we first revealed the gene expression profiles in RA-FLS regulated by FasL. The involvement of FasL-Fas/DcR3 signaling in the pathogenesis of RA is suggested.

P2-047

The expression of mRNA for metastasis-associated protein S100A4 in CD34+ cells of the bone marrow in rheumatoid arthritis

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Conflict of interest: None

[Object]: The calcium-binding protein S100A4 is known as a metastasis-specific gene product. Recent studies have disclosed that S100A4 is significantly increased in plasma and synovial fluid of patients with rheumatoid arthritis (RA). Furthermore, S100A4 correlated with disease activity in RA patients. The current study therefore examined the mRNA expression of S100A4 in bone marrow (BM) CD34+ cells from RA patients. **[Methods]:** CD34+ cells were purified from BM samples from 45 RA patients and 28 OA patients during joint operations via aspiration from iliac crest. The expression of mRNA for S100A4 was examined by quantitative RT-PCR. **[Results]:** The expression of mRNA for S100A4 was not significantly different in RA BM CD34+ cells compared to OA BM CD34+ cells. The S100A4 mRNA expression level was not correlated with the administration of MTX or oral steroid. S100A4 mRNA expression was significantly correlated with S100A9 and S100A12 mRNA expression in RA BM CD34+ cells. **[Conclusions]:** Although previous studies demonstrated that the expression of S100A4 protein is up-regulated in the synovial tissue of RA patients, it is possible that RA BM CD34+ cells might not contribute to the abnormal enhancement of S100A4.

P2-048

IgG anti-citrullinated protein antibody (ACPA)-IgM rheumatoid factor complex is detected in the serum of patients with rheumatoid arthritis as IgM ACPA

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Conflict of interest: None

Anti-citrullinated protein antibody (ACPA) is specifically produced in patients with rheumatoid arthritis (RA) and is implicated in the pathogenesis of RA. Although ACPA is primarily IgG isotype, detection of IgM ACPA in a portion of RA patients was also reported. As the presence of IgM antibody is a hallmark of ongoing immune responses, we measured IgM ACPA in a cohort of RA patients to identify “immunologically active” individuals. Although citrulline-specific IgM was detected in some samples, IgM reactive to both citrullinated and non-citrullinated peptides was detected in substantial number of samples. The presence IgM ACPA did not correlate with disease activity or other clinical variables, but IgM ACPA was detected in the samples with high levels of IgG ACPA. IgM ACPA also correlated with IgM rheumatoid factor (RF), and, importantly, protein G-mediated removal of IgG from the serum eliminated IgM ACPA activity, suggesting the presence of IgG ACPA-IgM RF complex. In fact, IgM RF was detected in the elution from protein G or citrullinated peptide coated beads. Thus, IgM reactive to both citrullinated and non-citrullinated peptides and IgG ACPA-IgM RF complex, which might be involved in the pathogenesis of RA, are detected in the serum of RA patients as IgM ACPA.

P2-049

Influence of disease activity for adipocytokaine in rheumatoid arthritis from the TOMORROW study

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Conflict of interest: Yes

[Objectives] Adipocytokaine is high so that disease activity is high in RA. We analyzed the influence of change of disease activity for change of adipocytokaine from the TOMORROW study (UMIN000003876). [Methods] 193 RA and 194 healthy individuals were entry. We compared change of leptin and adiponectin (Δleptin, Δadiponectin) between baseline and after 3 years. Correlation with disease activity and predictive factors for Δadipocytokaine in RA were investigated. [Results] Leptin increased in both groups. There were not significantly differences between groups (0.21, 0.18ng/ml: p=0.37). On the other hand, adiponectin decreased in both groups. There were significantly differences between groups (-1.8, -3.3μg/ml: p=0.01). Negative correlation between Δleptin and Δadiponectin was detected in RA (r=-0.29, p<0.01). Correlation between adiponectin and DAS28ESR was positive at both periods (r=0.22, p=0.01: r=0.18, p=0.01). However, it was not tendency about leptin. There was no correlation in Δadipocytokaine and ΔDAS28ESR. Lipid markers and %fat were predictive factors for Δadipocytokaine. [Conclusion] Leptin increased and adiponectin decreased during 3 years. Correlation with Δadipocytokaine and ΔDAS28ESR did not detected. Disease activity was high in adiponectin high RA.

P2-050

High HAQ score is a risk factor for locomotive syndrome in patients with rheumatoid arthritis - findings from CHIKARA study-

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Conflict of interest: None

[Purpose] Rheumatoid arthritis (RA) is often associated with sarcopenia, which can cause locomotive syndrome (LS). We investigated LS conditions in patients with RA. [Methods] 100 patients (78 female, average age 66 yo) were enrolled in CHIKARA study to investigate the correlation between disease activity and sarcopenia prospectively. We investigated their body composition, laboratory data, disease activity, HAQ and treatment. We made uni- and multivariate analysis of the correlation between each status and LS diagnosed by locomo 5. [Results] The percentage of LS was 52%. Univariate analysis showed that age (r=0.255, p=0.01), %body fat (r=0.244, p=0.014), body weight (r=-0.215, p=0.032), visceral fat rating (r=0.205, p=0.041), leg muscle score (LMS) (r=-0.359, p<0.001), rheumatoid factor (r=0.221, p=0.027) and HAQ (r=0.460, p<0.001) had significant association to LS. Patients with lower LMS (less than 90) had significantly higher prevalence of LS (OR3.77, p=0.001). LMS (OR0.91, 95%CI 0.84-0.97, p=0.005) and HAQ (OR8.78, 95%CI 2.66-29.0, p<0.001) were detected as significant factors by multivariate analysis. Disease activity and use of glucocorticoid or biological agents showed no significance. [Conclusions] RA patients with low LMS and high HAQ score were more likely to have LS.

P2-051

The mortality in patients with rheumatoid arthritis is still high even in new era of treatment: the result from TOMORROW study for 6 years

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Conflict of interest: None

Objectives: The aim of this study was to investigate risk factors for mortality in patients with rheumatoid arthritis (RA) compared to controls in the new era of treatment for RA. **Methods:** We started a prospective cohort study named TOMORROW in 2010. We compared all causes of mortality in 208 RA patients (half of them receiving biologics at baseline) and 205 age- and sex-matched controls from 2010 to 2016 and analyzed risk factors for mortality in patients with RA using Cox proportional hazard regression model. **Results:** Total deaths occurred in 10 (8.39/1000 person-year) of patients with RA and 1 (0.86/person-year) of controls. Mortality rate of RA was significantly higher ($p<0.01$) than that of controls. Cox proportional hazard regression model revealed that morbidity of RA per se was related to increased mortality rate among all participates (HR: 9.35 95%CI 1.18-73.8, p=0.034). Glucocorticoid (GC) use also increased mortality rate in RA patients (HR: 4.08 95%CI 1.04-16.1, p=0.044). Baseline disease activity, disease duration and the use of biologics did not affect mortality. **Conclusions:** The mortality rate was significantly higher in RA patients than controls during six years. Medicating with GC was apparently associated with mortality.

P2-052

Lower Gastrointestinal tract symptoms in rheumatoid arthritis (RA) patients using questionnaire survey

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Conflict of interest: None

【Introduction】It is well known that the gut immune system is involved in inflammatory bowel disease and the autoimmune disease, but little in RA. To investigate the relationship between gut immune system and RA, we performed questionnaire survey about the symptoms of lower gastrointestinal tract.【 Object and the method 】One hundreds thirty eight RA patients (29 males, 109 females, mean age 61.7± of 13.2 years) were studied for inflammation markers, disease activities, constipation scoring system (Dis Colon Rectum. 1996 Jun;39 (6): 681-5.) (CSS), and Bristol Stool Scale (Scand J Gastroenterol. 1997 Sep;32 (9): 920-4.) (BSS).【 Results 】Fifty-one patients (37.0%) were treated with biologics. The mean sores of CSS and BSS in RA patients were 3.5±4.4 and 3.7±1, respectively. The significant rank correlation was found between CSS and CRP ($\rho=-0.229$, $p<0.05$). Multivariate logistic regression analysis revealed that duration (OR 0.945, CI 0.8889-0.9939,), diabetes (OR 21.10, CI 2.89-492.961) and BSS (OR 1.956, CI 1.184-3.426) influenced the use of biologics significantly ($p<0.05$).【 Discussion 】BSS was related to the use of biologics and CSS to inflammatory reaction. These results might indicate that gut immune system plays a role in the pathogenesis of RA.

P2-053

Oldest- elderly patients with rheumatoid arthritis

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Conflict of interest: None

Purpose: The aim of this study was to evaluate the characteristics of oldest-old patients with rheumatoid arthritis (RA) in our hospital. Material and Methods: All patients in our hospital with RA according to the 2010 ACR/EULAR classification criteria from April 2011 to November 2016 were enrolled in this retrospective single-center study. We divided the patients into 3 groups according to their age: young < 65 years old; elderly 65-74, older elderly 75-84, and oldest elderly > 85. Results: Of the 246 RA patients, 77 were elderly, 61 were older elderly, and 18 were oldest elderly. Treatment: 5 patients were receiving DMARDs and glucocorticoid (GC), 1 was on biologics and GC, and 2 patients were treated with DMARDs without GC. 5 of 9 patients who were receiving only GC had histories of DMARDs treatment. Conclusion: In our hospital, three quarters of elderly patients were treated with GC.

P2-054

Clinical features of 106 cases of elderly onset rheumatoid arthritis and unclassifiable arthritis

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Conflict of interest: None

[Object] To identify the Clinical features of elderly onset rheumatoid arthritis (RA) and unclassifiable arthritis (UA). [Methods] One hundred and six cases of elderly onset RA and UA receiving DMARD in a recent five years were studied for clinical factors such as sex, age, duration to administration after diagnosis, serological data, disease activity and HAQ in two groups classified based on the absence or presence of rheumatoid factor (RF) and anti-CCP antibodies (ACPA). [Results] No significant difference was noted in the mean age at the first diagnosis. The male-to-female ratio and the rate of cases with a diagnosis of definite RA by the 2010 ACR-EULAR classification criteria for RA were significantly different between groups. In seronegative patients, it seemed that there was a tendency to be high disease activity in onset than seropositive patients. [Conclusions] It seemed to be different clinical features in elderly onset RA and UA depending on the presence or absence of RF/ACPA.

P2-055

Evaluation of the clinical features of seronegative rheumatoid arthritis to establish appropriate management

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Conflict of interest: None

[Objectives] The 2010 criteria for RA, which weight serology data, lead to confusion regarding diagnosis and therapy for seronegative (SE-) RA. To establish effective management of SE- RA, we evaluated its clinical features. [Methods] Newly-diagnosed RA patients were stratified as SE-(RF- and ACPA-) or seropositive, and the clinical features and therapeutic regimens were compared between the two groups. RA diagnosis and the therapeutic regimen were based on the individual physician's judgment. [Results] Among 69 patients (age 68 (20-90) yr, females 62.3%, RF positivity 56.7%, ACPA positivity 54.4%), the period from symptom onset to the start of therapy was 4 (1-24) mo, including one (0-22) mo of patient delay. The SE- group contained more elderly patients and had a higher swollen joint count, a higher CRP level, a lower score for the 2010 criteria, a higher rate of US application, a lower proportion of smokers, and higher PSL usage than the other group. There were no inter-group differences in disease duration, radiologic changes, and usage of DMARD. [Conclusion] Because patients with SE- RA have a high risk of disability due to old age and a high incidence of joint inflammation, prompt diagnosis is needed with appropriate referral from the home doctor and use of US examination.

P2-056

Clinical features of RA developed in male patients

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Conflict of interest: None

Objective) RA develops most usually in female. This study focused on whether any features unique to RA in male are. Methods) Male patients who visited to our hospital and diagnosed to have RA from 2014 to 2016 were included. Peak RF titer in each patient, and ACPA, Steinbrocker-Stage, and chest CT findings at the phase with the peak RF were examined retrospectively. Results) 32 patients aged 59.4±9.8 (31~71) were included. RF level was 488±1007 (4~8310) U/mL; 7 patients showed a level higher than 556 U/mL (mean +1SD, by Bando et al.). ACPA level was 836±1297 U/mL (>500: 7/18, >1000: 3/18). Positive ANA was 6/14. XP-Stage 0~4 was in 12, 4, 7, 3, 3, each. As for CT findings tested in 22, interstitial involvement was observed in 9, emphysema in 7, combined pulmonary fibrosis and emphysema (CPFE) in 3, others (old TB, pneumonia) in 2; no positive finding was in 7. Discussion)When compared to features known to be usually seen in female patients, male RA patients showed more frequently (22%) a high RF level, on the other hand, rather mild destructive arthritis, and pulmonary involvement was frequent (40%). Conclusion)Male RA patients had clinical features somewhat different from those of female patients, and pulmonary interstitial and/or emphysematous involvement were outstanding.

P2-057

Investigation of bronchofiberscopy (BF) for organizing pneumonia (OP) associated with connective tissue disease at our hospital

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Conflict of interest: None

[Background] In connective tissue disease, the frequency of complicated OP is high, but we have difficulties in diagnosis from a process similar to infectious diseases. We examined the implementation status of BF for suspicious OP cases in our hospital. [Methods] We retrospectively investigated information of patients suspicious OP with BF and patients diagnosed as OP from clinical course without BF at our hospital between 2014 and 2015. [Results] 10 cases suspicious OP were performed BF. 9 cases were diagnosed as OP (8 cases with preceding antibiotic treatment), and 1 case was diagnosed as lung cancer. 5 cases were presenting organized images by pathological findings. In all cases, we started steroid therapy (PSL 0.5-1.0mg/kg/day) regardless of accordance with tissue findings, and the therapeutic response was good. In 6 cases without BF, clinical diagnosis was made after the preceding antibiotic treatment. 3 cases naturally extinguished without treatment, and 3 cases were treated with steroid (0.3-0.5mg/kg/day). [Discussion] In our hospital, clinical course tended to be more important than pathological tissue findings in OP patients. Clinical judgment might be considered important for BF indication, because it is useful for differentiation of malignant tumor and granulomatous lesion.

P2-058

The case of fatal pulmonary arterial hypertension associated with rheumatoid vasculitis

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Conflict of interest: None

A 57-year-old man was diagnosed as interstitial lung disease in 2005 and had been treated with predonisorone (PSL) and cyclosporine (CsA). In 2008, he suffered from polyarthritis, and was diagnosed as rheumatoid arthritis (RA). Since 2010, he had been treated with PSL, CsA, and adalimumab. In 2013, he was pointed out the findings of mononeuritis multiplex and asymptomatic cerebral infarction, so he was diagnosed as rheumatoid vasculitis (RV). In 2016, his cough and dyspnea were exacerbated. Echocardiograms showed pulmonary hypertension (PH), and he was admitted to our hospital. He was diagnosed as pulmonary arterial hypertension (PAH) by right heart catherterization and pulmonary perfusion-inhalation scintigraphy, and it was suspected that his PAH was associated with RV. Although he received glucocorticoid therapy, he died because of rapidly progressive hypoxemia due to PH. Necropsy revealed the inflammation of pulmonary artery, indicating that his PAH was involved in RV. [Discussion] Connective tissue diseases, such as systemic sclerosis, mixed connective tissue disease, and systemic lupus erythematosus can be the cause of pulmonary hypertension, however the cases of RV are rarely reported. We report the quite rare case of necropsy-proved RV-PAH.

P2-059

Clinical Characterization of Interstitial Lung Disease and chronic airway disease in Rheumatoid Arthritis Patients in High Resolutional CT and Titer of Anti Citrullinated Peptide Antibodies

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Conflict of interest: None

Background/Purpose: To investigate clinical characteristics of interstitial lung disease (ILD) and air way disease in rheumatoid arthritis (RA) patients. Methods:494 patients with RA were treated at our hospital and followed up at least one year as newly onset RA. Results:101 out of 494 patients showed ILD at initial presentation (21.4%). 5 cases were excluded because of the other respiratory diseases. 96 RA-ILD cases were performed HRCT. In HRCT findings, 24 cases of RA-ILD showed widely spread at the initial presentation and higher extensive score of ILD (score4~6). Higher anti-CCP2 titers were found in higher extensive score of ILD (869.9+/-619.3 vs. 315.7+/-401.2, $p<0.01$). We also found that the patient with air way disease had higher anti-CCP2 titers (445.7+/-727.6 vs. 146.4+/-293.4, $p<0.01$). Conclusion: HRCT findings focused on the extension score at the initial presentation is a useful predictor of the RA-ILD and air way disease in RA. Anti-CCP2 is one of the related factor of the extension score.

P2-060

POEMS syndrome in a patient with rheumatoid arthritis

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Conflict of interest: None

POEMS syndrome (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal protein and Skin changes) is a rare multisystemic disorder which is characterized by increased serum levels of vascular endothelial growth factor (VEGF). We present here a case of POEMS syndrome which developed in a patient with rheumatoid arthritis (RA).【Case report】A 67-year-old man, in whom RA had been diagnosed and treated with tacrolimus 6 months previously, was referred to our clinic for right pleural effusion and mononeuritis multiplex. On physical examination, he also had hairiness, and skin pigmentation and angioma. Computed tomography indicated a sclerotic legion in the 9th rib, in which high 18-Fluorodeoxyglucose uptake was seen on positron emission tomographic scans. Serum levels of immunoglobulins were all normal, and monoclonal protein was not observed. Serum VEGF was extremely high at 5,530 pg/ml. Histopathological examination of a specimen obtained from the 9th rib showed IgA lambda type plasmacytoma. He was diagnosed with POEMS syndrome and translocated to Hematology department for taking chemotherapy.【Clinical significance】To date, there are few published reports on the case of RA patients developing POEMS syndrome. Rheumatologists should be aware of this syndrome.

P2-061

Clinical features of rheumatoid arthritis patients complicating with organizing pneumonia

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Conflict of interest: None

[Objective] Although organizing pneumonia (OP) is a rare complication in RA patients, it occurs in a variety of situations. This study aimed to clarify the clinical features of RA patients complicating with OP. [Methods] We reviewed medical records of our 220 RA outpatients in 2016. OP was diagnosed by trans-bronchial lung biopsy or typical clinical features. [Results] 17 OP events were recognized in 10 patients (7 males, 3 females). OPs were treated with steroid (PSL 20-60 mg/day) for 15 events and followed without steroid for 2 events; all OPs improved. Regarding treatment for arthritis, although the rates of steroid therapy (80.0 vs 67.1%) and MTX therapy (70.0 vs 70.0%) did not differ between OP and non-OP groups, biological DMARDs were administered significantly more often in OP than non-OP (50 vs 20.5%). 5 events occurred along with tapering RA therapy and aggravation of arthralgia (tapering steroid: 3 events, withdrawal of abatacept: 2 events). 3 events occurred 1-2 months after administration of anti-TNF biologics. [Conclusions] In RA patients complicating with OP, OP is susceptible to steroid therapy, but arthritis tends to remain refractory. We must pay attention to the occurrence of OP after tapering therapy, or administration of anti-TNF biologics.

P2-062

A pseudotumor of cervical spine in RA regressed by abatacept

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Conflict of interest: None

A 69-years-old female with RA treated with methotrexate (MTX) 8 mg/week and certolizumab pegol (CZP) 200 mg bow developed paralysis of bilateral lower limbs. X-ray of cervical spine showed atlantoaxial subluxation. A mass lesion of the cervical spine was revealed by MRI. No evidence of infection and malignancy, and the high disease activity of RA (CDAI was 27.1) indicated the mass an inflammatory pseudotumor of RA. CZP was switched to abatacept (ABT), then her neurological symptoms improved gradually, and MRI showed the reduction of pseudotumor. In this case, the TNF-inhibitor resistant mass regressed after administration of ABT, indicating the mass as a pannus of RA. The golden standard of the treatment of inflammatory pseudotumor of the cervical spine in RA with neurological symptom is the surgical resection. However, this case suggests that the control of RA activity is also a considerable approach in RA pseudotumor.

P2-063

To evaluate the efficacy of potassium-competitive acid blocker (vonoprazan) for patients with rheumatoid arthritis with failed treatment of proton-pump inhibitors for the gastroesophageal reflex

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Conflict of interest: None

(Objectives) Proton-pump inhibitors (PPI) are effective in patients with gastroesophageal reflex (GERD). However, PPI failure is sometimes experienced in the treatment of GERD. The purpose of this study was to investigate the efficacy of switching therapy from PPI to a potassium-competitive acid blocker (vonoprazan) in patients with rheumatoid arthritis (RA). (Methods) Twenty-four patients with RA who had GERD symptoms despite treatment with PPI were enrolled (esomeprazole, 22 patients; lansoprazole, 2 patients). The GERD symptoms were compared between before- and four weeks after switching to vonoprazan using a self-administered frequency scale for the symptoms of GERD (FSSG). Additionally, we evaluated the disease activity score (DAS28) and adverse events of vonoprazan. (Results) The mean scores of FSSG and DAS28 at baseline were 16.6 ± 8.7 (5–39) and 3.3 ± 1.1 (0.6–4.8), respectively. There was no correlation between the FSSG and DAS28 scores. The mean FSSG score at 4 weeks after the switching significantly decreased to 5.6 ± 6.9 (0–25) (p=0.004). (Conclusion) In RA patients with insufficient effect of PPI treatment for GERD symptoms, switching to vonoprazan is recommended.

P2-064

Today's situation and change from the past of treatment selection of Rheumatoid arthritis (RA) patients associated with chronic interstitial pneumonia (CIP) of our institute

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Conflict of interest: Yes

Background: We aim to know treatment selections of CIP-RA patients of our institute today. And we compare today's our selections to 2-year past our selections. Methods: We reviewed clinical data concerning treatment and DAS28CRP of our CIP-RA patients in August 2016. Results: Total CIP-RA patients today are 124 (51 males), and those 2-year past were 89 (41 males). MTX, Corticosteroid, Biologics, Tacrolimus, SASP and Bucillamin are prescribed for 17%, 49%, 33%, 56%, 32%, 10% of CIP-RA patients today, and for 19%, 61%, 27%, 56%, 28%, 10% of CIP-RA patients 2-year past. Remission rate and LDA rate in DAS28CRP are 57%,15% of CIP-RA patients today, and were 61%,20% of CIP-RA patients 2-year past. Conclusions: In the treatment of CIP-RA patients, we avoid MTX and preferred corticosteroid and tacrolimus and b-DMARDs. Among b-DMARDs, we preferred abatacept. This selection bias are not changed during past 2 years.

P2-065

A case of anti-ARS antibody positive was found, after interstitial pneumonia was exacerbated with rheumatoid arthritis

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Conflict of interest: None

A 54-year-old female treated for rheumatoid arthritis (RA) with Mizoribine (MZR), who underwent acute exacerbations of interstitial pneumonia (IP) at 49 and 50 years old respectively, and recovered by steroid pulse therapy was hospitalized because of sub acute progressive respiratory distress and spreading ground grass opacity in chest x-ray. After admission, a fine crackle was auscultated in both lower lungs, increasing KL-6 in blood test and chest CT examination showed ground grass opacity - infiltrative shadow along bronchial vascular bundle in bilateral lower lobe. We thought that IP exacerbation with RA, and changed MZR to Tacrolimus, but respiratory function worsened slowly. Arthralgia and myalgia appeared after hospitalization, blood test showed increasing CK value, so we re-measured autoantibody and found anti-ARS antibody positive. We thought her IP was due to anti-ARS antibody syndrome, and treated with steroid pulse therapy. After then the symptoms were improved. This case seems to be a combination of IP due to anti-ARS antibody syndrome and RA, or a series of symptoms of anti-ARS antibody syndrome. RA and anti-ARS antibody syndrome were difficult to distinguish. It is important to consider anti-ARS antibody syndrome when diagnosis or treatment of RA are difficult.

P2-066

Problems in elderly patients with rheumatoid arthritis

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Conflict of interest: Yes

The improved prognosis of rheumatoid arthritis (RA) and the prolonged life span of Japanese population resulted in the increased of elderly RA patients. In this study, we analyzed the prevalence of age-associated comorbidities, e.g. as dementia, renal dysfunction, and osteoporosis, in the outpatients in our clinic and discuss the measures to deal with the problems. Among RA patients who are more than 65 years of age (51% in 1647 patients), 0.5%(65-74y), 16%(75-84y), and 17%(>85y) are diagnosed with mild dementia. The patients with dementia often have problems in taking non-daily administrating drugs, such as MTX and bisphosphonate, especially in those who lives alone or with only elderly. The frequency of patients with renal dysfunction also increases with age, which result in the increased use of steroid instead of csDMARDs. This in turn causes steroid-induced osteoporosis, which however is difficult to treat because bisphosphonates are contraindicated in patients with renal dysfunction. Thus, the levels of ADL in elderly RA patients gradually decrease due to insufficient disease control and osteoporosis. The use of biologics and PTH should be considered in the treatment of elderly RA.

P2-067

【Case Report】69 years old man with RA developed refractory severe interstitial pneumonia, but rituximab was very effective for his lung disease

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Conflict of interest: None

【Summary】69 years old man. In December 2014, he was diagnosed with rheumatoid arthritis and treated with MTX + PSL. We started to treat him with TCZ in January 2016. From that time he was treated with MTX8mg+PSL5mg+IGU50mg+TCZ. In March 2016, he had Coughing, fever, respiratory distress and was delivered to our hospital emergency room. His both lungs appeared diffuse alveolar damage (DAD) type interstitial shadows. In addition, blood test showed complement reduction and rheumatoid factor elevation (RF:800U/ml → 3000U/ml). We diagnosed him as rheumatoid vasculitis. Steroid pulse therapy (mPSL1000mg/day, 3days) 4 courses and IVCY (500mg/2week) 8 courses were administered. At first, his interstitial pneumonia responded to that treatment, but gradually exacerbated. We selected rituximab and gave him 4 courses. (RTX375mg/week) Then his interstitial pneumonia turned to improve. And RF titer also decreased markedly. (RF: 3000U/ml → 80U/ml) The dose of PSL was reduced to 25 mg, he was discharged the hospital with home oxygen therapy (O2 1L/min) in August 2016. We report the case rituximab was very effective for refractory interstitial pneumonia due to rheumatoid vasculitis.

P2-068

Two cases of rheumatoid arthritis developed lymphoproliferative disorders initially presenting gastrointestinal manifestations during immunosuppressive therapy

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Conflict of interest: None

It has been reported that rheumatoid arthritis (RA) is associated with an increased risk of lymphoma. Although reasons of a link between RA and lymphoma are unclear, several mechanisms have been cited including systemic rheumatoid inflammation, reactivation of EB virus, Sjogren syndrome, and specific treatment. Among them, frequent extranodal lesions have been reported in iatrogenic immunodeficiency-associated lymphoproliferative disorders (LPD). We report two cases of RA developed LPD presenting rare gastrointestinal manifestations. [Case 1] A 69-year-old male RA patient with 10 years duration treated with MTX and etanercept (ETN) developed stomach discomfort. Endoscopic examination revealed multiple reddish protruded lesions with central concavity in stomach and duodenum. Pathological study demonstrated diffuse large B cell lymphoma (DLBCL) with negative for EBER. The lesions of LPD completely regressed in response to drug withdrawal. [Case 2] A 44-year-old female with RA and Sjogren syndrome treated with weekly methotreaxate developed acute abdomen. She was admitted and laparotomy was done under the diagnosis of perforation of intestine. Pathological findings showed DLBCL of intestine with negative EBER. Complete regression of LPD was achieved by MTX withdrawal.

P2-069

Do we need carotid artery ultrasonography in patients with rheumatoid arthritis?

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Conflict of interest: None

Background) Recent EULAR recommendations suggest to estimate the risk of cardio-vascular events in rheumatoid arthritis, actually carotid artery ultrasonography is recommended. Methods) In retrospectiveyl, from 2012 to 2016, we checked the prevalence of carotid artery ultrasonography abnormalities in rheumatoid arthritis. In addition, among green zone (Framingham risk factors) we also checked the prevalence of it. Results) We evaluated 154 patients and the prevalence abnormalities by carotid artery ultrasonography was 28%. Even in the Green Zone of Framingham score, the prevalence abnormalities by carotid artery ultrasonography was 8%. Discussions) In rheumatoid arthritis, carotid artery ultrasonography needs to be performed, even the patients with low traditional cardio-vascular risk factors.

P2-070

A case of relapse lympho-proliferative disorders (LPD) after introduction of abatacept

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Conflict of interest: None

Case:80 year-old female She was diagnosed RA in 64y.o., and started MTX in 66y.o. RA activity got worse when she was 70y.o., so we started infliximab. But after her first use, she got pneumonia, and we gave up using it. She started tacrolimus in 71y.o., and etanercept in74y.o. Her disease activity was mostly stable. She had abdominal pain in 78y.o. and biopsy appeared diffuse large B cell lymphoma and actinomycete infection at the hypertrophyic mucosal of the ileum, and we diagnosed MTX-LPD. We stopped MTX and etanercept, and started benzylpenicillin, and the mass got smaller in a month.and mostly disappeared in 3 months. RA activity relapse, we started abatacept after 16months. She got pyelonephritis with hydronephrosis due to swelling lymphnode. We recognized that MTX-LPD relapsed, and stopped abatacept and tacrolimus. Inguinal lymphnode got bigger and her left leg was so swalling that she couldn't walk. We started etoposide. agranulocytosis occurred at the first course, and we need to chanege the dosage and interval. It was quite effective. consideration:We must remember that using immunosuprressional drugs to the past OIIA-LPD patient is quite risky, and we should follow markers continuously.

P2-071

A case of Felty's syndrome with suspected overlapping of lupus nephritis

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Conflict of interest: None

A 71-year-old woman was admitted to our hospital because of proteinuria and lower leg edema. Rheumatoid arthritis had been diagnosed in her 20s, but she achieved remission in her 40s. Felty's syndrome had been diagnosed at the age of 65. The patient had histories of idiopathic

portal hypertension and suspected T- cell large granular lymphocytic leukemia (T-LGL). She had recurrent episodes of bacterial infection due to neutropenia. Six months before admission, she developed spinal muscle abscess. Thereafter, proteinuria gradually increased. Urinalysis revealed microhematuria and proteinuria (3.5 g/day). Laboratory data showed pancytopenia, renal dysfunction and hypocomplementemia; all of antinuclear antibody, anti-ds-DNA antibody and anti-citrullinated peptide antibody were positive. Renal biopsy revealed proliferative glomerulonephritis by light microscopy [(IV-G (A)] but IgG was negative by immunofluorescence study. Despite immunosuppressive therapy and plasmapheresis, she required continuous hemodialysis. After four months, liver enzymes suddenly increased. Abdominal CT showed severe liver atrophy. She finally died of hepatic failure. Reviewing her clinical course and renal pathology, hepatic glomerulosclerosis and infection-related glomerulonephritis were possible diagnoses.

P2-072

A case of granuloma annulare secondary to rheumatoid arthritis representing various reactions to antirheumatic drug

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Conflict of interest: None

An 85-years-old female was diagnosed rheumatoid arthritis (RA) 10 years ago. After methotrexate (MTX) was increased from 4 to 8mg/w, 3 subcutaneous nodules appeared to extensor of her elbow. Intravenous (iv) abatacept (ABT) injection was added to MTX, which markedly resolved the nodules in a few days. But after switching to subcutaneous ABT injection, the numbers of the nodule were increased. When she came to our hospital, 5 nodules with maximum size of 2 cm were noted in extensor of her elbow and forearm. We changed ABT/MTX to etanercept (ETN)/MTX. After each injection, the nodules became smaller in several hours but became larger several days later. When the nodules got worsened, biopsy was performed. The histopathology showed granuloma annulare (GA). We continued ETN and stopped MTX, and the nodules improved dramatically. [Clinical significance] The lesions of rheumatoid nodule are observed in subcutaneous tissue with poor mucin deposition. MTX and TNF inhibitors (TNF-I) are known to exacerbate rheumatoid nodules. In contrast, the lesions of GA are observed in epidermis with rich mucin deposition. In GA secondary to RA, MTX and TNF-I are known to be effective. However, as our case illustrated various reaction to anti-rheumatic drugs, individual treatment strategy is required.

P2-073

Two cases of exacerbation of interstitial lung disease (ILD) triggered by pneumocystis jirovecci pneumonia (PJP) in patients with RA

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Conflict of interest: None

Exacerbation of ILD is frequently induced by respiratory infections. We here report 2 cases of exacerbation of ILD triggered by PJP in patients with RA. Case 1 is a 78-years old woman who had been treated with PSL (9mg/day), MTX (6mg/week), and BUC, and IFX was added in May 2007. In Oct 2007, she was admitted to our hospital because of fever, dyspnea, and GGO in bilateral lung fields. She was diagnosed as PJP because of high serum beta-D glucan and positive PCR result of Pneumocystis jiroveccii in sputum. Large dose of methyl-PSL and S/T were administrated, and GGO improved once but exacerbated again with re-increase of serum KL-6. The dose of PSL increased and she finally improved. Case 2 is a 73-years old woman who had been treated with PSL (12.5mg/day) and MTX (12mg/week). In May 2016, she was admitted to our hospital because of fever, ssevere hypoxemia and widespread GGO in the lungs. Serum beta-D glucan was high and we diagnosed as PJP. Large dose of methyl-PSL and S/T were administrated, resulting in improvement of GGO. However, on day 15, GGO exacerbated again, and she was re-intubated with concomitant use of high-dose of PSL and cyclosporine, finally resulted in death on day 40. We should be cautious for that ILD may exacerbate after PJP.

P2-074

Prediction of Relapse After Discontinuation of Adalimumab by Ultrasonographic Assessment in Patients With Rheumatoid Arthritis in Clinical Low Disease Activity

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Conflict of interest: None

Objective. To determine whether the comprehensive ultrasound (US) assessment of synovial inflammation predicts relapse after discontinuation of treatment with adalimumab (ADA) in patients with rheumatoid arthritis (RA) in low disease activity (LDA). **Methods.** Twenty RA patients in remission (REM, DAS28 <2.6) and two RA patients in LDA (DAS28<3.2) receiving treatment with ADA, underwent a comprehensive US scan on synovial sites in 36 joints measuring total power Doppler (PD) and grey scale (GS) score before ADA discontinuation and were followed up clinically for 6 and 12 months. **Results.** Fourteen patients (63.6%) after 6 month and twelve patients (55%) after 12 month preserved LDA. Using the optimal cutoff values determined by ROC curve analysis, cut value was determined as ≥ 2 (odds ratio 11, P = 0.057; fisher extract test) for PD-US scores and ≥ 13 (odds ratio 16.5, P = 0.0201) for GS-US scores at the discontinuation with LDA after ADA free. Finally, nine patients recovered to LDA adding methotrexate, steroid, biologics (ADA 2, TCZ 1) among ten patients who did not preserve LDA during 12 months. Only one patient did not achieve LDA after ADA treatment. **Conclusion.** Ultrasound assessment is useful for predicted relapse within 12 months after discontinuation of ADA treatment.

P2-075

Observational analysis of the tapering of biologics, Etanercept

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Conflict of interest: None

Objectives: This study was to assess how to reduce biologics, Etanercept, in patients with rheumatoid arthritis (RA). Methods: RA patients with Etanercept were observed on their doses and injection intervals. Injection interval of Etanercept 25mg s.c.i. was adjusted due to clinical symptoms and data. Medical records were observed, retrospectively. Results: Of 42 RA patients (60.5 year old, male/female: 10/32) with the duration of 6.7 years, 9 patients were started with 50mg of Etanercept and 33 patients, of 25mg as the first dosage. Observation period was for 35.5 months. 17 patients were maintained on the first dosage, 8 patients were prolonged interval of 10~14 days, and 17 patients: 21~28 days with 25mg of Etanercept. Dose-tapered group: 64.0 y.o. of age was younger than dose-sustained one: 55.3 y.o. (p=0.043). Prescription of predonisolone were different, 2.6mg and 6.0mg (p=0.016). There was no significant difference in other factors such as BMI, stage, class of disease, duration of RA, value of ACCPA, RF, ESR, CRP, and MMP-3 and TJC or SJC). In minimally dose-tapered group, they could reduce to 50% at around 15.0 months and to 25% at 10.6 months. Conclusion: Among RA patients, rather elderly patients with low dose of steroid may reduce Etanercept.

P2-076

The anaysis of extension of therapy period in patients with rheumatoid arthritis (RA) who had intravenous Tocilizumab (TOC iv) therapy

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Conflict of interest: None

【Object】We examined effects of extension of therapy period in patients with rheumatoid arthritis (RA) who had achieved clinical remission (CR) by intravenous Tocilizumab (TOC iv) therapy.【Methods】We investigated into 11 RA patients who took treatment of TOC iv in our hospital for past 5 years. 5 patients of them achieved CR at average 25.8 months by TOC iv therapy, and then treatment interval was extended to every 6 weeks. We compared RA disease activity scores and their backgrounds of extension group (Group E) with those of non-extension group (Group N).【Results】DAS28ESR at first time of TOC therapy had no significant difference between both groups (5.8 vs 6.3). DAS28ESR at week 24 of TOC therapy had the difference from Group E and N (1.8 vs 3.8). Analysis of background factors showed some differences in ACPA titer, JHAQ score, MTX combination ratio and PSL usage rate, respectively, but no significant difference was observed because the number of analyzed objects was small.【Conclusion】Our analysis implicated that it is possible to extend the interval of TOC therapy while maintaining RA remission by carefully selecting patient.

P2-077

Survey of discontinuation and change of biological drugs for rheumatoid arthritis patients

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Conflict of interest: None

[Objectives] There has been no clear consensus for the hospital pharmacist's role in biological drug treatment for patients with rheumatoid arthritis (RA). However, such contributions have not been realized fully. In this study, we sought to investigate current situation to clarify what pharmacists needed in biological drug treatments. [Methods] A total of 350 patients were administered in biological drugs at Showa University Hospital outpatient clinic, 150 patients as subjects, who discontinued or switched to different medications. We retrospectively investigated reasons and subsequent responses to the discontinuation and change of the medications. [Results] The outcomes of 150 patients were as followings; remission / partial remission 13 (8.7%), first invalidity 38 (25.3%), secondary invalidity27 (18.0%), and adverse events 34 (22.7%). As the countermeasures for discontinuation and change, 68 patients (45.3%) were switched to another biological product, and 48 patients (32.0%) switched to other drug products with a different action mechanism. [Conclusion] The 22.7% of adverse events were resulted in reasons for the discontinuation and change. More positive contributions could be possible if pharmacist participates in monitoring side effects and countermeasures for the safety.

P2-078

Efficacy of Biologics Switch by Golimumab

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Conflict of interest: None

[Objects] We did Switching this time from a TNF inhibitor to Golimumab (GLM) in our institution and analyzed 63 clinical usefulness that were available for follow-up in retrospective more than 24 weeks. [Method] We divided 63 cases that we were able to analyze into Bio Naïve group (n=33) and the Bio Switch group (n=30) and weighed the clinical efficacy. Significant difference was found in a base-line CRP level between both groups. Also, we divided Bio Switch group into previous Bio distinction (IFX, ETA, ADA) more and there was a difference in efficacy of GLM by former Bio or weighed it. [Results] As for the change of DAS28CRP at 24 weeks, there was not the significant difference of the thing which a significant drop was seen in Bio Naïve group as compared with Bio Switch group (Bio Naïve group: 4.08 → 2.41 Bio Switch group: 3.71 → 2.40). It decreased in 2.47 from 3.90 in the previous ETA group (n=6), in 2.49 from 4.27 in the previous ADA group (n=11), in 2.34 from 3.45 in the previous IFX group (n=10). The significant difference between biologics was not found. During an observation period, there was not serious adverse events [Conclusion] A useful thing had GLM as 2nd Bio for the TNF inhibitor not as effective case.

P2-079

An evaluation of the effectiveness of golimumab for rheumatoid arthritis in patients with an inadequate response to first-line biological disease-modifying antirheumatic drugs

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Conflict of interest: None

[Object] We investigated the effectiveness of golimumab (GLM) as a second-line biological disease-modifying antirheumatic drug (bDMARD) following first-line treatment with other bDMARDs. [Methods] The study population consisted of 67 patients with rheumatoid arthritis (RA). GLM was administered to 35 patients as a first-line bDMARD (GLM-first group) and to 32 patients as a second-line treatment following inadequate response to former bDMARDs (GLM-second group). [Results] Six months after beginning treatment, the GLM-first group showed significant improvements from baseline according to the DAS28-ESR. Conversely, treatment was not as successful in GLM-second group. The DAS28-ESR improved significantly only in the group switched from abatacept; there was no improvement in the groups switched from other TNF inhibitors (TNFi) or tocilizumab (TCZ). [Conclusions] Although previous studies demonstrate that switching to GLM as a second-line treatment leads to significant improvement after insufficient response to other TNFi or TCZ, these results are still debated. There were variations in the clinical history of the patients who did not show improvements; therefore, the next therapeutic choice should take into account the diversity of pathophysiology in patients with RA.

P2-080

Clinical Impact of eGFR self-report on methotrexate prescription among patients with rheumatoid arthritis

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Conflict of interest: None

[Aim] Nagoya University Hospital started eGFR self-report from Dec in 2009. Prescription status of MTX was analyzed before and after eGFR self-report. [Methods] Study subjects were adult patients with RA who were treated by MTX from Sep to Nov in 2009 and 2010. GFR categories, prescribed dose, new prescription and discontinuation of MTX were analyzed before and after eGFR self-report. [Results] MTX was prescribed in 424 and 470 patients in 2009 and 2010, and average dose of MTX was 6.8±2.4mg/week. Numbers of patients according to eGFR categories in 2009 and 2010 were G1: 125, 170, G2: 246, 261, G3a: 37, 27, and G3b: 16, 12. MTX was not prescribed to patients with eGFR below 30, and number of MTX prescription to patients in G3a+b was decreased in 2010. New prescription to patients with G3b was observed in 3 patients in 2009, but none in 2010. Among 16 patients with G3b in 2009, no dose-increase and 4 discontinuation of MTX were observed in 2010, and all 3 patients with G3b, who were treated MTX at 8 mg/week and above, were reduced MTX dose in 2010. [Conclusion] Prescription status of MTX was different before and after eGFR self-report, suggesting its preferable effect to prevent adverse effect of MTX.

P2-081

Clinical response of patients with refractor adult Still's disease to subcutaneous administration of Tocilizumab

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Conflict of interest: None

The efficacy of infusions of biologics in treating adult Still's disease (ASD) is reported, but the information is still lacking and insufficient with subcutaneous (sc)-injected drugs. To prove the efficacy of sc-injcted Tocilizumab in refractory ASD treated high-dose of prednisolone (PSL), Methotrexate (MTX), and Infliximab (IFX), low-dose of PSL and sc-injected Tocilizumab was medicated. This female 31-years-old patient's ASD started at age of 19 with high fever, salmon pink rash, polyarthritis, and elevated ferritin. The tight treatment of high dose of MTX and Tacrolimus lead the patient to the remission after 10 years. She had stayed in drug free condition for two years, however, her disease of ASD relapsed with remitted fever, rash, and neck lymphadenopathy with throat pain. According to her wish and some condition of our clinics, she choices the sc-injection of TCZ, at first, one shot every two weeks, and then, two every two weeks with PSL. After the increase of sc-injection, the efficacy of TCZ was remarkable and sustained for weeks. This result indicated that the TCZ efficacy in the treatment of ASD depend not on the delivering route, but on the total dose.

P2-082

Clinical course of patients undergoing bio-free treatment after achieving remission in clinical practice

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Conflict of interest: None

Objective: To investigate the clinical course of patients in the treatment interruption group after achieving remission in clinical practice. **Subjects and Methods:** We attempt treatment interruption after at least 2 years of SDAI remission following administration of bio-drug upon patients' request. Patients whose treatment was interrupted for at least 6 months were included in this study. Recurrence of early morning stiffness, mild CRP increase, arthralgia, and joint swelling was observed as an end point of treatment interruption. HAQ and mTSS at the time of treatment interruption and immediately after recurrence were compared. **Results :** Out of 36 patients, 14 received IFX; 1, ETN; 13, TCZ; 3, ADA; 3, ABA; and 2, GML. The mean duration of treatment interruption was 2.2 (years) for IFXtreated group, 1.2 for ETN group, 1.2 for TCZ group, 1.8 for ADA group, 1.8 for ABA group, and 1.5 for GML group. The original biodrug treatment was resumed in all patients after recurrence, except for one, in whom, IFX treatment was switched with GML treatment. **Conclusion:** Differences were observed among each group and the duration of interruption was longer in the 1st-bio group than in the multiple-drug group. No change in HAQ or mTSS was observed after resumption of original bio-drug treatment.

P2-083

Survey of the dose reduction of biologics to treat rheumatoid arthritis (RA) patients in our related clinic

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Conflict of interest: None

[Objectives] To investigate the status of the reduction of biologics with RA patients. [Methods] 16 patients who reduced dosage after introduced biologics in our related clinic were included in this study. We investigated the introduction and reduction of biologics, change of the concomitant medication, RA disease activity score (DAS28CRP) and MMP-3. [Results] Duration of biologics introduction from the RA onset was 67.6 months. Etanercept (ETN) in ten cases, tocilizumab (TCZ) and adalimumab in two cases of each were administrated at first. In one case, TCZ were administrated as second biologics after invalided ETN. The concomitant medication at the introduction was methotrexate in 14 cases (87.5%), prednisolone (PSL) in nine cases (56.3%). Period of reducing biologics was 12.3 months after the introduction, PSL was stopped in eight cases at the time. DAS28CRP decreased to 2.07 from 3.79 at the time of reducing biologics, and continued remission after reducing biologics. MMP-3 decreased with 37.1 ng/ml from 160.3 ng/ml. Three cases increased biologics again, because flared up clinical symptom. One case was pregnant after reducing biologics, stopped biologics in the period of pregnancy. [Conclusions] Almost cases could be able to continue the remission after reduced biologics.

P2-084

Extension of Dose interval of Toricllizumab in Rheumatoid artritis

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Conflict of interest: None

[Object] We examined cases of rheumatoid arthritis with prolonged administration interval 6 months after remission maintenance by administration of Tocillizumab (TCZ). [Subjects and Methods] Among 36 patients who received TCZ, 11 patients (1 male and 10 females) who agreed to extend the administration interval, maintaining remission for an additional 6 months or more after achieving remission, had an average age of 56.4 years 31 -76), disease duration is 10.6 years (4-28) Steinbrocker Stage 3/1/3/3, Clas 3/6/2/0. The number of tender joints, number of swollen joints, patient VAS, physician VAS, CRP, ESR, MMP - 3, RF, SDAI, CDAI, DAS - CRP 28, DAS - ESR 28 were studied. [Results] Two out of three patients whose administration interval was extended at intervals of 5 to 6 weeks remained remission, and 1 had a slightly worsening tendency (remission to low disease activity). In addition, 4 out of 8 patients extended from 5-6 weeks to 8 weeks interval kept remission and 2 cases shortened to 6 week interval for relapse. [Conclusions] We should try to prolong the administration interval for cases where maintenance of remission was achieved by TCZ administration for 6 months.

P2-085

Possibility of Elongation of Adalibmab (ADA) Drug Interval in RA

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Conflict of interest: None

【Objective】To evaluate the efficacy of elongation of ADA drug interval.【Method】 RA patients in LDA after ADA drug therapy were enrolled in this study.6 patients maintained in LDA. Assessed patients backgrounds, existence of ACPA/RF, MTX/PSL Dose, Biologics (Naiive/Switching), timing of elongation, upper limit of elongation interval, and Complication.【Results】Mean age was 62.5 years old.5 patients had ACPA/RF. All patients used MTX (MeanDose8.5mg/week). Bio Naiive were 5 patients, another one was switching. Elongation began within 13week in average. Elongation began from 3week to 5weeks.1patients reflared in 6week, No complication occurs in this study.【Conclusion】 Within 5 week, we can elongate ADA drug interaval safely.

P2-086

Examination of effectiveness and safety by Tocilizumab shorten administration time for rheumatoid arthritis

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Conflict of interest: None

Introduction: Since May, 2013, it has been permitted to use subcu-

taneous injection of Tocilizumab (TCZ) for the treatment of rheumatoid arthritis. However, the intravenous drip infusion is still needed. Since May, 2013, we started TCZ administered at 30 minutes infusion. **Objectives**: We evaluated the effectiveness and safety by TCZ shorten administration time for rheumatoid arthritis. We used SDAI and CDAI for effectiveness evaluation. We examined all of the adverse events during full of the observation period for safety. **Method:** From February, 2013 until Jun, 2016 we administered at 30 minutes infusion to patients who had not been infusion reaction after 3 times TCZ administration. **Result:** We conducted 21 patients; male 5 / female 16, age 63.3±17.5 and SDAI 14.6±8.5 at the baseline. SDAI improved 4.2±3.0 after 6 month treatment, and remission rate was 50%. We encountered a case developed nausea in infusion reaction, although it could continue by switched administration time in 60 minutes. The other adverse events were observed 5 patients. **Conclusion:** We can administrate TCZ safely by administering while monitoring the infusion reaction. TCZ administration in 30 minutes can expect reduction of patients binding hours and burden on medical staff, and efficient use of treatment space.

P2-087

The case of progressive RA with operating pacemaker implantation who was successfully treated with TCZ and has been continued the drug free remission

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Conflict of interest: None

[Case] The case was 35 years old, women, Stave IV, Class 2, RA patient. RA was diagnosed in 2001 and she was operated pacemaker implantation because of congenital AV block. She was treated with SASP, BUC, MTX, and PSL, but these therapy were not effective and disease activity was increased (DAS28/ESR: 4.63). In 2008, June, she was treated tocilizmab (TCZ) by drip infusion. After TCZ therapy, disease activity and symptoms were improved and one year later, she achieved clinical remission (DAS28/ESR: 1.60). At the same time, both MTX and PSL were stopped and continued TCZ mono therapy. After that, the clinical remission was continued and then we tried to employ an extended-interval dosing method. In 2015, April, we stopped TCZ (drug free). In 2016, February, she was re-operated pacemaker implantation, but her heart function did not get worse before and after commencement of TCZ therapy and she has been continued the drug free remission. [Conclusion] We experienced the case of progressive RA with complicated heart disease who was successfully treated with TCZ and has been continued the drug free remission. It was suggested that there is possible to continue the drug free remission in which case of progressive RA patient that was well controlled disease activity during TCZ therapy.

P2-088

Investigation of patients in the AORA registry receiving biologic agents for the first time

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Conflict of interest: None

Purpose: We surveyed the backgrounds of patients registered in the AORA registry receiving a biologic agent for the first time. Patient age, disease duration on starting biologics, disease activity on starting biologics, combined use of MTX/PSL, and level of effectiveness were investigated. **Subjects:** Subjects comprised patients who received a first dose of infliximab (IFX; n=101), etanercept (ETN; n=176), adalimumab (ADA; n=15), tocilizumab (TCZ; n=40), and abatacept (ABT; n=25), up to July 2015. **Results:** By year, ETN has been the most frequently used agent since 2009. Mean age and disease duration at start of administration were: IFX, 57.6 years and 129 months; ETN, 59.1 years and 132 months; ADA, 57 years and 93 months; TCZ, 56.3 years and 134 months; and ABT, 65.6 years and 161 months, respectively. DAS28CRP at the start showed high disease activity: IFX, 4.22; ETN, 4.58; ADA, 4.40; TCZ, 4.11; and ABT, 4.29. Rate of combination MTX/PSL at the start of administration were: IFX, 100/74%; ETN, 77/47%; ADA, 93/87%; TCZ, 63/55%; and ABT, 52/52%. DAS28CRP at the time of the final survey was: IFX, 3.04; ETN, 2.64; ADA, 2.39; TCZ, 2.03; and ABT, 2.24. **Discussion:** As ETN is injected subcutaneously, and thus easily used on an outpatient basis, it is often used in clinics.

P2-089

The efficacy of half use of etanercept (ETN) for elderly or long-term morbidity RA patients

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Conflict of interest: None

«Objectives» The use of not enough amount of biological products affects the immunogenicity and encourages the antibodies of that. However, there are several Biological products for RA which have less immunogenic. This study is The efficacy of half use of Biologic therapies (Etanercept:ETN) for elderly patients without increasing the amount of Methotrexate (MTX) or long-term morbidity RA patients. «Methods» Sixteen patients (over 75 years or suffering from more than 20 years) has been treated by using half amount of ETN for more than 24 weeks (Man 3 Female 13). We evaluate the effect of half use of ETN therapies. «Results» 16 of 11 patients were keeping Low disease activity at 12week. No Patients must discontinue biologic therapies in all of the period. All patients had been Low disease activity at the last observation. But 5 Patients were dropped out of treatment because adverse event 2, Tumor was founded 2, self-discontinuation 1. «Conclusion» Half use of ETN are likely to be useful for elapsed RA patients more than 20 years from the onset with in recurrent or still have not been able to maintain a low disease activity, or 80 years or older without being able to receive aggressive arthritis treatment.

P2-090

Attempt to enable use of biological products and dosing interval study

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Conflict of interest: None

In rheumatoid arthritis (RA), biological products for its effectiveness and safety has been established. However, the burden of patients is large, health care and economic considerations there seems to be. Because of fear of the emergence of the neutralizing antibody during the administration of biological preparations, proper use and proper dosing interval is determined strictly. In our department Etanercept (ETN), Tocilizumub (TOC), Golimumab (GLM) for dosage reduction (tapering), expansion of the dosing interval (spacing) was performed on the patient consent. ETN,

25 mg was administered two times a week, but gradually spread the dosing intervals currently every 10 days keeps the low disease activity. TOC is an intravenous preparation every 4 weeks,5 weeks and now 6 weeks, its effects can be maintained. GLM is initially high disease activity in 100 mg every 4 weeks which remission status then enforced, extended to every 6 weeks, even 50 mg every 4 weeks in the follow-up period. And yet the number of cases are little and during a trial, but, according to individual tailor-made treatment may be suggested. To further increase the number of cases, establish effective dose and dosing interval.

P2-091

Successful switching to intravenous injection of tocilizumab after multi-use of biologics including subcutaneous injection of tocilizumab: A report of 2 cases

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Conflict of interest: None

【Case 1】80 y, F, BW: 52.9 kg. Her biologic therapy had been initiated with ETN 16 years after onset. However, she showed 2nd lack of efficacy (LOE) to treatment with both ETN and ADA, then switched to TCZ sc. Baseline CRP, MMP-3 and DAS28-ESR was 2.1, 147 and 3.49, respectively. At 4-week, no parameters were not improved. Then, she had been treated with CZP, GLM, Tofa, but neither was effective and finally treated with TCZ iv (400 mg/4 weeks). At 8-week, CRP, MMP-3, and DAS28-ESR was 0.01, 167, and 0.84, which showed marked improvement.【Case 2】58 y, F, BW:47.5 kg. Her biologic therapy had been initiated with ETN 2 years after onset. However, she showed primary LOE to treatment with both ETN and GLM, then switched to TCZ sc. Baseline CRP, MMP-3 and DAS28-ESR was 6.84, 630 and 5.23, respectively. At 52-week, CRP, MMP-3 and DAS28-ESR was <0.01, 83.2 and 1.75, which was clinical remission; however, she showed 2nd LOE thereafter. Then, she had been treated with ABT and Tofa, but neither was effective and finally treated with TCZ iv (400 mg/4 weeks). At 16-week, CRP, MMP-3, and DAS28-ESR was 0.01, 411.3, and1.89, which showed marked improvement.【Conclusion】When the patients showed insufficient efficacy to treatment with TCZ sc, switching to TCZ iv should be considered primarily.

P2-092

The efficacy of biologics to muscle strength in patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] To clarify the improvement of muscle strength in rheumatoid arthritis (RA) by biologics. [Methods] The total of 10cases, who were diagnosed as having RA, were subjected to be analyzed the grip powers and pinch powers before and after biologics treatments. [Results] Average age was 70.8±7.8 years old. Eight patients were female. All RA patients had a good response to biologics. Average grip power was increased from 98.3+58.3mmHg to 162.7+81.6mmHg. The average pinch power was also increased from 1.85+0.98kg to 3.23+1.85kg. In addition, the pinch powers were increased in relation to the decline of serum CRP levels. [Conclusion] We suggested that the biologics improved the muscle strength of RA patients, which resulted from suppression of inflammation.

P2-093

Medication for RA patients with long time remission

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Conflict of interest: None

Objective: To characterize the medication profile for the RA patients with long-lasting remission. We examined RA patients who admitted our clinic from July to September every year. In 2015 we examined 332 patients. We identified 65 RA patients with DAS-28CRP remission from 2011 to 2015. Among them, 24 patients (37%) were treated by biologics (group A). 40 patients had kept remission without biologics (group B). In 2015, 14 patients were DAS-CRP moderate and high activity even though treated by biologics (group C). Results: We used methotrexate (MTX) 27 patients in group B (68%) and 146 patients in 332 examined patients in 2015 (45%). Mean duration of disease were group A 13.6 years, group B 12.8 years, group C 13.9 years respectively. In group A, we used biologics in 7.7 years (mean) from onset, and treated 1 biologics in 14patients and 2 biologics in 8 patients (mean 1.4 biologics). In group C, we used biologics in 10.9 years (mean) from onset, and treated 1 biologics in 6patients, 2 biologics in 5 patients, 3 biologics in 1 patient and 4 biologics in 1 patients (mean 1.8 biologics). Compared 2 groups, years from onset to start biologics were not different significantly. But we used less biologics in Group A.

P2-094

Investigation of the efficacy and safety of the biological DMARDs for the elderly patients with rheumatoid arthritis

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Conflict of interest: None

Objectives: To evaluate the efficacy and safety of the biological DMARDs (bDMARDs) for the elderly patients over 75 years old with rheumatoid arthritis (RA). Methods: 34 RA patients treated with bDMARDs for the first time who were older than 75 years were evaluated. We analyzed continuation rate, clinical response, and safety at 1 year. Results: As for the bDMARDs first start, the mean average age was 78.6 years, the disease duration was 9.3 years, the MTX concomitant rate was 47.1%, the mean dose of MTX was 7.8 mg/week, and the PSL concomitant rate was 64.7%. Adapted bDMARDs were IFX (n=7), ETN (n=15), GLM (n=3), TCZ (n=1), and ABT (n=8). Tendency to choose ETN or ABT was observed. The continuation rate was good with 82.4% at 1 year. Disease activity index was also improved (DAS28: 5.01±1.30, 2.97±0.88, SDAI: 19.74±12.40, 5.45±5.32 (0, 1 year, mean± SD, LOCF)). Three cases (IFX:1, ETN: 2) were not effective, and another three cases were stopped from adverse event (pulmonary abscess (ABT), phlegmone (ETN), and colon cancer (ABT)), but all cases were recovered. Conclusion: bDMARDs is one of the choices of the treatment for RA patients over 75 years old. We should not hesitate to treat elderly RA patients with bDMARDs for taking QOL and complications.

P2-095

Clinical results of tocilizumab (TCZ) in patients with rheumatoid arthritis; more than 5 years follow-up

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Conflict of interest: None

Object; To investigate the efficacy and continuity of tocilizumab (TCZ) treated more than five years in patients with rheumatoid arthritis. Materials; 84 RA patients (male; 16, female; 68) started to treat with TCZ form August 2008 to December 2010. The average age; 56.6 years, the average duration of RA; 12.6 years, The average DAS28 (CRP); 4.00 at

the beginning of administration respectively. 58 patients had received TCZ as first-line and 26 as second-line. We investigated the efficacy and continuity of TCZ analyzed the reason of discontinuation. Result; Of 84, we could follow up 79 patients. Among 79, 43 were continuing. Among 58 who treated as first-line, 55 were followed and 29 were continuing with remission. Among 26 who treated as second-line, 24 were followed and 14 were also continuing with remission. 36 were not continuing. The reasons of discontinuation were caused by side effects (e.g. infectious disease and malignant disease), however, among 36, 10 were stopped with remission and all of them were maintaining remission at final follow-up. Conclusions; The continuation rate of TCZ more than 5 years was 54.4%. 53 which include both patients who have been continuing and have achieved discontinuation by remission have been keeping the efficacy of TCZ.

P2-096

The clinical outcome of subcutaneous tocilizumab in patients with rheumatoid arthritis

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Conflict of interest: None

【Objective】To examine the clinical outcome of subcutaneous-tocilizumab (TCZ-SC) in patients with rheumatoid arthritis (RA).【Methods】Forty RA patients (33 in female) who were introduced with TCZ-SC were registered. The age was 62 years old on average, and RA duration was 8 years on average. Bionaive cases were 30. Methotrexate (MTX) was used in 14 cases (35%) and 2.6 mg/week on average (4-10 mg/w). Methylprednisolone (PSL) was used in 15 cases (38%) and 2.3 mg/day on average (5-10mg/d). The persistency, DAS28, remission rate of DAS28, and discontinued cases were examined.【Results】The persistency rate was 88%. DAS28 (4.72 on the introduction of TCZ-SC) was decreased to 2.07 (at 3 months) and to 1.89 (at 12 months after TCZ-SC). The DAS28 remission rate was increased to 76%(at 3 months) and to 81%(at 12 months). Discontinued cases were 5. Of these, no efficacy was 1 case, and adverse events were 4 (nontuberculosis mycobacterium, drug eruption, surgical site infection, and interstitial pheumonia, respectively).【Conclusions】Based on the results that not effective case was just one in our 40 cases, and that TCZ-SC achieved high DAS28 remission rate just after 3 months and the remission was maintained until 12 months, we consider that TCZ-SC efficacy is so high.

P2-097

Efficacy of tocilizumab therapy in elderly rheumatoid arthritis patients in the AORA registry

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Conflict of interest: None

[Purpose] We investigated tocilizumab (TCZ) efficacy in elderly rheumatoid arthritis (RA) patients. [Methods] We investigated backgrounds, drug retention rates, and 28-joint disease activity scores based on erythrocyte sedimentation rate (DAS28-ESR) of 47 RA patients ≥ 65 years of age, in the AORA (Akita Orthopedic group on RA) registry. [Results] There were 7 men and 40 women with a mean age of 71 years. The mean disease duration was 139 months. Thirteen and 34 patients received intravenous and subcutaneous TCZ, respectively. Twenty-two patients were treatment naïve (N group) and 25 had switched from another treatment (S group). Methotrexate was administered to 27 and prednisolone to 34 patients at respective mean doses of 7.4 mg per week and 5.6 mg per day. As to DAS28-ESR scores, 24 patients had moderate disease activity and 14 had high disease activity. At study completion in 2016, 10 patients had dropped out. The 4-year drug retention rate was 77% in the N group and 73% in the S group. Of the 40 patients with clinical courses observable beyond 52 weeks, data on 37 were analyzed: 29 patients had achieved low disease activity with DAS28-ESR scores changing from 4.57 ± 1.28 to 2.42 ± 1.07. [Conclusion] Our findings confirm high efficacy of TCZ in elderly RA patients.

P2-098

Efficacy of intravenous drip fusion of Abatacept by patient body weight on rheumatoid arthritis using data from NinJa 2015

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Conflict of interest: None

[Object] The dose of intravenous drip fusion of Abatacept against RA is increased by patient weight 60kg and 100kg. We evaluated the efficacy of Abatacept by weight class using data from NinJa 2015. [Methods] The object was three hundred and one women patients who took 500 mg of Abatacept every four weeks intravenously and weighed under sixty kilogram among rheumatic patients recorded in NinJa 2015. Their mean age was 68.3 years, their mean disease duration was 15.3 years and their mean body weight was 48.2kg. They were divided into three groups; u40 group was patients under 40 kg by body weight, u50 group was patients whose weight was not less than 40 kg and under 50 kg, and u60 group was patients whose weight was not less than 50 kg and under 60 kg. The patients of u40 group was older than those of the other two groups. [Results] CDAI score and SDAI score in u60 group were significantly lower than those in the other two groups. HAQ-DI value and MDHAQ value in u60 group were significantly lower than those in u40 group. [Conclusions] Intravenous drip infusion of 500 mg of Abatacept every four weeks might be the most effective on patients whose weight was not less than 50 kg and under 60 kg and might be less effective on patients under 40kg by body weight.

P2-099

Comparison of administration techniques for biologic agents : restrospective cohort study

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Conflict of interest: None

Objectives. It has been a while since, the boilogic agents have let rheumatoid arthritis patients to early remmision, and improved their QOL. Comparison of administration techniques for biologic agents, whether DIV or SC would be better for the patient's QOL, has not been reported until this point. For the first time, we would like to report the difference. Methods.149 RA patients who treated with biologic agents were recruited. Design was retrospective cohort study. Comparing the SC group with the DIV group, the primary outcome was QOL (SF-36) after 6months' treatment. Result. The mean age of RA patients was 57.5±15 and 85% was female.50.3% was the SC group and 49.6% was the DIV group. Adjusted with age, sex, DAS28 ESR, HAQ, and disease duration, there was no significant difference between 6month MCS. But 6 month

PCS was significantly higher in DIV group (p=0.0409). Conclusion. There is a possibility that treatment with DIV would improve the 6 month QOL (PSC) compared with SC.

P2-100

A study of 30 early rheumatoid arthritis (RA) patients who have achieved a social remission

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Conflict of interest: None

Treatment results in RA patients have significantly improved, leading them to clinical, structural and functional remissions at high rates. The next goal to be pursued is "social remission," which means returning completely to the present post and thereby paying the same amounts of taxes as before. Achievement of a social remission requires the patient to become free of drugs. A drug-free remission can be achieved by inducing apoptosis in all of his/her TNF-producing cells. At our clinic, a social remission has been achieved in 30 early RA patients as described below. *Subjects and methods:* A TNF-α inhibitor and MTX were concurrently administered to 33 early RA patients suffering from the disease for not more than 6 months and untreated with an antirheumatic drug. The dose of the biological drug was increased to promptly lead the patients to a deep remission. After one year of the treatment, the patients were kept drug-free and followed up for another year. *Results:* Thirty of the 33 early RA patients became drug-free and achieve a social remission. *Conclusion:* Our method allows 91% of them to achieve a social remission, and is therefore superior in terms of medical economy to methods in which MTX is administered as the anchor drug.

P2-101

Subcutaneous tocilizumab for the treatment of RA in clinical practice

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Conflict of interest: Yes

Purpose: to examine the clinical results of subcutaneous tocilizumab treatment for the RA patients in clinical practice. Methods: 110 patients with RA (58.4 years old in average, 10.5 years of disease duration, Bio-switch: 63 patients and concomitant MTX: 61.8%) were included in this prospective multicenter study. DAS and CDAI remission, and retention rate were analyzed at 24 weeks. Results: CDAI improved from 4.8 to 2.3 points. DAS28 and CDAI remission was achieved in 66.2 and 28.0%, respectively. Retention rate was 7.3 at 24 weeks and concomitant MTX significantly influenced the retention of TCZ. There was no change of RF and ACPA values. Conclusions: Subcutaneous TCZ showed the comparable efficacy with intravenous TCZ for RA treatment, and one of the important options.

P2-102

Successful Treatment of Refractory Hematocytopenia (Evans Syndrome) with Mycophnolate Mofetil in A Patient with Systemic Lupus Erythematosus

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Conflict of interest: None

A 27-year-old woman was admitted to our hospital because of refractory autoimmune hemolytic anemia (AIHA) and thrombocytopenia (ITP). She was diagnosed as having systemic lupus erythematosus at 13 years of age and she frequently experienced attacks of AIHA from 9 years ago. Although her previous doctors treated her with prednisolone, rituximab and tacrolimus for long term, AIHA never achieved complete remission. On admission, she had low hemoglobin (Hb) level (4.3 g/dl) and thrombocytopenia (48,000/μl). Further examination showed that she had AIHA and ITP (Evans syndrome). Since we considered that her hematocytepenia was induced by the recurrence of SLE, we tried to treat her with mycophenolate mofetil (MMF) in addition to the increase in prednisolone in order to potentiate the immunosuppressive effect. After then, her hematocytopenia gradually improved to 10 g/dl of Hb level. Although further study is necessary, MMF might be a candidate for the treatment of refractory AIHA and ITP in lupus patients.

P2-103

The efficacy of Tocilizumab therapy in patients with rheumatoid arthritis

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Conflict of interest: None

Objective. To examine the efficacy and safety in tocilizumab therapy of intravenous and subcutaneous injection with rheumatoid arthritis (RA) and an inadequate response to biologic disease-modifying antirheumatic drugs (DMARDs). Methods. This study comprised ten patients with rheumatoid arthritis intolerant to biologic DMARDs. Patients received tocilizumab therapy with intravenous or subcutaneous injection with or without methotrexate for 6 months. The outcomes were evaluated with the disease activity during 6 month 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 4.1 to 2.2) and CDAI (from 8.0 to 6.3) decreased significantly from baseline to Week 24. DAS28ESR Remission achieved in 6 cases at Week 24. Tocilizumab monotherapy was also effective with RA patients of in adequate response to TNF inhibitor therapy. The retension rate of tocilizumab at 24 weeks was 100%. The average dose of methotrexate tapered from 9.7mg to 6.7mg. The average dose of glucocorticoid also tapered from 4.3mg to 2.0mg. Conclusions. These results demonstrate that tocilizumab therapy is effective in patients with RA of an inadequate response to biologic DMARDs.

P2-104

Biologic-free remission after certolizumab pegol therapy for patients with rheumatoid arthritis: Report of two cases

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Conflict of interest: None

We describe two rheumatoid arthritis (RA) patients who achieved biologic-free remission by treatment with certolizumab pegol (CZP). [Case 1] A 64-year-old male with rheumatoid arthritis had received methotrexate (MTX). His disease duration was 7 months. Even though he had been treated with MTX at 12 mg/w, his RA disease activity had remained high. We started to treat him with CZP. He achieved clinical remission at 4 weeks after the start of CZP treatment. We discontinued CZP at 44 weeks. His clinical remission has continued for 2 years and 3 months since stopping CZP. [Case 2] A 37-year-old male with RA had received MTX at 14 mg/w. His disease duration was 13 months. Even though he showed low disease activity, some joint swelling remained. We added CZP. He achieved clinical remission at 8 weeks after the start of CZP treatment. We discontinued CZP at 25 weeks. He showed stable clinical remission for 1 year after stopping CZP. [Conclusion] To achieve biologic-free remission, CZP, with neither antibody-dependent cellular cytotoxicity activity nor complement-dependent cytotoxicity activity, has been considered unfavorable. However, the achievement of biologic-free remission with CZP is possible.

P2-105

Investigation of periprosthetic femoral fracture in total hip arthroplasty for rheumatoid arthritis

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Conflict of interest: None

【Purpose】We examined the characteristic and the problems of periprosthetic femoral fracture of THA for the RA.【Patients and Method】11 cases with for periprosthetic femoral fracture of THA for RA, all female. The mean age was 76.8. The analysis was the cause of the bone fracture, period of RA, THA passed years, fracture type, operation method, drug, complications.【Results】The cause of the fractures were 10 falls and 1 fall down. Average period of RA was 19 years and 5 months. THA passed years, an average of 11 yrs and 9 months. Fracture type, as for Vancouver type B1 4, B2 1, B3 1, C 5, the operation method, as for 10 osteosynthesis, 1 re-THA. Stem fixation were 5cases using bone cement, cementless 6 cases. Other joint replacement, TKA 6, THA 7, TSA 1, TEA 1. RA drugs were Biological products 2, MTX 7, steroid 5. The complications was one re-fracture of the re-THA. The implans of osteosynthesis were LCP 3, NCB 9, all cases bone union【Discussion】The infection and the bone union imperfection were not seen in this examination. There are many cement using THA and many joints replacement cases in the RA. Not to mention the infection prevention for the operation and the careful choice of the therapeutic method, the prevention of fall and bone fracture with the medication were thought to be important.

P2-106

Consideration of THA cases difficult to treat in RA patients

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Conflict of interest: None

We experienced three cases difficult to treat, and these three cases related to RA, such as suspected infection, repeated revision. Case 1 was a 76 years old male. Cementless THA was performed with acetabular bone grafting. 6 years after first THA, a remarkable loosening was generated on the acetabulum, and revision surgery was performed. However, after that, two more revised surgeries were needed. Case 2 was a 69 years old female. The main complaint were bilateral knee pain. However the left hip joint was ankylosis due to tuberculosis, at first the operation was performed in the order of right TKA, left THA, left TKA, and it takes three months or more. Case 3 was a 73 years old male. Although TCZ was being administered, infection was suspected just before the right THA, the surgery was postponed. During the final follow-up observation there was no loose surgery site and the course was good. THA's attention to RA includes poor bone quality / polyarthritic disorder / reduction of immunity (easy infectivity). Even in this series each case was consistent with those problems.

P2-107

Outcome of curved intertrochanteric varus osteotomy for osteonecrosis of the femoral head

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Conflict of interest: None

We reviewed the outcome of curved intertrochanteric varus osteotomy for osteonecrosis of the femoral head. We reviewed 21 hips in 17 patients with mean follow-up of 64.2 months. There were 11 women (14 hips) and 6 men (7hips), with a mean age of 32.6 years at the time of surgery. We investigated etiology, causative disorder, preoperative stage and type, postoperative progression of stage and conversion to total hip arthroplasty. 4 hips had collapse of femoral head but they don't need total hip arthroplasty. In one hip, total hip arthroplasty was done due not to collapse of the femoral head, but to progression of osteoarthritis. We conclude that curved varus osteotomy can be used to preserve the hip joint in patients with osteonecrosis of the femoral head.

P2-108

The outcome of total knee arthroplasty for valgus deformity with rheumatoid arthritis

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Conflict of interest: None

[Objectives] The aim of this study is to estimate the outcome of total knee arthroplasty (TKA) for valgus deformity with rheumatoid arthritis (RA) in our institution. [Patients & Methods] In whom we had performed primary TKA surgery for RA, we evaluated 64 knees in 59 cases with less than 170 degrees of FTA at pre-surgery, that were performed by the same prosthesis type, midvastus approach for joint capsule exposure, and without lateral release of capsule. The follow-up period was 7.8 years. We investigated JOA RA knee score and Knee and Function score according to Knee Society Score as clinical outcome, the range of motion (ROM), the findings of roentgen photograph, and complications. [Results] JOA RA knee score, Knee score and Function score were significantly improved from 46.4, 36.3 and 35.4 points at pre-surgery to 87.8, 94.8, and 71.3 points at final follow-up, respectively. The ROM changed from 13-113.4 degrees to 0.3-119.8 degrees after surgery. The tilt angle of patella in patella-femoral joint showed only the spread of 1.8 degrees to lateral side. There were observed infection, wound dehiscence, and hematoma/bleeding in 2 knees, respectively and pulmonary embolism in 1 case. [Conclusion] The good results were showed for the outcome of TKA for valgus deformity with RA.

P2-109

Journey 2 total knee arthroplasty for rheumatoid arthritis knee

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Conflict of interest: None

[Object] We evaluated Journey 2 total knee prostheses with the guide motion for rheumatoid arthritis knee. [Methods] We evaluated for 4 rheumatoid arthritis knees which performed Journey 2 TKA. The all cases woman, the age at operation were an average of 68 years old (57-81). In preoperative JOA score, an average of 61 points (55-70 points), the knee flexion angle were an average of 126 degrees (120-130 degrees). We operated using a trivector approach and measured resection technique. After three months post-op, we evaluated JOA score and knee flexion angle. [Results] Mean tourniquet time were 101 minutes (80-112 minutes), and mean flexion angle at op were 131 degrees (125-135 degrees). We operated three knees using Journey 2 BCS type, and one knee using Journey 2 CR type, because of femoral too small size and osteoporosis. At three months post-op, mean JOA score were 81 points (70-90 points), and the knee flexion angle were 120 degrees (100-130 degrees). [Conclusions] Journey 2 total knee arthroplasty with guided motion were useful for rheumatoid arthritis knee.

P2-110

Comparison of implant gap in TKA for Rheumatoid Arthritis and osteoarthritis

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Conflict of interest: None

Objective: We compared the implant gap value measured during primary TKA for rheumatoid arthritis (RA) and osteoarthritis (OA) of varus knee. **Material and Methods:** Twelve patients with RA and 62 patients with OA were treated with CR- TKA. Patients with flexion contracture over 20 degree, with valgus deformity and treated with PS-TKA were excluded. In the OA cases, MCL deep layer and in some cases, in company with posterior oblique ligament (POL) was released. In the RA cases, same procedure or no ligament release was undergone. Osteotomy was undergone with measured resection technique. After trial femoral component was inserted, implant gap was measured at 0°, 30°, 45°, 60°, 90° and 120° knee flexion by an Offset type tensor under a detachment force of 40 Ibs applied on the knee joint. **Results:** There was a tendency that the implant gap value was large in the RA group compared with the OA group at each knee flexion angle. Furthermore, it was significantly larger in the RA group than the OA group at 90° and 120° knee flexion, that suggests significant joint laxity at these angle. **Discussion and Conclusion:** It is suggested that implant gap in CR-TKA is larger, that is looser, in the RA than the OA when knee joint is flexed more than 90°.

P2-111

Consequence of initial treatment for periprosthetic joint infection in patients with RA − study of effectiveness to treated with continuous local washing irrigation −

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Conflict of interest: None

【Purpose】To study the consequence of initial treatment for periprosthetic joint infection (PJI) with RA patients, especially of effectiveness to treated with continuous local washing irrigation.【Materials and Methods】Until August 2016, we have treated 13 PJI cases, of 9 cases were operated at our hospital, 4 cases were other. 11 cases were RA patients, two were OA. TKA cases were 11 cases, THA was one case, and TEA was also one. MRSA cases were two, MRSE was one, MSSA was one, and the other were four, not detected the bacteria cases were four.【Results】6 cases were cured only after washing and continuous local washing irrigation. One case could be successed by one stage revision, and two were two stage revisions. 4 cases were failed, of two were arthrodeses and other were resection arthroplasties.【Discussion】We have been treated against PJI with several appropriate antibiotics and with continuous local washing irrigation for the initial treatment. Without the cases that caused by drug resistant bacteria, in taking PSL for amount, and having general complications, will be able to rescue and restore the implant to treat with continuous local washing irrigation for initial period of PJI.

P2-112

Effect of total knee arthroplasty on medication in patients with rheumatoid arthritis

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Conflict of interest: None

Objective: This study evaluated the effect of total knee arthroplasty (TKA) with capsulosynovectomy on disease activity and medication in patients with rheumatoid arthritis (RA). Methods: Seventy-seven patients with RA who underwent primary TKA with more than one year of follow-up were retrospectively reviewed to assess postoperative disease activity and drug administration. Results: RA disease activity was significantly decreased in DAS28-CRP one year after surgery. (3.9 vs. 2.7, $p<0.01$) DAS28-CRP after TKA in patients who were treated with the same or reduced medication was significantly lower compared with in those who were treated with additional or altered medication. (2.5 vs. 3.2, $p<0.01$) Conclusion: TKA with capsulosynovectomy improves disease activity after surgery in patients with RA.

P2-113

Two-stage bilateral total knee arthroplasty for rheumatoid arthritis patients

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Conflict of interest: None

【Introduction】Rheumatoid arthritis (RA) knees were characterized with bilateral involvement and flexion contracture. We treated bilateral RA knees with TKA one by one because of preoperative anemia and prolonged surgery raising risk of infection and DVT. The purpose of this study is to report results of one by one TKA for bilateral RA knees.【Materials and Methods】10 RA patients received bilateral TKA (20 TKA) were followed over one year. We reviewed disease duration, time of start to gait after surgery, duration of hospitalization. Femorotibial angle (FTA), range of motion (ROM) and JOA score were evaluated before and after surgery.【Results】Mean disease duration was 18.8 years, mean duration of hospitalization was 31.9 days. There was no significant difference the time of start to gait and duration of hospitalization between the first and the second TKA. FTA was 174.2° before surgery and 175.2° after surgery. Mean ROM (ext./flex.) changed from -16.4°/107.1° to -1.3°/104.6°. JOA score improved from 46.4 to 78.3 mainly by reduced pain score and flexion contracture. Significant improvement was seen in flexion contracture and JOA score after surgery.

P2-114

Cementless TKA using the NexGen trabecular metal modular tibial component in patients with rheumatoid arthritis: effect of bone grafting in the peg holes

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Conflict of interest: None

[Objectives] When cementless total knee arthroplasty is performed with the NexGen trabecular metal modular tibial component, initial fixation may be enhanced by grafting resected cancellous bone into the peg holes before insertion of the modular component. In this study, clinical and X-ray findings were compared between a standard operation group and a bone graft group. [Subjects and methods] This study investigated 21 patients (26 knees) with rheumatoid arthritis, including 13 patients (16 knees) in the standard operation group and 8 patients (10 knees) in the bone graft group. Baseline characteristics of both groups were similar. Postoperative clinical and X-ray findings were compared between the two groups. [Results] There were no significant differences between the two groups. At 6 months postoperatively, new bone formation was seen in 25% of the standard operation group versus 70% of the bone graft group. [Discussion] Fixation can be enhanced by placing crushed cancellous bone into the peg holes because the bone fragments will infiltrate the porous base of the peg after insertion of the component. [Conclusion] Grafting of crushed resected cancellous bone into the peg holes enhances initial fixation of the NexGen trabecular metal modular tibial component.

P2-115

Patellar non-resurfacing in total knee arthroplasty for rheumatoid arthritis

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Conflict of interest: None

[Background] Patellar resurfacing in total knee arthroplasty (TKA)

remains controversial. However, a number of authors have recommended routine patellar resurfacing of patella in patients with rheumatoid arthritis. [Objective] To investigate whether patellar resurfacing in TKA is appropriate in patients with rheumatoid arthritis. [Methods] A total of 13 primary TKAs without a resurfacing patella were studied in 9 patients with rheumatoid arthritis. TKAs were performed at our institution between January 2000 and December 2007. All patients were females, and the mean age at the time of surgery was 64.9years. The mean follow-up period after surgery was 10.5 years (range 8 –12 years). Clinical assessments after surgery were evaluated by a Japanese Orthopedic Association score and Patella scoring system at all intervals, and Range of motion. [Results] There was a significant difference in JOA score between preoperation (86.3±8.7) vs. postoperation (86.3±8.1) at follow-up $p<0.05$). The rate of occurrence of anterior knee pain was 0%. During the follow-up period, no patient underwent revision surgery for symptoms related to the patellofemoral joint. [Conclusion] A non-resurfacing patella in TKA for rheumatoid arthritis could obtain good long-term results.

P2-116

Intra-observer and inter-observer reliability of preoperative CT-based 3D planning for total knee arthroplasty

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Conflict of interest: None

【Object】Preoperative planning is an important factor of total knee arthroplasty (TKA). Recent studies suggest the usability of preoperative CT-based 3D planning for TKA, but few studies show its intra-observer and inter-observer reliability. The aim of this study is to document the reliability of preoperative CT-based 3D planning for TKA.【Methods】Twenty knees who underwent TKA at our hospital were included. The indication was primary osteoarthritis in ten and rheumatoid arthritis in ten. All knees were planned with zed knee system (Lexi) by six orthopaedic surgeon independently twice at more than 2-week interval. We studied about femoral and tibial component size, the degree of valgus and external rotation of femoral component.【Results】We achieved 99.2% intra-observer and 82.3% inter-observer agreement within 1 size in femoral component size and 90.0% intra-observer and 83.1% inter-observer agreement in tibial component size. The average errors of the degree of valgus were 0.67 ° in intra-observer and 1.03 ° in inter-observer, and those of the degree of external rotation were 1.42 ° in intra-observer and 1.79 ° in inter-observer.【Conclusions】We studied about the reliability of preoperative CT-based 3D planning for TKA.

P2-117

Patient background of joint-preserving toe arthroplasty for rheumatoid arthritis

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Conflict of interest: None

[Object] Since 2011, we perform joint-preserving toe arthroplasty, the first metatarsal osteotomy or tarsometatarsal arthrodesis for hallux valgus deformity and proximal shortening metatarsal osteotomy for dislocation of the second to the fifth metatarsophalangeal (MTP) joints. We report on the backgrounds of patients in whom we performed joint-preserving toe arthroplasty. [Methods] The study included 12 cases in 15 feet, 2 feet of 3 males, and 10 feet of 12 females. The mean age of the patients was 61.8 years. We evaluated the hallux valgus angle (HVA) and intermetatarsal angle (IMA), and modified Sharp score (van der Heijde) on radiographic images. [Results] Erosion had a mean modified Sharp score of 7.7 points (perfect score, 60 points); and joint space narrowing, 16.5 points (perfect score, 24 points). The HVA and IMA improved from 45° to 16°, and from 17° to 10° after operation. [Conclusions] While erosion had a low modified Sharp score, joint space narrowing had a high score, which relatively maintained the bone form of the joint face. Patients with dislocated MTP joints and a subdislocation could consider several treatment options. Therefore, many patients seem suitable for joint-preserving toe arthroplasty.

P2-118

Hindfoot arthrodesis using retrograde intramedullary nailing for rheumatoid arthritis

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Conflict of interest: None

[Object] Hindfoot arthrodesis using retrograde intramedullary nailing was performed for hindfoot disorder in patients with rheumatoid arthritis (RA). [Methods] The patients included four with RA, two with a varus deformity, one with a valgus deformity, and one with ankle joint distraction. Of the patients, one was male and three were female. The mean age was 64.8 years. All the patients had damaged ankle and subtalar joints. The nails used were Biomet Phoenix in one patient and Stryker T2 Ankle Arthrodesis Nail in 3 patients. After the treatment, load bearing was permitted under the cast below the knee, except in 1 patient who had an artificial bone graft in the bone defect part. [Results] Bone union was attained within 3–5 months. [Conclusions] A retrograde intramedullary nail was inserted from the plantar side through the ankle and subtalar joints for fixation of the tibia. The cases showed good indications for operation for hindfoot deformity by RA or talus necrosis. We obtained good results of hindfoot arthrodesis for our RA patients by using retrograde intramedullary nailing.

P2-119

Surgical treatment for hallux valgus by rheumatoid arthritis use planter fixation locking plate

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Conflict of interest: None

[Purpose] thorn great changes with the advent of biologic treatment of rheumatoid arthritis (RA), for foot toe surgery of articulated conservative surgery recently performed now. The RA outside the consideration of cases using bottom mounted locking plate for a fixed valgus toe transformation surgery. [How to] the RA5 example from 5/2015, all in women average age is 63 years old. Results: out of valgus toe angle average improved after 20 degrees 60 degrees. JSSF RA foot ankle scale from 35 observed delayed 65 one wound, healing light treatment with you. Conclusion: outside is a complex osteotomy, valgus surgical method in a variety of ways, but if the RA as seen bone weakening. To get stable if you simplify osteotomy should be solid fixed. Case of osteotomy fixed previously, using K wires in our hospital, but with fixed wanting to re deformation observed. Recently, the outside was likely after the anti mother toe correction osteotomy fixed with locking plate. I thought RA disrupted plate installation problems as larger incision and that the plate is somewhat difficult, but less than as a fixed valgus foot surgery is not useful or not.

P2-120

Rapidly destructive coxarthrosis-like arthritis in rheumatoid arthritis patient treated with biologic disease-modifying antirheumatic drugs

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Conflict of interest: None

A 74-year-old woman with rheumatoid arthritis (RA) presented to our outpatients clinic because of a 3-day-history of left coxalgia. She was treated with methotrexate 14 mg/week and abatacept 125 mg/week, but

her disease activity remained high. Magnetic resonance imaging revealed bone edema of left hip bone and femoral head. There was no crystal in the synovial fluid. Cultures of synovial fluid yielded no bacteria and mycobacterium. Although we consulted orthopedic surgeons about operation, they hesitated because of the concern over infection with elevated C-reactive protein. On day 68, X-ray revealed marked destruction of her left femoral head and rapidly destructive coxarthrosis (RDC) was suspected. On day 113, the left total hip arthroplasty was performed. After the operation, she became to be able to walk by herself. Once RDC is developed, operation is the only treatment. Although differentiating RDC from septic arthritis is difficult, we should perform operation after fluid culture turned out to be negative. There are a few reports of RDC-like arthritis in RA patient, whose disease activity was tended to be high. We should closely monitor patients considering the possibility of RDC-like arthritis if the coxalgia develops rapidly in RA patient with high disease activity.

P2-121

A case of Chronic Expanding Hematoma with Loosening of Total Hip Arthroplasty in RA patient

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Conflict of interest: None

We treated a patient who developed hip swelling and pain due to a chronic expanding hematoma 12 years after revision total hip arthroplasty, in whom the acetabular implant had loosened and become dissociated. Should aseptic loosening occur, not only adverse reactions to metal debris but the underlying condition must also be included in the differential diagnosis and treatment to be carried out. Should it occur after total hip arthroplasty, it may be associated with bone destruction, in which case early revision surgery must be performed.

P2-122

One case of the chronic rheumatoid arthritis that enforced total hip arthroplasty in Mayo Conservative Hip Prosthesis

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Conflict of interest: None

Because we experienced a case of the chronic rheumatoid arthritis that enforced total hip arthroplasty, using Mayo Conservative Hip Prosthesis which is a bone preservation type stem, we report it. [CASE] She is a 45 years old woman. There was a rheumatic career from 34-year-old time and has received medication medical treatment in nearby doctors. There was the left coxalgia than about 40 years old. Her coxalgia gradually turned worse and became hard to walk, she received total hip arthroplasty. Because there was some possibility of revision in the future when we considered age, the femoral stem used Mayo Conservative Hip Prosthesis. One year five months passes after operation, she can walk without cane. And there is no loosening of prosthesis. [DISCUSSION] Mayo Conservative Hip Prosthesis is short stem which assumed the fixation in the proximal bone end by multipoint contact, the bone preservation by the minimum bone aggression, restraint of thigh pain a concept. There are many reports that this implant was good results using for coxarthrosis, but there are only a few reports that it was used for the chronic rheumatoid arthritis. We concluded that Mayo Conservative Hip Prosthesis is useful for total hip arthroplasty in patients with the young chronic rheumatoid arthritis.

P2-123

A case report of total knee arthroplasty in one stage for RA destructive knee joint with patellar fracture

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Conflict of interest: None

[Case] 69 year woman. RA onset at 60 years. Medical therapy is provided now in MTX6mg/w. Destruction and the swelling sharp pain of the right knee developed than about 68 years old, and surgery medical treatment was considered. After having fallen down, we were injured and were introduced the right patella fracture in a surgery purpose in our institution. After having performed patellar ostheosynthesis, we performed TKA at the same time. Postoperatively, it started than a CPM40 from the next day and ROM0 - 125 degrees at the discharge eight weeks later after operation [Discussion] The complication of treatment by operative procedure for the patella fracture after TKA and the incidence of reoperation are extremely high and are often reported when, if it is possible, they should avoid it. This patient was anticentromere antibodypositive and, with antiSSA antibody positive, was associated with CREST syndrome. After having performed patellar ostheosynthesis, surgery was under the medical treatment in one stage because what we avoided was thought to be desirable for performing TKA which added greater operative stress to the same location of the knee. It was thought to be useful to perform one-stage operations depending on a state and the primary disease of the preoperative knee.

P2-124

Recurrent Hemarthrosis after Total Knee Arthroplasty: A case report

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Conflict of interest: None

Recurrent hemarthrosis in the knee joint after total knee arthroplasty (TKA) is a rare complication of TKA. We report a case of recurrent hemarthrosis on a RA patient who was performed TKA in our hospital four years ago. A 67-year-old woman, who was affected with RA and well controlled, we performed TKA for rheumatoid arthritis of left knee. Four years later, she twisted her left knee and developed intra articular hematoma of knee. We tried conservative therapy, but hematoma was not controlled. Therefore we performed first operation, removed hematoma, changed the surfase and coagulated the capsle of the joint. One month after first surgery, hematoma recurrenced after initial walking. Hematoma did not recovered with conservative therapy and we performed second surgery. We coagulate articular surface again, and replaced thick polyethylene insert. At the 2-month follow up, the hematoma did not recurrence. We think that this complication was probably due to blood vessel fragility of RA patients.

P2-125

One-stage total knee arthroplasty (TKA) for rheumatoid arthritis (RA) patients. —A report of 3 cases—

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Conflict of interest: None

We performed one-stage bilateral TKA in 3 RA patients with malalignment or flexion contracture of knee joints and reported our results. 【Case 1】54 y-o male with difficulty in gait by pain. FTA was over 200° and ROM (ext./flex.) was -30°/90° on the right and -10°/100° on the left. Operation time was 5 hours and 5 minutes, hospital stay was 32 days. FTA was 175° on the right and 176° on the left, ROM was 0°/95° and 0°/100° respectively. 【Casa 2】65 y-o female with difficultly in gait. ROM (ext./flex.) was -20°/80° on the right, -20°/90° on the left. Operation time was 5 hours and 6 minutes, hospital stay was 22 days. ROM was 0°/100° and 0°/110° respectively. She could walk without cane on discharge. 【Case 3】53 y-o male unable to gait for 1 year. ROM was -30°/140° on the right, -20°/140° on the left. Operation time was 3 hours and 50 minutes, hospital stay was 43 days, ROM improved -15°/130° and -10°/130° respectively. He could walk with walker on discharge. 【Conclusion】One

stage bilateral TKA was performed in 3 RA patients. In RA patients without complications, one stage bilateral TKA may shorten hospital stay and enable early rehabilitation.

P2-126

Hemophagocytic lymphohistiocytosis secondary to systemic lupus erythematosus treated with the combination of immunoglobulin, steroid pulse and tacrolimus

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Conflict of interest: None

36-year-old Japanese female was admitted to our hospital presenting erythema, high fever, arthralgia and lymphadenopathy. Laboratory examination revealed leukopenia, thrombocytopenia, positive dsDNA antibody and the elevated levels of LDH and CRP. Bone marrow testing showed hemophagocytosis. We diagnosed her as hemophagocytic lymphohistiocytosis (HLH) secondary to systemic lupus erythematosus (SLE). SLE is a chronic autoimmune disease affecting multiple organ systems with protean manifestations. HLH is a potentially fatal condition and a rare complication of several autoimmune disorders, including SLE. Our case was successfully treated with the combination of intravenous immunoglobulin therapy, intravenous methyl predonisolone pulse therapy and oral tacrolimus.

P2-127

A case of CLE that developed AAHS

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Conflict of interest: None

A 17-year-old woman, with no previous serious illness, was admitted to our hospital due to continuous fever, lasting 2 weeks and arthralgia, She received NSAIDs for fever and arthralgia had a only partial response, presented with an erythematous rash involving the nose, nasolabial folds, and upper arm. Laboratory examination on admission revealed leukocytopenia and anemia, elevated ferritin (5087ng/ml) and asparate transaminase (AST: 542U/L, ALT:349U/L). Bone marrow punctute showed hemophogocytosis. After mPSL pulse therapy, oral PSL 60mg/d was started and her symptoms immediately relieved. We denied virus infections disease, and malignancy as existing cause of HPS from labolatory test and diagnostic imaging. Laboratory examination showed leukocytopenia, ANA positive, anti-SS-A/Ro antibody positive, arthralgia was not satisfy the classification of SLE criteria. She was diagnosed as CLE, from the results of skin biopsy. So she was diagnosed as autoimmune associate hemophagocytic syndrome (AAHS). Several cases was reported SLE-related HPS, although patients who developed HPS from CLE is rarely reported.

P2-128

Successful treatment of macrophage activating syndrome (MAS) and hemophagocytic lymphohistiocytosis (HLH) by intensive therapy including continuous hemodiafiltration with a cytokine-adsorbing hemofilter (AN69ST-CHDF, sepXirisTM) and plasma exchange in a pat

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Conflict of interest: None

We report a case of MAS and HLH in refractory SLE patient. To this hospitalization 5 months ago, he was treated with Glucocorticoid (GC) pulse therapy (mPSL 1g/day), rituximab (RTX) and intravenous cyclophosphamide (IVCY), since he merged serositis (pleuritis and pericarditis) and aseptic meningitis associated with SLE. On this admission, he was hospitalized in our department, so as to investigate hepatic disorder. After admission, he developed leukocytopenia (WBC 2,700/μl) and showed hyperferritinemia (41,068ng/ml). We suspected MAS/HLH, so we started GC pulse therapy. It was temporary improvement, however, to 22nd day, pancytopenia was worsen. Additionally, he became a multiple organ failure (MOF). We started 2nd course of GC pulse therapy. But, MOF progressed. He was admitted to the ICU. Hypercytokinemia (IFN-ɤ 7,600pg/ml, TNF-α 27.6pg/ml) and hyperferritinemia suggest MAS was in progress, so we started combination therapy of cyclosporine A, RTX and plasma exchange (PE). However, immunosuppressants and PE had a limited effectiveness. Hence, we started using AN69ST-CHDF in order to reduce cytokines level. It's all because intensive therapy, he recovered from MOF. AN69ST-CHDF could be an effective option for MAS/HLH in a patient with connective tissue disease including SLE.

P2-129

Systemic Lupus Erythematosus in Middle Aged Woman Presented Only with Pancytopenia Due to Hematopoietic Failure

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Conflict of interest: None

A 66 year old woman with no previous diagnosis of lupus erythematosus was referred to our hospital for the evaluation of severe anemia. Upper and lower gastrointestinal endoscopy were held with no proven active bleeding. Thrombocytopenia and leukocytopenia were also presented, leading to the examination of bone marrow. Bone marrow biopsy showed hypocellularity with significant increase in the amount of reticulin fibres. C4 and C3 level were low and antinuclear antibody was significantly high, with positive dsDNA antibody. Lupus erythematosus was suspected, but no other typical features such as malar rash, serositis, or glomerulonephritis were found. Pancytopenia due to hematopoietic failure rather than peripheral destruction in lupus erythematosus was rarely reported. Some reports have shown resolution of pancytopenia after treatment with steroids. We started prednisolone 40 mg daily, thereafter pancytopenia and low complement were normalized. Recognition of lupus erythematosus which presents only with pancytopenia caused by hematopoietic failure is important, since glucocorticoids alone is effective, and unnecessary bone marrow transplantation could be spared.

P2-130

Vascular involvements as the manifestation of systemic lupus erythematosus: 3 case reports

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Conflict of interest: None

We describe 3 cases of systemic lupus erythematosus (SLE) with several vascular involvements. **[Case reports]** Case 1: 53-year-old man had the development of abdominal angina together with limb gangrene, even though he had treated with prednisolone (PSL) and anticoagulant agent (ACA) since the diagnosis of SLE. Remission was achieved by additional immunosuppressant and antiplatelet drug. Case 2: 35-year-old woman had digital gangrene during treatment with PSL. Peripheral arterial occlusion on extremities and multiple coronary aneurysms were demonstrated. Digital symptom was improved after administration of immunosuppressant and ACA. Case 3: 31-year-old woman, who had treated with PSL, had the occurrence of intestinal perforation and toe gangrene ascribable to arterial occlusion. Symptoms were recovered by additional ACA and immunosuppressant. **Conclusion:** All patients indicated gangrene on fingers and/or toes as well as severe vascular lesions belonging to vital organ, suggesting that it may be necessary to perform systemic

survey of angiopathy related to organic disorder in the existence of gangrene on extremities.

P2-131

Vasculitic neuropathy as a key finding to diagnose systemic lupus erythematosus with secondary Sjogren syndrome : a case report

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Conflict of interest: None

(Background) Vasculitic neuropathy is observed in various rheumatic diseases as an accompanying symptom, and its incidence is diverse. It is sometimes observed in systemic lupus erythematosus (SLE) and Sjogren syndrome (SS) but rarely plays a key role in the diagnose of these diseases. (Case) A 28-year-old woman presented to our hospital because of numbness, pain and subsequent finger pulp nodules in her fingers. In addition, a blood test revealed coexistence of hypocomplementemia, which implied latency of immune-complex vasculitis. Finally, a diagnosis of SLE was made in accordance with the presence of anti-nuclear antibody and elevated ds-DNA-IgG level. A renal biopsy performed on a later date revealed asymptomatic lupus nephritis. Additional survey revealed the presence of anti-SSA antibody, keratoconjunctival disorder, and lip biopsy findings, which led to the diagnosis of SS. After the diagnoses were confirmed, immunosuppressive therapy was started with oral prednisolone (0.8 mg/[kg×day]), which improved both the neuropathy and finger pulp nodules. (Meaning of this case report) We report this case because it indicates diversity of symptoms caused by rheumatic diseases and the importance of physical examination in making the diagnosis.

P2-132

Superior mesenteric artery syndrome in systemic lupus erythematosus

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Conflict of interest: None

[Introduction] Superior mesenteric artery syndrome (SMAS) is characterized by compression of the third portion of the duodenum due to narrowing of the space between the superior mesenteric artery and aorta. We report 2 cases of women diagnosed with systemic lupus erythematosus (SLE) complicated by SMAS. [Case reports] A 25-year-old female with SLE reported postprandial abdominal pain, which changed with body position, associated with weight loss of 7 kg over the last 2 years. Computed tomographic (CT) showed duodenal obstruction with a cutoff in the third portion. The aorto-mesenteric artery angle (AMA) was 13° and the aorto-mesenteric distance (AMD) was 8 mm. These findings supported the diagnosis of SMAS. A 23-year-old female was diagnosed with SLE and given methylprednisolone and cyclophosphamide.1 month later, She reported periumbilical pain. Lupus enteritis was suspected, but symptom didn't respond to additional immunosuppressive therapy. CT showed an obstruction of the duodenum, the narrow AMA and the short AMD. She was diagnosed with SMAS. [Clinical significance] SMAS should be examined if SLE patients have postprandial or postural abdominal symptoms which don't correlate with disease activity and are not improved by immunosuppressive therapy.

P2-133

2 cases of systemic lupus erythematosus (SLE) patient with severe retinopathy

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Conflict of interest: None

Case1: A 27 year-old woman presented initially with headache and blurred vision 5 months prior to admission. Then, butterfly rash, erythema on her upper arms and visual loss developed, so she visited an ophthalmologist. Ophthalmological examination revealed multiple cotton wool spots and she was diagnosed with SLE, complicating retinal involvement and central nerve system. Treatment with glucocorticoids (GCS) was immediately initiated and has provided good response. Case2: A 33-year-old woman diagnosed as SLE 13 years ago. She was treated with 10 mg of GCS and kept remission. One month prior to admission, she visited an ophthalmologist because of loss of vision of her left eye. She had multiple cotton wool spots and leakage of contrast medium out of vessel of the retina. She was diagnosed retinopathy due to SLE and treated with methylprednisolone pulse therapy, which brought complete (partial?) remission of visual loss. [Conclusion] Ocular involvement has been reported as a manifestations of SLE, however severe retinopathy as a first presentation of SLE shown in case 1 is rare. Furthermore, case 2 showed retinal involvement as the only manifestation of relapse. The course of the cases indicate necessity to give close attention to retinal lesions as one of the manifestation of SLE.

P2-134

A case of lupus erythematosus with steroid-resistant massive ascites responding well to enalapril

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Conflict of interest: None

A 40-year-old female was admitted with one month history of progressive hypertension, and renal dysfunction. She was diagnosed as SLE with lupus nephritis 14 years ago. She had been treated successfully with prednisolone and tacrolimus. Laboratory test revealed hemolytic anemia, thrombocytopenia, normal levels of anti-ds-DNA antibody, negative for coombs test, and positive for schistocytes on peripheral smear. As her clinical features were compatible with thrombotic microangiopathy, Methylprednisolone (MP, 1 g for 3 days) and plasma exchange (PE) were started. Although her anemia and thrombocytopenia were gradually improved, she presented with anasarca, and a CT scan showed massive ascites and bilateral pleural effusions. In addition to pulse MP, intravenous cyclophosphamide (500 mg/4 weeks) was undertaken, however, her anasarca continued. The both fluids were transudates and extremely high serum levels of renin and aldosterone were detected. We initiated therapy with Enalapril, one of angiotensin converting enzyme inhibitors and increased the dosage gradually. Thereafter, her ascites and pleural effusions were decreased and finally disappeared. Renin-angiotensin-aldosterone system may be involved in the mechanism of steroid-refractory ascites in lupus erythematosus.

P2-135

Two cases of rheumatoid arthritis and systemic lupus erythematosus overlap syndrome with liver cirrhosis and portal hypertension who were successful treated by abatacept

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Conflict of interest: None

Rheumatoid arthritis-systemic lupus erythematosus overlap syndrome (RA/SLE-OL) complicated with liver cirrhosis (LC) and portal hypertension (PoH) is rarely recognized. We experienced 2 patients who were successfully treated by abatacept (ABT). [Patient 1] A 57-year-old woman. She was treated with methotrexate (MTX) for 17 years. She had photosensitivity, thrombocytopenia, positive antinuclear and anti-DNA antibodies and diagnosed as having SLE. After prednisolone (20 mg daily) was initiated, she developed LC and PoH. MTX was discontinued and ABT was initiated for RA. She had sustained clinical remission of RA/

SLE-OL, even though steroid dose was decreased. [Patient 2] A 55-year-old woman. She had been treated with MTX for 11 years and adalimumab (ADA) for 3 years. Because of esophageal varix rupture, she was diagnosed as having PoH. Liver biopsy suggested MTX-associated liver cirrhosis. ADA and MTX were discontinued and tocilizumab was started. One year later, she had pancytopenia, positive anti-DNA and anti LKM-1 antibodies, indicating RA/SLE-OL with autoimmune hepatitis. After ABT was initiated, pancytopenia was ameliorated along with RA moderate response. [Conclusion] Our cases suggested that ABT may be effective for extraarticular manifestations of RA/SLE-OL patients.

P2-136

A case of SLE patient with renal serositis

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Conflict of interest: None

[Case] 42 years old, woman [Chief complaint] General malaise [History of Present Illness] In 2003, She was diagnosed as SLE because of antinuclear antibody, anti-ds-DNA antibody, arthralgia and pericarditis. PSL 30 mg was started, and it led to remission. Then, PSL 6 mg was the maintenance dosage. In 2015, She was diagnosed as organized pneumonia. From that time on, there was an increase in anti-DNA antibody, and proteinuria tended to increase, suggesting an increase in the activity of SLE. [Progress after hospitalization] A low absorption region was recognized around the kidney by CT and renal serositis accompanying SLE was suspected. Renal biopsy could not be performed, but nephropathy was supposed to be lupus nephritis type III or IV from clinical findings. As a treatment, a steroid semi-pulse was administered, and PSL 35 mg/day was started. After that we combined with MMF and plasma exchange. This treatment led to remmision. [Discussion] In SLE patients, pleurisy and pericarditis are common complications, but at this time we experienced a case with renal serositis. With the treatment of SLE, it showed an improvement tendency, and for this reason, it was considered to be caused by SLE. At this time, a report on renal serositis (accompanying SLE) has been made with some literature consideration.

P2-137

Successful treatment of protein losing enteropathy with combination of Mycophenolate mofetil and Tacrolimus in a patient with SLE

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Conflict of interest: None

We report the case of a 32-year-old woman who was diagnosed as Systemic Lupus Erythematosus (SLE) at our hospital in 20XX-5. She was treated with Prednisolone (PSL) and Cyclosporine A (CsA). Laboratory data showed Alb <3.0g/dl, CH50 <15.0U/ml from 20XX-3, CsA was changed to Tacrolimus (TAC), and treatment with PSL 8mg/day and TAC 3mg/day was continued. Nevertheless, Laboratory data showed Alb 2.0g/dl. ^{99m}Tc-HAS-D showed albumin loss from ileum to ascending colon, this finding led to a diagnosis of protein losing enteropathy (PLE). Treatment was increased to PSL 50mg/day and Mycophenolate mofetil (MMF) 2g/day in addition to TAC. After three month, her laboratory data improved Alb 3.8g/dl and CH50 20.7U/ml. There is no randomized controlled trials on treatment because PLE associated with SLE is rare condition. Patient mainly have been treated by PSL and used in combination of immunosuppressive therapy. Especially, the effectiveness of AZA has been reported, but patients of SLE with sequentially presented PLE need for more potent immunosuppressive therapy. This patient showed good response to combination therapy with MMF and TAC. The combination therapy with MMF and TAC was considered to be one of effective treatment options for a refractory case of PLE associated with SLE.

P2-138

A case of necrotizing histiocytic lymphadenitis with SLE mimicking malignant lymphoma

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Conflict of interest: None

A 41 year old woman was admitted to our hospital because of fever and right cervical lymphadenopathy. She had been suspected of having rheumatological disease because of Raynaud's phenomenon and polyarthritis for 3 months. High fever has been appeared for 1 month before admission. On admission, physical examination showed multiple lymphadenopathy in right cervical region without tenderness and FDG-PET showed intense uptake in same region. She was diagnosed of SLE because of polyarthritis, leukocytopenia, positive of antinuclear antibody and anti-Sm antibody. Biopsy of right cervical lymph node showed no malignancy and necrotizing histiocytic lymphadenitis. Though, she was also suspected to having hemophagocytic syndrome because of persistent high fever, hyperferritinemia, mPSL pulse therapy improved her clinical course.

P2-139

Rectal ulcer in systemic lupus erythematosus (SLE) : Is it activity of the disease?---A case report and literature review

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Conflict of interest: None

A 69-year-old woman admitted to our hospital with bloody stool. She was diagnosed as mixed connective tissue disease and treated by prednisolone (PSL) at 43 of age. When she was 57 y.o., she experienced rectal ulcer which was successfully treated by moderate-dose PSL. However, intravenous cyclophosphamide were needed because her rectal ulcer repeated recurrence. When she was 63 y.o., mizoribine and tacrolimus were started because she developed lupus nephritis. When she was 68 y.o., abdominal pain and diarrhea occurred without SLE activity. Images of computed tomography indicated phlebosclerotic colitis. She improved by fasting and antibiotics. After a year, she was hospitalized for bloody stool without abdominal pain nor SLE activity, which partially improved by fasting and antibiotics. However, mild fever and slightly positive CRP continued. Colonoscopy revealed rectal ulcer with severe stricture. We determined surgical resection to avoid rectal perforation, resulting in improvement of her condition without strengthening immunosuppressive treatment. Rectal ulcer is rare complication in SLE, which sometimes occurs without SLE activity. Because rectal perforation results in extremely poor prognosis, careful choice of treatment and appropriate surgical intervention are needed.

P2-140

The efficacy of hydroxychloroquine with treatment of active lupus skin lesions

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Conflict of interest: None

【Object】8 patients, that skin lesions affected by cutaneous lupus erythematous (CLE) and systemic lupus erythematous (SLE), were treated by hydroxychloroquine (HCQ). We evaluated that efficacy against the skin manifestations. 【Method】8 patients with SLE or CLE having active cutaneous symptoms in our hospital were administrated HCQ after ophthalmological screenings for retinopathy. We analyzed the changes of skin lesions before and after HCQ. 【Result】1 male patient and 7 female matients were included. Mean age was 48.3 ± 5.7. Average dose of pred-

nisolone was 10.7 ± 0.9 mg, conbination immnunosupressive therapies were tacrolimus (5cases), mizoribine (2cases), mycophenolate mofetil (1case) and azathioprine (1case). One patient having extensive alopecia with discoid lupus erythematous showed no response, so HCQ was discontinued. Others were acute malar rash (5cases), discoid lupus erythematous (3cases), Lupus profundus (2cases), chilblain lupus (1case), Bullous lupus (1case), severe skin ulcer (1case), showed response for HCQ obviously. 1 patient developed side effect, mainly represented diarrhea, so led to reduce dosage, but no other adverse problems have been found. 【Conclusion】Although our cases are few, HCQ is efficacy to active and various skin lesion with SLE and used safely.

P2-141

A case of lupus profundus requiring differential diagnosis from subcutaneous panniculitis-like T cell lymphoma with painless nodules on the cheek

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Conflict of interest: None

A 37-year old woman had been aware of the subcutaneous nodule of the left cheek for a year and she visited our hospital. US finding showed the swelling of subcutaneous tissue and increased echo level of fat tissue on the size of thumb, and MRI suggested neoplastic lesion. Whole body CT scanning indicated subcutaneous nodules in both upper buttocks and upper extremities similar to the cheek portion and the swelling of axillary lymphnodes. Nodules biopsy and flow cytometric analysis showed that subcutaneous panniculitis-like T cell lymphoma should be denied. She was admitted to our department to examine systemic muscle and joint pain in the morning for 3 months. Laboratory examinations showed as follows;WBC 5100/μl, CRP 0.05mg/dl, ANA x80, anti ds-DNA antibody 19 IU/l, sIL-2R 803 U/ml. Pathological findings revealed that confirmed the deposition of immunoglobulin in the plasma cells of the subcutaneous fat tissue. Finally, these results shows lupus profundus. Treatment with PSL 20mg/day had started. Nodular lesions and joints pain disappeared. Appearance of subcutaneous nodules at unique sites may delay diagnosis of lupus erythematosus, which is resulted in the dented skin and scar. Therefore, early diagnosis and treatment are required from the cosmetic aspect in female patient.

P2-142

A case of systemic lupus erythematosus [SLE] complicated with Sacroiliitis [SI]

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Conflict of interest: None

[CLINICAL MEANING] SI is very rare in SLE patients. I report the case of SI in a SLE patients treated with TNFαinhibitor [TNFi]. [CASE] 46-years old woman was introduced for the treatment. She had butterfly rush and abdominal pain and was diagnosed SLE and treated by steroids for 10 years. She also had progressive low back pain for 5 years. Physical exam showed 157cm and 78kg. She had arthritis of both wrist, and knee, and severe low back pain. Manual “Newton test” was positive. Laboratory exam showed that CRP was 1.07mg/dl. HLA B-27 and blood culture was negative, and hip MRI was normal. Bone scintigraphy showed SI. Those suggested that she had a SI during non-active SLE. For very bad QOL, she was treated with Infliximab effectively She had infusion reaction in third time, and switched to Adalimumab and relapsed. She had been remission with Certolizumab Pegol [CZP]. [DISCUSSION] This is the case that had long-term SI during non-active SLE by manual exam and bone scintigraphy, and treated successfully with CZP. CZP is structurally concentrated on inflammatory areas. The reports were seen CZP for Axial spondyloarthritis in abroad. I need to watch her carefully in case SLE is relapsed because of TNFi.

P2-143

A case of arytenoid chondritis as a manifestation of relapsing polychondritis in a paitient with systemic lupus erythematosus

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Conflict of interest: None

A 50-year old female who had been detected ANA and Anti-Ro antibody visited our hospital complaining 2 weeks history of lymphadenopathy and fever of 39℃. Physical examination revealed oral ulcer, malar rash, and poly-lymphadenopathy in the bilateral neck, axillae, and subclavian. Inflammation of the cartilage of nose and auricles were also detected. In combined with the laboratory results of lyphopenia and anti-Sm antibody positivity, she was diagnosed as having a relapsing polychondritis (RP) related to systemic lupus erythematosus. On the second day of the admission, she also reported hoarseness. Although contrast computed tomography was negative for cricoiditis nor bronchial stents, otorhinolaryngological examination demonstrated arytenoid chondritis. She was treated with oral prednisone at a dose of 25mg every other day, and all of the symptoms were alleviated. Additional otorhinolaryngological examination showed the complete recovery of the arytenoids chondritis. RP is an autoimmune disorder with chondritis as a prominent clinical feature that has been found to coexist in some patients with systemic lupus erythematosus. Air way manifestation of RP is a one of a critical symptoms, therefore, early detection and treatment of arytenoid chondritis are required.

P2-144

A case of systemic lupus erythematosus with drug-induced hypersensitivity syndrome

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Conflict of interest: None

22 year-old female was admitted for SLE. She was found to have fever, malar erythema, and arthralgia for 3 months prior to admission. Treatment was initiated with 20 mg/day of PSL on day 5, and subsequently hydroxychloroquine (HQ) was started on day 11. Significant improvement was achieved, though painful cervical lymphadenopathy appeared on day 14. Elevated liver enzymes and eosinophilia were found on day 19. She was febrile with an exanthem of the trunk, arms and legs, that appeared on day 23. HQ and sulfamethoxazole/trimethoprim (ST) were discontinued, then methylprednisolone pulse therapy was started. Subsequentry PSL was increased to 40 mg/day. Skin biopsy revealed spongiosis in the superficial dermis, which was consistent with the finding of drug eruption. The clinical and laboratory findings satisfied the criteria for drug-induced hypersensitivity syndrome. The skin lesions disappeared after treatment with 40 mg/day of PSL for 2 weeks. We could not determine the titers of IgG antibodies to HHV 6 because of high levels of autoantibodies. Because DLST for HQ and ST were negative, the causative drugs were not identified. Because of the difficulty in distinguishing cutaneous lupus from a drug eruption, we present this case with some discussion and literature review.

P2-145

The study of pregnancy with systemic lupus erythematosus flare : report of 8 cases

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Conflict of interest: None

【Object】Because SLE is most frequent among young women, cases

of pregnancy with SLE are not rare. However, since few reports have been reviewed on cases of SLE flare during pregnancy in Japan, we report cases experienced at our hospital. 【Methods】From March 2010 to September 2016, there were 39 cases of pregnancy with SLE delivered at our hospital. The 8 cases of SLE flare during pregnancy are investigated about clinical course, treatment, and outcomes. 【Results】In 8 cases, treatment was strengthened primarily due to joint pain, thrombocytopenia, proteinuria, hypertension. 3 patients who had proteinuria and hypertension were difficult to differentiate preeclampsia from SLE flare. Among 39 cases of pregnancy with SLE, there were 3 cases newly developed / diagnosed during pregnancy, 2 cases were severe with hypertension and proteinuria, one of which was the result of neonatal death. 【Conclusions】 Because preeclampsia and SLE flare often coexist, when it is difficult to distinguish between them, the patient should be regarded as having SLE flare, and should be treated aggressively. In addition, it is reported that new onset case of SLE during pregnancy is an independent risk factor of obstetric complications, therefore we need to manage carefully.

P2-146

KRAS gene mutation in a patient of systemic lupus erythematosus with persistent monocytosis

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Conflict of interest: None

The somatic mutations of genes involved in RAS/MAPK signaling pathway are implicated in various malignant conditions, whereas their germline mutations cause developmental disorders, termed RASopathies. Recently, Lupus-like autoimmune conditions have been reported in RASopathies and patients with somatic mutations of RASs in hematopoietic cells. **Case**; 60 years old, female patient was diagnosed as SLE based on polyarthritis, thrombocytopenia, and the presence of anti-nuclear antibodies. While her symptoms, laboratory abnormalities were resolved by glucocorticoid and tacrolimus, the patient later developed encephalomyelitis at 67 years old, which was refractory to intensive immunosuppressive therapies. On the other hand, the patient presented persistent monocytosis from 65 years old. Repeated examination for chronic myelomonocytic leukemia (CMML) did not show any evidence of malignancy. Genetic analysis revealed *KRAS* gene mutation (c.35G>A;p.G12D) consistent with a previously reported case of RAS-associated autoimmune lymphoproliferative syndrome (RALD). **Discussion**; Although it is still uncertain for discriminating from CMML, we report a case of elderly-onset RALD. In addition, the case indicates a novel pathogenetic role of RAS/MAPK pathway in autoimmune diseases.

P2-147

A case of systemic lupus erythematosus with pseudo-Pelger-Huët anomaly in the peripheral blood

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Conflict of interest: None

The patient is a 62-year-old woman with a history of ovarian sarcoma who had been in remission for 8 years. She was treated with carboplatin, paclitaxel and pazopanib, and also underwent hysterectomy and bilateral oophorectomy. She presented with 2 months history of fever, general malaise and alopecia. She was referred to our hospital because of pancytopenia and cervical lymphadenopathy disclosed by PET scan. Pseudo-Pelger-Huët anomaly (pseudo-PHA) was seen in the peripheral blood. Bone marrow revealed small amount of pseudo-PHA in myeloid lineage with no sign of hematological malignancies. She was diagnosed as SLE based on pancytopenia, proteinuria, ANA and specific antibodies. Therapy with intravenous methylprednisolone was initiated at a dose of 60 mg/day. On day 3 of treatment, pseudo-PHA disappeared from peripheral blood. After steroid pulse and IVIg, her symptoms markedly improved. During the subsequent 6 months of follow-up, she has been in remission and pseudo-PHA hasn't re-appeared. Although a few cases with pseudo-PHA due to MMF in SLE have been reported, pseudo-PHA related to SLE itself is rarely seen. We report the case with review of the literatures.

P2-148

Seronegative full house nephropathy: a 2-case reports and literature review

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Conflict of interest: None

We report 2 cases of seronegative (ANF-negative) full house nephropathy and review literature. <Case 1> A 22-year-old female with a 2-year history of proteinuria (2g/gCr) underwent renal biopsy. She was seronegative, and had no extra-renal symptoms such as rash, arthralgia or serositis. Immunofluorescence (IF) microscopy revealed full house pattern (IgG/IgA/IgM/C3/C1q-positive) and electron microscopy (EM) showed deposits in mesangial and subepithelial areas. <Case 2> A 35-year-old female with a 20-year history of proteinuria/hematuria underwent renal biopsy because of increase in proteinuria (3 g/gCr). The patient had received renal biopsy 3 years ago, which showed "minor glomerular abnormality". She was seronegative, and had no extra-renal manifestations. IF showed full house pattern with mesangial, endothelial, and subepithelial deposits on EM. <Discussion> While these histological findings were strongly suggestive of lupus nephritis (ISN/RPS Class II), neither of them fulfilled SLE criteria of ACR or SLICC. Prednisolone (0.5-0.6 mg/kg/day) failed to make them enter remission within a month. Differential diagnosis is necessary in our cases to exclude other glomerulopathies, and careful monitoring to detect appearance of extra-renal symptoms and seroconversion will be needed.

P2-149

Monocyte CD64 as a useful biomarker for predicting recurrence of systemic lupus erythematosus: a case report

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Conflict of interest: None

Background: The expression of CD64 on monocytes (mCD64) is upregulated by macrophage colony-stimulating factor (M-CSF) and interferon (IFN)-α, key cytokines in systemic lupus erythematosus (SLE). We previously reported the association between mCD64 and the disease activity of SLE. Case: A 28-year-old woman with a 20 year history of lupus nephritis (WHO class III) presented with fever and erythema in August 2016. The levels of complement and anti-dsDNA antibody were normal, and other SLE-like symptoms were not observed. Viral infection was suspected, but her erythema was getting worse. Skin biopsy was performed and the results indicated SLE. PSL dosage was increased from 2 to 20 mg/day. Hypocomplementemia appeared 2 weeks later. Baseline expression of mCD64 was about 20,000 molecules/cell. The mCD64 expression increased to 31,849 molecules/cell 2 weeks before the appearance of erythema and to 43,242 molecules/cell at the appearance of erythema. It decreased after the treatment. Discussion: Relapses of SLE are frequent. There are no useful markers for predicting the SLE flare. It is reported that a rise in M-CSF is an earlier predictor than conventional markers and symptoms for lupus nephritis flare. This case suggests that mCD64 may be a marker for predicting SLE relapse.

P2-150

A case of lupus nephritis associated with mantle cell lymphoma

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Conflict of interest: None

A 74-year-old Japanese male was admitted to our hospital presenting general fatigue, rapid progressive renal dysfunction with massive proteinuria. Laboratory examination showed anemia, thrombocytopenia, elevated peripheral mantle cell counts, elevated serum creatinine level, massive proteinuria, positive anti-ds-DNA IgG antibody and serum and urine monoclonal gammopathy (IgMλ). Renal biopsy revealed the coexistence of lupus nephritis class IV-S (A) and the direct invasion of mantle cell lymphoma cells in the kidney. Both LN and MCL were improved by the combination therapy of steroid, rituximab and bortezomib.

P2-151

The coexistence of systemic lupus erythematosus and myasthenia gravis

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Conflict of interest: None

【Case】A 45-year-old woman with medical history of generalized myasthenia gravis (MG) was admitted to our hospital with painful paresthesias of the feet and hand. She was diagnosed systemic lupus erythematosus (SLE) on the basis of 1997 ACR classification criteria and 2012 SLICC classification criteria [arthritis, mononeuritis multiplex, hypolymphemia, antinuclear antibody and antiphospholipid antibodies (aPL) seropositivity and hypocomplementemia]. Mucocutaneous symptoms or abnormal urinalysis were not observed. After treated with oral prednisolone, the nerve conduction velocity was improved. 【Discussion】MG is one of the NP-SLE and the coexistence of MG and SLE is rarely reported. Patients with SLE and MG are reported as older, have lower incidence of mucocutaneous and renal manifestations, and higher frequency of anticardiolipin antibodies and lupus anticoagulant. We report our experience of 5 patients with both diseases with focus on their clinical characteristics. We then review the literature on patients with SLE and MG, and the high prevalance of other autoimmune diseases in patients with MG.

P2-152

A case of SLE complicated by miliary tuberculosis resulting in severe pancytopenia

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Conflict of interest: None

When we see pancytopenia in systemic lupus erythematosus (SLE) patients, increased disease activity, drugs, cytomegalovirus (CMV) reactivation, and hemophagocytic syndrome (HPS) are usually considered as differential diagnosis. Here we report a case of SLE who showed pancytopenia refractory to usual treatments, and was later found out to be complicated by miliary tuberculosis (TB). A 62-year-old woman, who was diagnosed as SLE 16 years ago, was admitted to our hospital because of painful oral ulcer. Two months before admission, the diagnosis of class IV lupus nephritis was made by renal biopsy, and immunosuppressive treatment with prednisolone, mycophenolate mofetil, and tacrolimus had been started. Although the ulcer responded well to CMV treatments, pancytopenia developed within the next few weeks, which did not improve with discontinuation of suspected drugs. Bone marrow examination was consistent with mild HPS, but additional immunosuppressive treatment did not work either. Next month, she had sustained fever and was diagnosed as miliary TB by sputum and blood culture. CBC returned normal 4 months after the start of multiple-drug TB treatment. We must not forget miliary TB when SLE patient shows unexpected clinical course.

P2-153

A case of Systemic Lupus Erythematosus complicated with autoimmune neutropenia and pulmonary lesions resembling multicentric Castleman's disease

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Conflict of interest: None

A 78-year-old woman was referred to our hospital due to leukopenia. Her leukocyte and neutrophil counts were very low (WBC 1500/μL, neutrophil 375/μL respectively), and bone marrow examination showed no abnormalities. Laboratory findings revealed positive for anti-nuclear antibody, anti-double stranded DNA antibody, anti-CLβ2GPI antibody and anti-neutrophil antibody, so she met the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus (SLE). She was diagnosed as SLE complicated by autoimmune neutropenia (AIN). Computed tomography scan of the chest showed ground-glass opacity and multiple nodular and cystic lesions in the bottom of both lungs. Biopsy specimens from right lower lobe obtained by video-assisted thoracoscopy revealed remarkable infiltration of mature plasma cells with polyclonal characteristics. The histological findings were diagnosed as multicentric Castleman's disease (MCD). It has been reported to complicate with MCD-like lymph node lesions in SLE. On the other hand, MCD is known to express the various autoantibodies, and to complicate with conditions resembling autoimmune diseases. Because SLE complicated with AIN is a rare case, there is a possibility that MCD was associated with the development of SLE.

P2-154

Antiretroviral therapy improved HIV-associated encephalopathy which has autoantibodies

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Conflict of interest: None

A 35 year old man. A leg dysesthesia was admitted 6 months ago, more than 39 ℃ of fever and shingles were repeated. Ablood test, the nerve conduction velocity, and head MRI were done. An abnormality wasn't admitted in MRI. On the other hand, an anti SS-A/B antibody and an anti Sm antibody were positive and nerve conduction disorder of a musculus gastrocnemius was admitted. Syphilis and an HIV antibody were seropositive, and peripheral blood CD4+ cells were 86/mm^3. It was diagnosed as the AIDS with HIV encephalopathy because cell numbers and protein in fluid were also increased. In SLE, he also could be diagnosed as SLE and fullfilled with SLICC and ACR classification. Antiretroviral therapy was started at 27 days later of hospitalization. HIV-RNA copies were not detected after HAAART therapy. In SLE, antiretroviral therapy also improved synovitis and decreased complement value and increased complement value. Disease activity also decreased. The frequency of rheumatological syndromes in human immunodeficiency virus (HIV) patients varies from less than 1 to 60% with the positive of autoantibodies. I suggest the HIV infection was important as a differential diagnosis in a rheumatic disease.

P2-155

Refractory liver dysfunction with systemic lupus erythematosus dramatically improved after the treatment with chelating agents of Wilson's disease

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Conflict of interest: None

A 29-year-old male admitted to our hospital because of high fever, arthralgia and oral ulcers. Laboratory investigation showed elevated

transaminase levels, proteinuria, positive anti-double strand DNA (dsDNA), and hemolytic anemia. He was diagnosed as systemic lupus erythematosus (SLE) and was treated with pulse intravenous methylprednisolone followed by oral steroid therapy. Then, arthritis, hemolytic anemia, and proteinuria were improved. However, he developed neuropsychiatric symptoms and hemophagocytic syndrome. He was additionally treated with pulse intravenous cyclophosphamide. Most of the symptoms were improved. However, high titers of transaminases (400-500IU/L) and dysphagia were not improved. We ruled out drug-induced hepatitis, autoimmune hepatitis, and viral hepatitis. Laboratory findings showed low serum ceruloplasmin and low serum copper levels along with increased 24-hour urinary copper. Liver biopsy detected the copper in hepatocytes. We diagnosed him as Wilson's disease (WD) and started to treat with chelating agents. Two month later, the liver enzymes go back to a normal level and neurologic disorder was also dramatically improved. We report a rare case of SLE with varied clinical manifestations caused by coexisting WD.

P2-156

Two cases of systemic lupus erythematosus (SLE) complicated with primary central nervous system lymphoma (PCNSL)

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Conflict of interest: None

Purpose:To understand a feature of SLE complicated with PCNSL under treated with immunosuppressants. Case1:26-years old female. she was diagnosed as SLE at 20 and treated with PSL. At 23 azathioprine (AZA) was added. 2 months ago, she admitted for headache and sensory disorder. Brain MRI showed intracranial mass. Biopsy showed EBV positive B-cell lymphoma (BCL). She was treated with MTX and radiation. She has no recurrence until now. Case2:35-years old female. She was diagnosed as SLE at 21 and treated with PSL. At 27, cyclosporine (CyA) was added. CyA was changed to tacrolimus (TAC) for insufficient effect at 33. She developed lupus nephritis type III at 34 and treated with PSL, TAC and MMF. 2 months ago, parinaud sign appeared and brain MRI showed intracranial mass extended for middle brain to thalamus. Biopsy showed EBER positive diffuse large BCL (DLBCL). Size of mass didn`t change despite discontinuation of TAC and MMF. She is treated with MTX now. Disscussion: Some report showed PCNSL are occurred in 0.3% of kidney transplant recipients treated with AZA, TAC and MMF. Most of these cases are related to EBV positive DLBCL. Our cases have some similarities to transplant cases. Conc: We should consider the occurrence of PCNSL, when treat SLE with combination immunosuppressants.

P2-157

Clinical evaluation in patients with limited cutaneous systemic sclerosis (lc SSc) ~retrospective analysis of 30 cases for 20 years ~

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Conflict of interest: None

[Objectives] To evaluate complications and the prognosis in patients with lc SSc. [Patients] 30 patients (29 females, mean 59.0 years old, mean duration after appearing Raynaud' phenomenon; 10.8 years), Sjogren's syndrome; 22, Primary biliary cirrhosis (PBC); 8, Pulmonary arterial hypertension (PAH); 3, Interstitial pneumonia diagnosed by chest X-ray film; 1. [Methods] Organ involvements, survival rate and the cause of death were surveyed by medical records for 20 years. [Results] 1) Eight patients were transferred to other hospitals and unknown in details. 2) Two of three patients with PAH were dead and the other was transferred to the other hospital. Two patients were newly developed to PAH and one patient was dead of heart failure. 3) One of eight patients with PBC was dead of liver failure and three patients were transferred to other hospitals. One patient was newly developed to liver cirrhosis and dead finally. Eight patients were dead (mean 71.1 years old); 3PAH (mean 63.0 years old), 2 liver failure (mean 79.5 years old), 1 intrahepatic cholangioma (73 years old), 1 esophageal cancer (65 years old),1 cerebral infarction (83 years old). [Conclusion] PAH and PBC are frequently overlapped in patients with lc SSc. It was reconfirmed that PAH was a serious complication.

P2-158

Clinical features of systemic sclerosis with pulmonary arterial hypertension (SSc-PAH)

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Conflict of interest: None

[Objective] To investigate the clinical features of SSc-PAH. [Methods] We studied patients with SSc-PAH who visited our clinic between January and April 2014. Clinical and laboratory data were collected from their medical records. [Results] A total of 24 patients with 21 females (87.5%) and 3 males (12.5%) were enrolled. Among these patients, 15 patients (62.5%) had diffuse cutaneous type and 9 patients (37.5%) had limited cutaneous type. There were no significant autoantibodies associated with SSc-PAH. Digital ulcer was higher in SSc-PAH patients (P=0.002). All the patients classified by WHO functional class (WHO-FC): 2 patients were class II, 18 patients were class III and 2 patients were class IV. Twenty-three patients were treated with beraprost, 4 were treated with endothelin 1 receptor antagonists (ERA), 6 were treated with phosphodiesterase type 5 (PDE5) inhibitors and 12 were treated with both ERA and PDE5 inhibitors. Mean pulmonary artery pressure, right ventricular systolic pressure, NT-pro BNP and WHO-FC were significantly improved after these treatments. [Conclusion] Patients with SSc-PAH in our clinic might have been diagnosed and treated in earlier stages of the disease. Our treatment could improve clinical symptoms, echocardiographic and hemodynamic variables.

P2-159

Frequency of autoimmune diseases associated with limited cutaneous systemic scleroderma with anti-centromere antibody

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Conflict of interest: None

[Objectives] Autoimmune diseases are often associated with each other. However, diseases likely to be complicated by each autoimmune disease are different. Our goal was to study the prevalence of autoimmune diseases associated with anti-centromere antibody (centromere Ab) positive lcSSc. [METHODS] 65 centromere Ab positive lcSSc patients who had hospitalized in our outpatient clinic from 2012 to 2016 were enrolled. We assess the correlation between the clinical characteristics and data. [RESULTS] Female were 60 (92.3%). Mean age was 68.0 years old. The duration between onset of Raynaud phenomenon and first visit was 10.7 year. Comorbidities were as follows; Sjogren syndrome (SjS) 56.9%, primary biliary cirrhosis (PBC) 46.1%, Hashimoto's disease 30.7%, CKD 30.7%, pulmonary hypertension 30.7%, and interstitial pneumonia 27.6%. Incidence of antibodys were as follows; anti-SS-A Ab 46.1%, anti-SS-B Ab 7.6%, anti-TPO Ab 16.9%, anti-TG Ab 20.0%, M2 Ab 30.7%, anti-dsDNA Ab 10.7%, anti-ssDNA Ab 7.6%, anti-Sm Ab 0.0%, RF 20.0%, CCPAb was 1.5%, anti-RNPAb 6.18%, MPO-ANCA 3.0%, PR3-ANCA 0.0%, GBM Ab 0.0%, ARS Ab 0.0%, Scl70 Ab 0.0% and RNAP III 0.0%. [CONCLUSIONS] Centromere Ab patients could be likely to have present overlapping syndrome with lcSSc, SjS, PBC, and

Hashimoto's disease.

P2-160

Consideration of rheumatoid overlap syndrome in conjunction with calcinosis

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Conflict of interest: None

Rheumatoid overlap syndrome is not a unique disease but calcinosis with the disease is under adequate clarification. A 74-year-old Japanese woman visited us due to both neck pain and numbness in upper extremities, whose past history was overlapped with rheumatoid arthritis, Sjogren's syndrome, and systemic sclerosis. Image examination has revealed that there was not only a multiple tiny calcification in her soft tissues of chest wall, but also a huge mass-like lesion at the atlanto-axial vertebrate joint region. Local pain and tenderness in the neck and shoulders and the associated weakness and stiffness in her upper limbs gradually exacerbated, and the mass was resected. The mass was with a milk-like liquid containing a chalky semifluid substance and powder. Above different two types of calcification were both dystrophic. It was noted that both tiny and huge calcification resided within the same patient with rheumatoid overlap syndrome. The consequences, such as calcification, glycation, oxidation, and amyloid change, being suggestive of due to the inflammatory disease activity, are should be discussed in relation to rheumatoid overlap syndrome.

P2-161

A case of systemic sclerosis (SSc) with IP and PH. Capillaroscopy is of use in the diagnosis of SSc

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Conflict of interest: None

An 88 years old female was followed up on finger swelling and slight interstitial pneumonia (IP) from 2008. In January 2014, she admitted to our hospital because IP exacerbated, but detailed examination did not lead to a diagnosis of underlying disease. It showed IP, finger swelling, antinuclear antibody (speckled pattern) positive, and aspergillus infection. She was followed up by at-home-oxygen introduction without immunosuppressive therapy. In September 2016, anasarca and dyspnea developed with a common cold and she was admitted to our hospital. SpO2 was 93% with 2L nasal cannula, chest CT showed cardiac dilatation, and IP worsened slowly. Echocardiography showed EF 78%, TRPG 67.5 mmHg, ePASP 77.5 mmHg. Capillaroscopy revealed the abnormality of the capillary and leaded to definitive diagnosis of systemic sclerosis (SSC). We distinguished the cause of pulmonary hypertension (PH), and diagnosed as acute heart failure with SSC-PH. After starting diuretic, TRPG improved to 42.9 mmHg. We administered tadalafil and ambrisentan, and TRPG improved to 27.4 mmHg. The periodical screening of PH is important when SSC is doubted. And, early capillaroscopy inspection helps the early diagnosis. We report it including consideration from literatures.

P2-162

Systemic sclerosis (SSc) with anti-centriole antibody positive, effective to immunosuppressive therapy

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Conflict of interest: None

A 62 years-old woman presented with two-years exertional dyspnea. It has got deteriorated for a year, an electro-cardiogram showed right heart load findings. In echocardiography, tricuspid regurgitation pressure gradient (TRPG) elevated to 90 mmHg, and mean pulmonary arterial pressure (mPAP) and pulmonary capillary wedge pressure was 54 mmHg and 8 mmHg respectively in a cardiac catheter test. She was diagnosed with pulmonary arterial hypertension and antinuclear antibody was positive, it was anti-centriole pattern. Then she was admitted to our hospital. First, she was treated by oral vasodilators, but they were not much effective because of side effects. It was expected that immunosuppressive therapy was effective due to Nitric monoxide load test positive and anti-centriole antibody positive. Moderate dose of prednisolones and cyclophosphamide had improved her mPAP to 33 mmHg two months later. Generally immunosuppressive therapy is not much effective for SSc-PAH. For SSc-PAH with anti-centriole antibody, immunosuppressive therapy is possible to be effective. If it is proved, the measurement of anti-centriole antibody will be significant in a use of immunosuppressive therapy.

P2-163

A Case of Systemic sclerosis with Chronic thromboembolic pulmonary hypertension developed from Recurrent pulmonary thromboembolism

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Conflict of interest: None

A 63-year-old woman with progressive dyspnea and Raynaud's phenomenon. We found bilateral pulmonary artery thrombus and pulmonary hypertension (PH). Tricuspid regurgitation pressure gradient was elevated to 82mmHg by echocardiography. Also, she was diagnosed as Systemic sclerosis (SSc) with skin thickening of fingers, Pitting scars, and anti-centromere Ab positive. As a result of right heart catheterization after anticoagulation therapy, it was diagnosed as pulmonary thromboembolism (PTE) based on the data of 20mmHg of mean pulmonary artery pressure (mPAP), so we introduced warfarin. There was no relapse and we stopped warfarin at patient'srequest 2years later, but 2months later PTE relapsed and mPAP was elevated to 25mmHg, so we continued warfarin and introduced beraprost.7months later mPAP is elevated to 36mmHg. Pulmonary blood flow scintigram and pulmonary angiogram showed that combined disease with Chronic thromboembolic pulmonary hypertension (CTEPH) and Pulmonary arterial hypertension (PAH) was considered, and so we introduced tadalafil40mg. MPAP decreased to 20mmHg 1year later. PH associated with SSc develops complex cardiopulmonary lesions in which multiple groups are mixed, but the merger of CTEPH is a rare. We report on the cases of SSc that developed from recurrent PTE to CTEPH with PAH.

P2-164

A case of Anti-RNA polymerase III antibody positive diffuse cutaneous systemic sclerosis with breast cancer developed scleroderma renal crisis and 7 years later presented pulmonary arterial hypertension

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Conflict of interest: None

A case of systemic sclerosis (SSc) in a 59-years-old woman who complain dyspnea. She was diagnosed as SSc by thickening of the skin on the limbs, face and trunk in 200X-8. She had no visceral involvement. Antinuclear antibodies was elevated (×640, speckled type), anti centromere antibody and anti topoisomerase I antibody were negative. She got scleroderma renal crisis (SRC) after 7 months, treated with ACE-I and ARB. In same time, She diagnosed as left breast cancer, had total masectomy and tamoxifen were administered. In 200X, she presented shortness of breath and edema. She didn't have any interstitial pneumonia and

myocardial damage, diagnosed as pulmonary arterial hypertension (PAH) by a right heart catheterization revealed pulmonary arterial pressure (PAP) was 60/21mmHg. Anti-RNA polymerase III antibody (a-RNAP) was positive. 2 months later, dyspnea worsened and momentarily went into cardiopulumonary arrest. Cardiac ultrasound reveald estimated PAP was 90mmHg. She diagnosed acute exacerbation of PAH and sildenafil, bosentan, beraprost were started. After the treatment, estimated PAP went down 38mmHg. 5 months pass, dyspnea don't get worth. In SSc patient, SRC and PAH are complicated in 0.45% and 45% of these patient had a-RNAP. Also in this case, a-RNAP was positive.

P2-165

A Pediatric patient with Mixed Connective Tissue Disease with Pulmonary Hypertension

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Conflict of interest: None

【Case】a 14-year-old girl【Chief complaints】Peripheral coldness, facial erythema, Raynaud's phenomenon, exertional dyspnea【Clinical history】The patient developed peripheral coldness and facial erythema followed by Raynaud's phenomenon and exertional dyspnea in November 2013. Connective tissue diseases were suspected due to a high ANA titer (>1:10240) and elevated ESR by a referring physician. She was admitted to our hospital in February 2014. She had Raynaud's phenomenon, swollen fingers, facial erythema, hypergammaglobulinemia and positive anti-RNP antibody. Echocardiogram showed increased TRPG (58mmHg) and right heart catheterization showed elevated mPAP (38mmHg). She was diagnosed with Mixed Connective Tissue Disease (MCTD) with pulmonary hypertension (PH). She was treated with mPSL pulse therapy followed by oral PSL (1mg/kg/day) and intravenous cyclophosphamide pulse therapy. After the treatment, clinical and laboratory findings were improved and right heart catheterizations were performed in August 2015 and in August 2016 that showed marked improvement.【Conclusions】PH has been considered as an important prognostic factor of MCTD. Careful follow-up of mPAP is essential although PH is improved by the treatment. We present the case with a review of the literature.

P2-166

A case of the renal crisis which developed at 11 years after the onset for a systemic sclerosis complicated with interstitial pneumonia treated with Prednisolone and Tacrolimus

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Conflict of interest: None

A 51 years old male developed Raynaud's phenomenon, dyspnea, and visited our hospital in 2005. He had finger skin hardening, interstitial pneumonia (IP), and antinuclear antibody (nuclear pattern) and had a diagnosis of systemic sclerosis (SSC). Because the IP exacerbated subacutely, 20 mg/day of prednisolone (PSL), and 2 mg/day of tacrolimus (TAC) were initiated. The blood pressure was in the normal range. In September 2016, he was pointed out disturbance of consciousness of JCS1-1, high blood pressure (BP) (230/170 mmHg), and an elevation of serum creatinine (Cr), and admitted to our hospital. Blood examination showed Cr 2.08 mg/dL, LDH 790 U/L, Hb 12.2 mg/dL, platelet 118000 / μL, haptoglobin lower than sensitivity, no crush red blood cell. We stopped TAC and started nicardipine, but the condition was not improved. After starting enalapril, the clinical manifestations, blood pressure, LDH, Cr, and platelets were gradually improved. And he was diagnosed as scleroderma kidney crisis (SRC). It is reported that SRC often accompanies thrombotic microangiopathy (TMA). On the other hand, PSL and TAC which are often used for SSC-IP treatment can cause SRC and TMA. It is necessary to be careful about SRC in the SSC treatment. We report it including consideration from literatures.

P2-167

Refractory interstitial lung disease in anti-U1RNA antibody positive systemic sclerosis

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Conflict of interest: None

A 32-year old woman was admitted to the hospital because of progressive skin induration in her hands four years ago. She was diagnosed with systemic sclerosis by Raynaud phenomenon, interstitial pneumonia, and skin induration of her hands. Despite the high titer in anti-nucleolar antibody (speckled pattern), all of anti-RNP antibody, anti-centromere antibody, anti-Scl-70 antibody and anti-RNA polymerase III antibody were negative. The chest CT at the first visit revealed interstitial pneumonia accompanied with diffuse, centrilobular ground glass opacities. In December 2012, methylpredonisolone pulse therapy was administered due to exacerbation of interstitial pneumonia, and then mycophenolate mofetil 1g/day was started. She experienced exacerbation of interstitial pneumonia three times during next year. With the cooporation of the department of molecular pathology of skin in Kanazawa University, autoantibodies associated in systemic sclerosis were screened, and it was recognized that anti-U1RNA antibody was positive. Ground glass opacities in centrilobular lesions gradually changed in multiple cystic lesions and emphysema. We report on an example of systemic sclerosis positive for anti-U1RNA antibody with interstitial pneumonia exhibiting atypical CT image findings.

P2-168

2 cases of gastric antral vascular telangiectasia (GAVE) complicated with anti-RNA polymerase III antibody associated systemic sclerosis (SSc)

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Conflict of interest: None

Case 1: 64 year-old female consulted our clinic with one-year history of Raynaud's phenomenon and stiffness of upper extremities. She was diagnosed having SSc by the presence of proximal skin sclerosis and anti-RNA polymerase III antibody. She was admitted to our hospital complaining anemia and interstitial pneumonia. Gastric endoscopic examination revealed GAVE. However, her anemia was resistant to the endoscopic electrocoagulation. Interestingly, anemia improved after intermittent intravenous cyclophosphamide therapy for interstitial pneumonia. Then, improvement of GAVE was confirmed endoscopically. Case 2: 75 year-old female was diagnosed having SSc by skin sclerosis of the face and extremities with anti-RNA polymerase III antibody. Endoscopic examination for anemia revealed GAVE, and telangiectasia of the jejunum was also found by capsule endoscopic examination. The gastric and jejunal telangiectasia were treated with electrocoagulation using double balloon endoscopic electrocoagulation. Then, her anemia improved after therapy. Discussion: Close relations between anti-RNA polymerase III antibody and GAVE with SSc have been suggested. Vascular telangiectasia should be considered through the upper to lower intestinal mucosa in SSc patients with anti-RNA polymerase III antibody.

P2-169

A case of mixed connective tissue disease with unexplainable hypoalbuminemia

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Conflict of interest: None

Protein-losing enteropathy (PLE) is a condition in which excessive loss of serum protein from gastrointestinal tract leads to severe hypoalbu-

minemia. PLE is an uncommon complication of systemic lupus erythematosus (SLE), the incidence of which is reported to be 1%. Here we report a case of mixed connective tissue disease (MCTD) patient with unexplainable hypoalbuminemia, which was later diagnosed as PLE. A 37-year-old woman, who had been diagnosed as MCTD due to Raynaud's phenomenon and positive result of anti-U1 RNP antibody, was admitted to our hospital with severe ischemia of her left toes. During the clinical course, progressive hypoalbuminemia and large amount of ascites appeared. Urinary protein was negative and liver function was normal, thus PLE was suspected. We started high-dose pulse methylprednisolone therapy followed by 1mg/kg of oral prednisolone, along with intermittent intravenous cyclophosphamide pulse therapy. α-1 anti-trypsin clearance test in stool was later found out to be positive, which led to the diagnosis of PLE. PLE is reported to be a first symptom of SLE in 27-75% of SLE-related PLE cases. PLE should be considered as a differential diagnosis of hypoalbuminemia in MCTD patients, regardless of whether they had other symptoms of SLE or not.

P2-170

A case of chronic intestinal pseudo-obstruction in systemic sclerosis with muscle weakness

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Conflict of interest: None

A 30-year- old woman was diagnosed with systemic sclerosis from skin sclerosis, Raynaud's phenomenon and positive anti-centromere antibodies. At the age of 33 years, she developed chronic intestinal pseudo-obstruction (CIPO) and repeatedly admitted due to vomiting and diarrhea. Medical management such as erythromycin, metronidazole and metoclopramide ended in failure and her ADL (Activities of Daily Living) weakened and nutritional status gradually declined. At the age of 35 years, she was hospitalized for a long time due to fall and fracture, and she lost her job. At the age of 37, she was admitted to our hospital for treatment of CIPO. On admission, her BMI was 14.6 and she was unable to autonomously walk. She was treated with central venous nutrition and rehabilitation, and her nutritional status improved. Furthermore, she treated with hyperbaric oxygen therapy and prokinetic agents such as pantothenic acid, dinoprost and neostigmine, and she was able to eat 600 kcal. [Clinical significance] We experienced the case of chronic intestinal pseudo-obstruction, whose ADL has weakened. In order to avoid ADL weakening, it was considered that use of central venous nutrition was also necessary at an early stage.

P2-171

A case of diffuse cutaneous systemic sclerosis with massive ascites and pleural effusion

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Conflict of interest: None

A 63-year-old woman presents complaining of screlodactylia with digital pitted scars for the past 13 months. She noted the onset of Raynaud's phenomenon at the same time. Interstitial pneumonia was detected on computed tomography screening. Serology tests showed a positive anti-nuclear antibody. Anti-topoisomerase I (anti-Scl 70) antibody was strongly positive. The patient was diagnosed with diffuse cutaneous systemic sclerosis. She was treated with oral steroid, cyclophosphamide pulse, endothelin receptor antagonist. However, she abruptly developed pericardial, pleural effusion and ascites with renal dysfunction and low grade fever. Blood test revealed anemia with schistocyte, thrombocytopenia, a reduction of the activity of ADAMTS-13 and an elevation of the lactate dehydrogenase level. On this basis, we made a diagnosis of scleroderma renal crisis involving thrombotic thrombocytopenic purpura. Angiotensin converting enzyme inhibitor, tocilizumab and plasma exchange therapy were started, leading to complete remission of thrombotic thrombocytopenic purpura, renal dysfunction continued developing and she finally needed hemodialysis. Skin fibrosis and interstitial pneumonia became moderate but massive ascites and pleural effusion remained unchanged, requiring every week drainage.

P2-172

A case of limited cutaneous systemic sclerosis progressed to generalized morphea-like systemic sclerosis

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Conflict of interest: None

[Case] A woman in her 60s visited our clinic 4 years before admission because of the right hand pain. Despite the findings included positive anti-nuclear antibodies, positive anti-centromere antibody, she did not have scleroderma. Two years before admission, she had Raynaud phenomenon, nail fold bleeding and distal scleroderma. She diagnosed with limited cutaneous systemic sclerosis (SSc). Two months before admission, she had erythemas on her abdomen, thigh, and axilla. Histological examination revealed edema of the dermis and thickening and homogenization of collagen bundles. The findings that eruptions occured in symmetry, their boundaries were clear with normal skin, and accompanied with redness, led to the diagnosis with generalized morphea (GM)-like SSc. The expansion of GM-like eruptions was stopped and edema improved after treatment with oral prednisolone 30mg/day. **[Clinical Significance]** A disease concept, GM-like SSc was mainly used among Japanese dermatologists, and often considered as a subtype of diffuse cutaneous systemic sclerosis. This case has features of limited cutaneous systemic sclerosis except GM-like eruptions. There is not exposure history of organic solvent. It was considered to be a valuable case showing the diversity of GM-like SSc.

P2-174

A recurrent case of mixed connective tissue disease complicated by acquired thrombotic thrombocytopenic purpura (TTP) with severe deficiency of ADAMTS13 activity

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Conflict of interest: None

[Case] A woman in her 30s was diagnosed as mixed connective tissue disease (MCTD) 17 years ago, based on Raynaud's phenomenon, puffy edema of dorsal hand, pulmonary arterial hypertension, and anti-U1RNP antibody. She was treated with high dose steroids, intravenous cyclophosphamide (IVCY), and plasmapheresis. Prednisolone (PSL) was gradually reduced to 4 mg/day. After 15 years of quiescent disease, her MCTD flared with macroscopic hematuria, purpura of limbs, breathing difficulty at the time of exertion, and she was admitted to our hospital for an emergency. She had high fever and neurologic symptoms, and her lab exams revealed thrombocytopenia (6,000/μl), microangiopathic hemolytic anemia (Hb 5.7 g/dL) with schistocytes: she was diagnosed as thrombotic microangiopathy (TMA). She was treated with high dose steroids, IVCY, and plasmapheresis. Subsequently, her labs revealed severely decreased ADAMTS13 activity, and ADAMTS13 inhibitor, which led to the final diagnosis of acquired thrombotic thrombocytopenic purpura (TTP). All the manifestations of TTP ameliorated, the steroids were gradually reduced, and she was discharged home. **[Clinical Significance]** We reported a very rare case of MCTD complicated by acquired TTP with severe deficiency of ADAMTS13 activity.

P2-175

Successful treatment of refractory thrombocytopenia by rituximab therapy in a mixed connective tissue disease patient: a case report

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Conflict of interest: None

Refractory thrombocytopenia is a rare complication in mixed connective tissue disease (MCTD). We described a 60-year-old woman with a 12-year history of MCTD who was successfully treated by rituximab (RTX). She experienced an onset of high fever, worsening of Raynaud's phenomenon, leg edema, thrombocytopenia ($19\times10^3/\mu L$), elevation of proteinuria (1.5g/g·Cr), and high CRP levels (4.1mg/dL) in May 20XX although she kept low disease activities until that time. Since high disease activity of MCTD was suggested, she initially received prednisolone at a dose of 40 mg/day and tacrolimus (Tac) at a dose of 3 mg/day. However, because these treatment was not effective, Tac was switched to oral cyclosporine 150mg/day and an intravenous cyclophosphamide pulse therapy at a dose of 500mg was added. She failed to respond to the second therapy, then we added RTX on 4 occasions during 4 consecutive weeks at a dose of 375mg/m^2. After the RTX treatment, both clinical symptoms and platelet count were significantly improved. B-cell depletion with RTX could be one of the therapeutic strategies for the refractory thrombocytopenia associated with MCTD.

P2-176

An autopsy case of mixed connective tissue disease accompanied by thrombotic thrombocytopenic purpura

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Conflict of interest: None

A 59-year-old woman was carried to our hospital in an ambulance because of dyspnea and consciousness disorder. She noticed Raynaud's phenomenon at the age of 36. Antinuclear antibodies were elevated (×1280) with speckled pattern. Anti-U1-RNP antibodies and anti-SSA/Ro antibodies were positive. At the age of 38, she was hospitalized for pneumoniae and pleurisy. Physical examination revealed scleroderma. She had a diagnosis of mixed connective tissue disease (MCTD), and she had received prednisolone in a dose of 10mg/day for about 20 years. On admission she was confused with a Japan Coma Scale of 10 points. Laboratory data showed haemolytic anemia with presence of red cell fragmentation, thrombocytopenia and renal dysfunction. She got a seizure and underwent tracheal intubation. A diagnosis of thrombotic thrombocytopenic purpura (TTP) was made. Plasma exchange was immediately carried out. Inspite of intensive care, she died due to multiple organ failure after 4 days of hospitalization. Autopsy results revealed microthrombus in the brain, both lungs and both kidneys. Secondary TTP in association with MCTD is extremely rare. This is the first report of MCTD complicated with TTP describing the histological findings obtained by brain autopsy.

P2-177

Successful treatment of severe skin sclerosis of systemic scleroderma with intravenous cyclophosphamide pulse therapy and low dose steroid after the treatment of thrombotic microangiopathy

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Conflict of interest: None

We describe a 64-year-old female patient with rapidly progressive skin sclerosis of systemic scleroderma after the treatment of thrombotic microangiopathy (TMA), which was successfully treated with intravenous cyclophosphamide (IVCY) and low dose prednisolone (PSL). She was diagnosed systemic scleroderma with diffuse skin sclerosis, a positive test result for Scl-70 antibodies, and interstitial lung disease in September 2015. In November 2015, she admitted to our hospital due to fever, thrombocytopenia, and hemolytic anemia with fragmentation of red blood cells. She was diagnosed with TMA and treated with repeated plasma exchange and angiotensin-converting enzyme inhibitor. Then, TMA improved. However, one month later, she admitted again because of rapidly progressive skin sclerosis. At that time, the modified Rodnan total skin score (MRSS) was 32. We began to treat her with IVCY 12.5mg/kg monthly and PSL10mg/day. In four months, her skin sclerosis started to improve. After the treatment with 6 courses of IVCY, her MRSS improved to 11.

P2-178

A case of SSc with metronidazole-induced encephalopathy

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Conflict of interest: None

A 68-year-old woman was diagnosed with systemic sclerosis (SSc) in X-16, and administered prednisolone at a dose of 5mg/day, beraprost, and mosapride. She had been constantly in and out of hospital repeatedly to show symptoms of ileus. In March X, diarrhea and feebleness appeared and in April, she was dignosed with intestinal pseudoobstruction. Although the symptoms were not improved by pantethine and dinoprost, the symptoms were disappeared by metronidazole. Metronidazole were administered at a dose of 1500mg/day. However, in September, dysphemia and cerebellar ataxia were appeared. MRI T2 and FLAIR images showed bilateral high signals in cerebellar dentate nucleus, splenium, and brain stem. She was diagnosed with metronidazole-induced encephalopathy. Metronidazole were stopped immediately. On the 4th day, the symptoms were improved, and on the 14th day, the symptoms were disappeared. Metronidazole-induced encephalopathy was reported sometimes in Japan. There are the reports that the patients had used metronidazole in the total dose of 100g, however, the patient use in the total dose of 150g. Metronidazole is effective to intestinal pseudoobstruction associated with SSc. It is important that we recognize metronidazole-induced encephalopaty as a rare advanced event.

P2-179

A case of interstitial pneumonia with dermatomyositis with positive anti-MDA5 antibody treated with mycophenolate mofetil

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Conflict of interest: None

[Case] A 46-years-old woman She noted eyelid rash and arthralgia in April 2016 and visited our hospital in May. She had rash characteristic of dermatomyositis (DM) without muscle symptoms. Her chest CT showed interstitial pneumonia (IP) suspecting clinically amyopathic DM. The combination of 70mg/day of prednisolone (PSL) and 250mg/day of cyclosporine (CYA) was initiated with temporary improvement of IP. Prompt relapse of IP followed and anti-MDA5 antibody was positive. Although we added intravenous pulse cyclophosphamide (IVCY) 2 times, a new lesion of IP appeared. Mycophenolate mofetil (MMF) was administered in addition to IVCY, against refractory and her DM-IP improved. Repeated infections of cytomegalovirus were observed, but controlled with foscarnet. PSL and MMF were tapered to 20mg/day and 1.5g/day, respectively, in November 2016, and IP has not relapsed. [Conclusion] DM-IP with positive anti-MDA5 antibody progresses rapidly like this case and there are several reports that it is lethal even if treated early with

PSL, calcineurin inhibitor and IVCY. This paper presents MMF is a potential drug for the treatment of DM-IP. There are few reports on the use of MMF in this disease, followed by review of the literature.

P2-180

Successful combination therapy with mizoribine in interstitial lung disease associated with anti-MDA-5 antibody positive dermatomyositis: a case report

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Conflict of interest: None

We describe a case of 66-year-old woman with slight fever, loss of appetite, and arthralgia, who was diagnosed as clinically amyopathic dermatomyositis (CADM) according to typical erythema along with skin ulcer on her extremities. She indicated hypoxia with respiratory symptom and interstitial lung disease (ILD) on CT finding as well as anti-MDA-5 antibody (MDA-5Ab) positivity. She was concomitantly administered methylprednisolone pulse and cyclosporine A (CsA) intravenously; however, exacerbation of hypoxia was demonstrated even though intravenous cyclophosphamide (IVCY) was immediately administered as an additional agent. Furthermore, IVCY was terminated because of myelosuppression ascribable to adverse event of this agent. Subsequently, mizoribine (MZR) was administered, resulting in amelioration of respiratory failure together with prednisolone- and oxygen-sparing effect. The combination therapy with immunosuppressive agents would be required in patients with acute progressive and refractory ILD related to MDA-5Ab positive DM. Meanwhile, only two cases of DM which described the efficacy of MZR have been reported so far. This is a first report that demonstrated the usefulness of MZR as a part of combination therapy in ILD associated with MDA-5Ab positive DM.

P2-181

Successful treatment with multi-immunosuppressants, PMX, and rituximab for anti-MDA5 antibody positive dermatomyositis complicated with rapid progressive interstitial pneumonia

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Conflict of interest: None

Introduction: Anti-MDA5 antibody positive dermatomyositis (DM) complicating interstitial pneumonia (IP) progress rapidly and resist to immunosuppressive therapy. Case: A 57-year-old female was admitted to our hospital with 4-week history of fever, erythematous eruptions, cough and dyspnea. Her physical examination revealed Gottron's sign and Heliotrope rash, but no signs of muscle symptoms were observed. The serum ferritin level was elevated (697 ng/mL), and $AaDO_2$ level was high (41.8 mmHg). Chest HRCT findings showed IP in the lower lobes. She was diagnosed with DM complicating rapid progressive IP (RPIP) and underwent treatment with high-dose prednisolone combined with cyclosporine and intravenous cyclophosphamide. However, her clinical condition deteriorated with progression of IP, polymyxin-B direct hemoperfusion (PMX-DHP) was performed. Following PMX-DHP, mycophenolate mofetil was added on. To further add to rituximab, the disease was led to remmision. In this case, anti-MDA5 antibody was positive. Conclusion: We conclude that multidisciplinary therapy is worth trying in such patients if they fail to respond to conventional treatment.

P2-182

Successful treatment of steroid, cyclosporine, cyclophosphamide intermittent infusion combination therapy-resistant antiMDA5 antibody-positive dermatomyositis with rituximab

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Conflict of interest: None

A 54-yaer-old woman was aware of nail wall erythema, palm exanthema 2years ago. She experienced joint pain, finger swelling, and slow progressive muscle weakness later. She was annoyed for daily life, and visited the dermatology office for progressive exanthema. Dermatologist implicated dermatomyositis as her exanthema and made a referral to our hospital for rapidly progressive interstitial lung disease. We diagnosed as clinically amyopathic dermatomyositis by lack of elevated levels of CPK and aldolase, rapidly progressive interstitial lung disease, inverse gottron papules, and liver enzyme and ferritin levels elevation. We gave glucocorticoids pulse therapy and oral cyclosporine, but not improved. The blood exam revealed anti-MDA5-positive, we added intravenous cyclophosphamide. Instead of nine course of IVCY, interstitial pneumonia has worsened. Treatment with rituximab started, and interstitial pneumonia was dramatically improved. AntiMDA5 antibody-positive amyopathic dermatomyositis associated with rapidly progressive interstitial pneumonitis frequently has a poor prognosis. We report a case with refractory CADM treated with rituximab successfully.

P2-183

A case of rapid progressive interstitial lung disease associated with anti-MDA5 antibody positive dermatomyositis successfully treated by single filtration plasma pheresis

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Conflict of interest: None

A 48-old women was complaining fever, face erythema, and muscle weakness three weeks before admission. She was suspected as dermatomyositis by elevating CK (2395U/L) and admitted to our hospital. After admission, she was diagnosed as dermatomyositis by Gottron's phenomenon, reverse Gottron's phenomenon, mechanic's hand, arthralgia, and elevating C-reactive protein. She had a sign of interstitial pneumonia in chest CT scan and hypoxemia (PaO2 52.9mmHg). After admission, as her oxygenation and chest imaging got worse in a week, we diagnosed her as rapid progressive interstitial lung disease (RP-ILD) and started treatment by intensive regimen of combined immunosuppressive therapy. Anti-MDA5 antibody was detected after started treatment. Because her oxygenation was not improved at all, we started single filtration plasma pheresis (SFPP) and her RP-ILD were improved. She could withdraw from SFPP 2 months after starting treatment. However RP-ILD got worse after that, we added intravenous immunoglobulin and following her. RP-ILD associated with anti-MDA5 antibody has a high mortality rate. There were few reports suggesting the effectiveness of SFPP but we thought it could be one of the treatment for RP-ILD with anti-MDA5 antibody.

P2-184

A case of anti-MDA5-positive dermatomyositis with interstitial pneumonia, ameliorated by IVCY and TAC

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Conflict of interest: None

Case1:A 36 years old female was suffered facial erythema and muscle weakness in September 2015. Gottron's sign appeared in December, and she was admitted to our hospital in January 2016. Although serum CK was in normal lange, heliotrope rash, shawl sign, Gottron's sign, mechanic's hand, polyarthritis were identified. Her laboratory data revealed positive test for anti-MDA5 antibody. IP was identified in bilateral inferior lobes in CT exam, so she was diagnosed as CADM with IP. CADM and IP were improved by steroid pulse therapy followed by oral administration of PSL55mg/day in combination with IVCY and TAC. Case2:A 50 years old female was suffered rough hand, chest erythema in January 2016. She was admitted to our hospital in April. Heliotrope rash, Gottron's sign, muscle weakness and polyarthritis were identified. Her labo-

ratory data revealed positive test for anti-MDA5 antibody. IP was identified in bilateral inferior lobes in CT exam, she was diagnosed as to have DM with IP. DM and IP were not improved by steroid pulse therapy followed by PSL60mg/day. Second steroid pulse therapy in combination with IVCY and TAC showed effectiveness with decreased anti-MDA5 antibody titre. Combination treatment with IVCY and TAC may be a useful option for IP associated MDA5-positive DM.

P2-185

Clinical characteristics in patients with anti-MDA5 antibody

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Conflict of interest: None

[Purpose] We examined clinical characteristics in patients with anti-MDA5 antibody [Method] For 105 cases who examined anti-MDA5 antibody with sera at the diagnosis, among 108 patients that we applied Bohan and Peter Criteria for the diagnosis of polymyositis (PM) and dermatomyositis (DM) that has been diagnosed from 2008 to 2016 in our hospital. I prepared that the antiMDA5 antibody-positive group and negative group about their profile, patients' backgrounds, complications, and Myositis specific antibodies. [Result] The mean follow-up period was 41 months, mean ages were 48 years old, and the sex ratio was 22 men and 83 women. Forty-five patients were diagnosed PM, and 60 patients were diagnosed DM. Patients with anti-MDA5 antibody were all cases DM in 23 cases. By the comparison between group of anti-MDA5 antibody positive and negative group, I got statistical significant difference at CK, ALD, KL-6, Ferritin, complication with interstitial pneumonia, complication with rapidly progressive interstitial lung disease (RP-ILD), and application rate that intensive regimen of combined immunosuppressive therapy. [Conclusion] In this study, the supportive result was provided about the effectiveness of the intensive regimen of combined immunosuppressive therapy.

P2-186

A case of clinically amyopathic dermatomyositis (CADM) presenting with central nervous system lesions

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Conflict of interest: None

The patient is a 42-year-old female who admitted to her local doctor because of flulike symptom, arthralgia and oral ulcers at Jan 2016. She was diagnosed as RA and prescribed 5mg/day of prednisolone, but these symptoms were remained. Gradually, she became weak to be difficult to move. Since her consciousness had been altered, she admitted to our hospital. At the time of admission, purpura was found on her iliac crest, back and sacrum. Blood examination showed sever liver injury, hyperferritinemia and pancytopenia. Chest CT revealed the existence of interstitial pneumonia (IP). Cerebrospinal fluid examination showed albuminocytologic dissociation. Brain MRI (FLAIR) had the findings of high intensity signal at bilateral striatum. From these results, we diagnosed as macrophage activation syndrome associated with immune-associated encephalitis, and started the high dose glucocorticoid therapy. At this time, it was found that anti MDA5 antibody was positive. Thus we diagnosed her as CADM. Although the cyclophosphamide and tacrolimus were added, she died in the exacerbation of IP. Since it was rarely found that CADM occurred in combination with CNS lesion, we report this case with some literature review.

P2-187

Analysis of clinical features in patients with dermatomyositis of anti melanoma differentiation-accociated gene 5 (MDA-5) antibody-positive

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Conflict of interest: None

Objective: Anti melanoma differentiation-accociated gene 5 (MDA-5) antibody-positive dermatomyositis is complicated by rapidly progressive interstitial pneumonia, the prognosis is poor. We have examined clinical features in patients with dermatomyositis of anti-MDA-5 antibody-positive. Methods: We intended for 10 patients of anti-MDA-5 antibody-positive dermatomyositis we diagnosed from April in 2008 to June in 2016. Results: The average age was 48±14 years. Gottoron signs in all cases, heliotrope rash in 4 patients, showed a fever in 9 cases. At the start of treatment, KL-6 is 5 cases within the reference value, the mean value of 882 ± 740 U / ml, ferritin three cases within the reference value, the mean value is 1079 ± 355 ng / ml, CK is 7 cases within the reference value. In 4 of 5 patients with anti-MDA-5 antibody normalization, KL-6 is within the reference value, interstitial pneumonia image on chest CT had disappeared. Onset of from January to April was observed 8 cases. Conclusion: The anti-MDA-5 antibody-positive dermatomyositis patients, there is a possibility that the course of therapy and anti-MDA-5 antibody titer is associated. Further, the onset of this disease is likely to be associated with season.

P2-188

Validation of Clinically amyopathic dermatomyositis (CADM) with Interstitial Lung Disease in 10 cases – can KL-6 and Ferritin be a short-term responsiveness Biomarker?

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Conflict of interest: None

[Object] Abnormally high serum KL-6 and Ferritin at the onset of treatment leads to poor outcomes, but a short-term responsiveness is still unclear. We aimed to evaluate the usefulness of 2 biomarkers and a marker of poor prognosis. [Methods] In total, 10 CADM patients with ILD were included. Clinical and laboratory data were retrospectively collected and statistically analyzed. [Results] Duration of respiratory symptoms had positive correlation with KL-6. All cases were treated with PSL, CY and calcineurin inhibitors. 6 cases including 1 fatal were anti-MDA-5 antibody positive group, 4 cases were negative. No significant difference of Ferritin at 0 or 4 weeks between groups. KL-6 was significantly higher in anti-MDA-5 antibody negative group at 4 weeks. In comparison with successful treatment of 7 cases without home oxygen therapy (HOT) and 3 cases including 2 HOT cases and 1 fatal case, strong association was approved between increased Ferritin amount and a poor prognosis (18.68ng/ml/week, AUC 0.8571). [Conclusion] Ferritin value was suggested no direct correlation with disease activity by itself. Meanwhile, increased Ferritin amount might be a marker of disease activity and prognosis. Adequate and aggressive treatment is preferred whether anti-MDA-5 antibody is positive or not.

P2-189

Two cases of anti-MDA (melanoma differentiation-associciated protein) 5 antibodies positive clinically amyopathic dermatomyositis (cADM) which took a completely different outcome

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Conflict of interest: None

A 45-year-old female presented with non-productive cough, exertional dyspnea, Gottron's signs and polyarthritis. Hypomyopathic findings and positive anti-MDA5 antibodies were revealed, so we diagnosed her as cADM. Since chest CT showed organized pneumonia (OP), administration of high dose steroid, calcineulin inhibitor and intravenous cyclo-

phosphamide, namely a triple therapy started on day 4. Intravenous immunoglobulin was added, but OP worsened. A methylpredonisolone pulse therapy, 3 times of plasma exchange and rituximab (RTX) were administrated. Cerebral infarction was occurred on day 48. RTX was administrated on day 54. However, hypoxemia was progressed and mediastinal emphysema and bilateral pneumothorax were developed. She died on day 60. A 55-year-old female presented with Heliotrope rashes, Gottron's signs and polyarthritis. Hypomyopathic findings and positive anti-MDA5 antibodies were revealed, so we diagnosed her as cADM. Since linear shadows had been increasing on chest CT in a week, a triple therapy started on day 5. Then, skin and lung lesion was improved. Anti-MDA5 antibodies positive cADM has a poor prognosis because of a rapid progressive interstitial lung disease. We report two cases of them which took a completely different outcome with some literature review.

P2-190

A case of clinically amyopathic dermatomyositis complicated with massive retroperitoneal hematoma

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Conflict of interest: None

An 80-year-old woman was referred to our hospital for erythema of chest and back. She was suspected as clinically amyopathic dermatomyositis (CADM) from findings of gottron's sign without muscle pain or weakness, and normal serum creatine phosphokinase level. After admission, she developed hypoxemia with radiographic features of mild degree of interstitial pneumonia. She was treated with prednisolone (PSL) 50mg/day. After that, Anti-MDA5 antibody was found to be positive. She was diagnosed as CADM. 10 days after starting the treatment, she complained back pain with low blood pressure. Computed tomography scan of abdomen and pelvis demonstrated a large right-sided retroperitoneal hematoma. Emergent angiography showed multiple contrast medium extravasation from the lumbar arteries. Transcatheter arterial embolization of the lumbar arteries was performed. These findings suggested that CADM was involved in vascular lesions. We added intravenous cyclophosphamide and oral tacrolimus, and massive hemorrhage was controlled successfully. We reported a case of CADM complicated with retroperitoneal hematoma. Although bleeding manifestation in dermatomyositis is rare, we propose that the patients with CADM may have a risk of life-threatening bleeding.

P2-191

Anti-MDA-5 positive Clinically Amyopathic Dermatomyositis Presenting with Rheumatoid Arthritis Like Polyarthritis

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Conflict of interest: None

【Introduction】Anti-MDA-5 positive clinically amyopathic dermatomyositis (CADM) is a fatal disease frequently complicated with rapidly progressive interstitial lung disease. We report anti-MDA-5 positive CADM presenting with rheumatoid arthritis (RA) like polyarthritis. 【Case】The bilateral hand, wrist, shoulder, knee, ankle and toe arthritis from January brought 20-year-old female to our clinic. Gottron's papules and signs existed on the extensor side of MCP, elbow and knee joints. There were tender palmar papules on DIP, PIP and MCP joints, no abnormal lung sounds and no muscle weakness. Laboratory data showed no muscle enzyme elevation. Chest CT revealed slight ground glass opacities on bilateral peripheral lower lobes. We commenced mPSL pulse therapy followed by 1mg/kg/day of PSL, calcineurin inhibitor and intravenous cyclophosphamide (IVCY) treatment. After the first IVCY dosage, anti-MDA-5 antibody result turned out positive. A total of 6 IVCY dosages were infused until July and her arthritis was in remission, her chest CT abnormality disappeared. 【Clinical significance】Anti-MDA-5 antibody positive CADM can masquerade as RA. Awareness of demartomyositis rash and palmar papules can lead to prompt diagnosis and treatment of anti-MDA-5 positive CADM.

P2-192

Anti-MDA5 antibody positive dermatomyositis with clinical features resembling anti-aminoacyl-transfer RNA synthetase syndrome: Two case report

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Conflict of interest: None

Anti-aminoacyl-tRNA synthetase antibody (anti-ARS Abs) syndrome is a subtype of dermatomyositis characterized by distinctive findings such as Raynaud's phenomenon, arthritis, fever, interstitial lung disease (ILD) and mechanic's hand. On the other hand, Anti-MDA5 Abs positive dermatomyositis often presents rapidly progressive ILD and poor prognosis. We described two cases of anti-MDA5 Abs positive dermatomyositis showing clinical features resembling anti-ARS Abs syndrome. Case1: A 51-year-woman was admitted to our hospital suffering from a 2-year history of elevated hepatobiliary enzyme, a 1-year of erythema of the fingers, and 4-month of arthritis and ILD. Since we empirically diagnosed her with anti-ARS Abs syndrome from clinical findings, she was given prednisolone (PSL) and Tacrolimus (Tac). Case2: A 59-year-woman was referred to our hospital complaining of a 6-month history of similar symptoms to Case1. She received PSL, Tac, and intravenous cyclophosphamide pulse therapy because she had deterioration of respiratory function. Their clinical symptoms were rapidly improved following the initial treatment. Contrary to our expectations, it turned out that both patients were negative for the anti-ARS Abs, but instead positive for the anti-MDA5 Abs.

P2-193

Comparison of Prognosis in Interstitial Lung Disease Between Polymositis/ Dermatomyosis Patients with Anti-Jo-1 Antibody and Anti-EJ Antibody

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Conflict of interest: None

Background: Anti-aminoacyl-tRNA synthetase (ARS) autoantibodies are polymyositis/dermatomyositis (PM/DM) specific autoantibodies. However, there is few study for the clinical characteristics of interstitial lung disease (ILD) with regard to different anti-ARS antibodies. Here, we evaluate differences in prognosis of ILD between anti-Jo-1 and EJ antibodies. **Methods**: Thirty five patients diagnosed as having PM/DM and ILD with anti-Jo-1 and anti-EJ antibodies at Tokai University Hospital between 2011 and 2016 were selected. Autoantibodies are identified by immunoprecipitation assays and ILD is diagnosed based on CT or XR. The cumulative survival rates were estimated with the Kaplan-Meier method and the differences in groups were compared with the log-rank test. **Results**: Of the 35 patients, 14 were positive for anti-EJ antibodies and 21 were positive for anti Jo-1 antibodies. Induction rates of home oxygen therapy during follow-up period were higher in anti-EJ antibody group than in anti-Jo-1 antibody group (30.0% vs. 10.5%: $p = 0.31$). Cumulative survival rates were worse in patients with anti-EJ antibody than in anti-Jo-1 antibody. **Conclusions**: These findings suggest that patients with anti-EJ antibody might have worse prognosis of ILD compared to those with anti-Jo-1 antibody.

P2-194

Clinical features and long term outcome in anti-PL7 patients with Antisynthetase syndrome (ASS)

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Conflict of interest: None

[Object] The aims of the present study were to assess clinical features and long term outcome in anti-PL7 patients with Antisynthetase syndrome (ASS). [Method] The clinical date of ASS with anti-PL-7 Abs from 4 hospitals were retrospectively obtained from the medical records. [Result] 12 patients were enrolled. Overlap syndrome were as followed:SSc (n=3), RA (n=3). Median serum CK value was 1629±1874 IU/L.11 patients had ILD and 2 patients had malignancy.11 patients were treated by glucocorticoids (PSL) plus immunosuppressive drug (IS), including 7 patients with PSL pulse therapy and 2 patients with IVCY therapy.2 patients experienced myositis relapse, 3 patients experienced ILD relapse, and 3 patients received additional therapy through entire period.5 patients were carried out PFT before and after treatment, and 2 of them showed reduced PFT value. 4 patients died due to rapid progressive ILD in 1 patients, cancer death in 2 cases. 1 patient required HOT therapy. [Disccution] We confirmed that anti-PL7 patients with ASS had lower CK levels and high frequency of ILD, complication of SSc.2 patients with ILD died and some patients showed reduced PFT value regardless of maximum therapy. It indicated that anti-PL7 patients with ASS could be refractory to PSL plus IS therapy.

P2-195

Examination of the clinical characteristics of 29 polymyositis and dermatomyositis patients with anti-tRNA-synthetase autoantibodies

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Conflict of interest: None

[Background] The anti-tRNA-synthetase autoantibodies (ARSs) positive patients have myositis and lung comorbidities, but the difference of clinical course is reported by the specificity of the each ARSs. We examined the difference between the anti-Jo-1 antibody positive and negative groups. [Method] From April 2005 to September 2016, 29 patients positive for ARSs were extracted. We examined the patient's background (age, sex, autoantibodies, treatment, and recurrence) based on the medical record. [Result] The anti-Jo-1 antibody positive group (23 patients) had more muscle weakness as presenting symptoms than an anti Jo-1 negative group (anti-PL-7 antibody; n=1, anti-PL-12 antibody; n=2, anti-EJ antibody; n=1, anti-KS antibody; n=2: 65.2% vs 0%, $p<0.05$). The anti-Jo-1 negative group had much Raynaud's phenomenon (13% vs 37.5%, $p<0.05$) as presenting symptoms, and the delay of diagnosis was found (6.2 months vs 15 months, $p<0.05$). Both groups had high rates of pulmonary comorbidities, recurrence, and required immunosuppressive treatment. [Conclusion] Differences were found in the initial symptoms, but no differences were found in the clinical course and therapeutic response. It is important to make early diagnosis by using ARSs.

P2-196

Anti-PL-7 antibody positive dermatomyositis with pathological finding of necrotizing myopathy: a case report

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Conflict of interest: None

We describe a case of 46-year-old woman with dermatomyositis (DM), who indicated general fatigue, slight fever, Raynaud's phenomenon, mechanic's hands and Gottron's sign, and proximal muscle weakness with increased level of creatine kinase. The examinations demonstrated histopathological finding of necrotizing myopathy (NM), which consists of muscle fiber necrosis, and macrophagic phagocytosis without infiltration of lymphocytes. As well as the positivity of anti-PL-7 antibody (PL-7Ab), she was concomitantly treated with prednisolone (PSL) and tacrolimus (TAC), and resulting in immediate achievement of clinical remission. In patients with PL-7Ab, which is categorized as one of the anti-ARS antibody, Raynaud's phenomenon and cutaneous involvement along with muscle symptom are specific features; however, only 4 cases of NM with PL-7Ab positivity were described to our knowledge. It was recognized that majority of patients with NMrequire additional immunosuppressant, because of their resistance to PSL alone. Accordingly, we herein not only report PL-7Ab positive DM with showing NM as a rare case, but also suggest that early co-administ is useful for achieving favorable outcome.

P2-197

A case of anti-aminoacyl tRNA synthetase antibody positive amyopathic dermatomyositis with interstitial pneumonia

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Conflict of interest: None

A 56-year-old woman was admitted for fever and edematous lid erythema. On admission, her laboratory data showed that C-reactive protein level was 8 mg/dL, KL-6 lelvel was 530 U/mL, but creatine kinase level was normal. Her computed tomographic scanning showed infiltrative shadow of bilateral lower lobe. Antimicrobial agent was not effective, and anti-aminoacyl tRNA synthetase antibody was positive. The biopsy specimen of skin showed small round cell infiltration. We diagnosed with amyopathic dermatomyositis with interstitial pneumonia. Anti-MDA 5 (melanoma differentiation-associated gene 5) antibody was negative. She was succesfully treated with methylprednisolone pulse therapy, predonisolone (30mg/day), and tacrolimus. [Clinical significance] We discuss about amyopathic dermatomyositis with interstitial pneumonia with literature review.

P2-198

A case of anti-signal recognition particle (SRP) antibody-positive polymyositis which has rapid progression of dysphagia

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Conflict of interest: None

Case: The patient was a 69-year-old man who visited our hospital for a chest pain. An elevated serum creatinine kinase (CK) level of 1,857 IU/L was noted and the patient had findings of myalgia and muscle weakness. Therefore, the patient was suspected polymyositis. Due to observed progression of dysphagia, rapid therapeutic intervention was deemed necessary. Steroid pulse therapy was started and prednisolone was given at 1 mg/kg as an after treatment. However, the patient showed no improvement in the CK level or dysphagia. The identification of anti-signal recognition particle (SRP) antibody positivity during the same period led to a judgment of a steroid-resistant disease. Upon initiation of intravenous high-dose cyclophosphamide and intravenous immunoglobulin (IVIG) combined with tacrolimus, a decrease in the CK level and improvements in dysphagia were seen. Clinical significance: Anti-SRP antibody-positive myositis is known to be resistant to steroids, and has been reported to respond well to immunosuppressants and IVIG. In the present case, the patient exhibited a disorder of the swallowing muscles. A multidrug combination of immunosuppressants and IVIG proved effective against this disorder, which we considered of significance as an experience of treatment of polymyositis.

P2-199

Two cases of myositis with anti-SRP antibody that complicated interstitial pneumonia and normalized CK value

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Conflict of interest: None

In this report, two cases of myositis with anti-SRP antibody are presented. First case, a 71-year-old woman complained of lower leg pain and shortness of breath. We diagnosed this case as interstitial pneumonia combined polymyositis with anti-SRP antibody, and it combined with breast cancer. We treated it with corticosteroid plus tacrolimus and intravenous immunoglobulin (IVIG). Treatment for breast cancer was added in the process of reducing steroids, and CK value was normalized. Second case, a 81-year-old woman after left breast cancer operation complained of shortness of breath on a slope. We diagnosed this case as interstitial pneumonia combined dermatomyositis with anti-SRP antibody. We treated it with corticosteroid plus tacrolimus. Although it improved in the beginning, but the data worsened in the process of reducing steroids, so we added IVIG and CK value was normalized. Myositis with anti-SRP antibody is refractory. It is said that IVIG is effective, but there are some cases not to recover completely. And it is reported that many do not combine with interstitial pneumonia and skin lesions. In this report two cases were accompanied by interstitial pneumonia, and one had skin lesions. In both cases, normalization of CK value could be achieved by treatment.

P2-200

Clinical features of anti-Mi-2 antibody positive dermatomyositis and polymyositis

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Conflict of interest: None

[Objectives] We evaluated the clinical features in anti-Mi-2 antibody (Ab) positive dermatomyositis (DM) and polymyositis (PM) patients. [Methods] Three anti-Mi-2 Ab positive patients were included. Anti-Mi-2 Ab was measured by EUROLINE. [Results] All patients were females; case 1 was PM (76-years old), case 2 was DM (79-years old), and case 3 was DM (25-years old). Case 1 and 2 had acute/subacute interstitial pneumonia (IP). All patients had speckled pattern of anti-nuclear antibody (titers were 1:640 or higher), and case 1 had anti-U1-RNP Ab. In IP patients, serum laboratory findings were below; CK 584, 2494 U/L, ferritin 123, 87.3 ng/mL, KL-6 864, 488 U/mL, A-aDO_2 58.5, 19.7 mmHg, respectively. In pulmonary function test results, %VC were 60.3, 116.9%, %DLco were 80.2, 63.7%, respectively. They received prednisolone (55, 20 mg/day) and immunosuppressants (case 1: cyclosporine 200 mg/day, case 2: tacrolimus 7.5 mg/day). One patient (case 1) died due to aggravation of IP. [Conclusion] The anti-Mi-2 Ab positive DM/PM was reported a low risk of IP and good response to treatments, but we should remind to consider that some IP cases may progress rapidly.

P2-201

Succesful treatment with rituximab in aortitis as a manifestation of refractory granulomatosis with polyangitis

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Conflict of interest: None

The patient is a 47 years old man. At the age of 44 years old, he had been diagnosed with upper respiratory tract lesion of granulomatosis with polyangitis (GPA), on the basis of refractory middle otitis and right facial paralysis with PR3-ANCA. He improved after received intravenous methylprednisolone pulse therapy (1000mg daily for 3 days), followed by oral prednisolone 70mg daily. Additional Azathioprine therapy was initiated. 3 years later, this patient was found to have hypertrophic pachymenigitis and elevated serum levels of PR3-ANCA. Despite high dose corticosteroid therapy, his hypertrophic pachymenigitis was relapsed as tapering prednisolone. FDG-PET showed abnormal uptake in the aortic root and spinal cord. Echocardiography revealed aortic regurgitation. After the rituximab treatment at a dose of 375mg/m2 weekly for 4 weeks, his symptom disappeared and the level of PR3-ANCA were normalized. Large-vessel involvement as a manifestation of GPA is very rare. It was reported that efficacy of rituximab for refractory large-sized vasculitis associated with GPA. We report this case with review of the literature.

P2-202

A rare case of AA amyloidosis caused by ANCA-associated systemic vasculitis

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Conflict of interest: None

[Case] A 73-year-old woman was pointed out the abnormal chest findings first detected by X-ray 10 years ago. Between the ages of 65 and 70, she developed otitis media, appetite loss, chronic diarrhea, and weight loss. After the gastrointestinal (GI) amyloidosis, slightly elevated MPO-ANCA, and bronchiectasis were detected, she was referred to our hospital for further examination. A bronchoscopy demonstrated amyloid protein deposits and colonization of *Pseudomonas aeruginosa* and *Aspergillus* spp. A renal biopsy revealed interstitial nephritis, which was treated with corticosteroid for 6 months. At age 73 years, she experienced GI symptoms, hematuria, renal dysfunction, and high levels of MPO-ANCA. A colonoscopic biopsy revealed AA amyloidosis immunohistochemically. The changes in the chest CT findings were not remarkable. Vasculitis with fibrinoid necrosis was demonstrated by the muscle and renal biopsies, and ANCA-associated vasculitis (AAV) was diagnosed. Concurrent administration of anti-fungal agent and high dose corticosteroid was begun. Her general condition improved immediately without any complications. [Clinical significance] Although AAV complicated by AA amyloidosis has rarely been reported, early diagnosis and comprehensive treatment may improve the prognosis.

P2-203

Three cases of relapsing granulomatosis with polyangitis successfully treated with rituximab

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Conflict of interest: None

[Case-1] A 65-year-old woman, who had been diagnosed as having granulomatosis with polyangiits (GPA), admitted to our hospital because of ophthalmodynia and rhinalgia. She was treated with prednisolone (PSL) and cyclophosphamide (CY), but the disease relapsed several times. Rituximab (RTX) of 375 mg/m^2/week was administered. Her clinicalsymptoms including ophthalmodynia and rhinalgia were relieved. [Case-2] A 32 year-old man, who had been diagnosed with GPA, developed severe bronchial stenosis. Oral CY failed to suppress disease activity and RTX of 375 mg/m^2/week was administered. Although bronchial stenosis was not improved, other clinical symptoms such as rhinorrhagia and ear fullness were ameliorated. [Case-3] A 60 year-old woman was diagnosed with ANCA-associated vasculitis and oral PSL and CY were initiated. Her right visual dysfunction appeared, and MRI brain scan revealed the presence of pseudotumor in her right orbit. She was diagnosed

as having GPA and RTX of 375 mg/m^2/week was administered. Visual acuity was recovered after RTX treatment. [Conclusion] RTX was efficient for patients with GPA, who were refractory to CY. No adverse events were observed in all three cases, thus suggesting its efficacy and safety for treating with patients with relapsing GPA.

P2-204

Rituximab for the treatment of dual-positive anti-myeloperoxidase (MPO-ANCA) and anti-glomerular basement membrane antibody (anti-GBM) vasculitis with pulmonary-renal syndrome

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Conflict of interest: None

[Case] A 79-year old female. [Chief complaint] Fatigue. [Clinical course] She was admitted to our hospital due to rapidly progressive glomerulonephritis and pulmonary alveolar bleeding. After admission, methylprednisolone 1000 mg / day Intravenous injection for 3 days started treatment. Subsequently, prednisolone 50 mg / day was administered intravenously. Dual-positive of anti-GBM antibody and MPO-ANCA was found. Based on the above, it was diagnosed that this case was pulmonary-renal syndrome, and plasma exchange therapy was used in combination. Due to deterioration of renal failure, hemodialysis was performed. In renal biopsy, IgG, C3 deposits were observed linear in the glomerular capillary wall with fluorescent antibody, crescent forming glomerulonephritis was observed by optical microscopic findings, and it was a finding consistent with anti-GBM nephritis. Rituximab 500 mg was also used as a remission induction therapy. Bloody sputum has disappeared at present. Both anti-GBM antibody and MPO-ANCA titer were low and creatinine improved to about 3 mg / dl, but urine volume was insufficient and hemodialysis therapy continued. [Discussion] There are few reports that Rituximab is used for pulmonary-renal syndrome.

P2-205

Recent analysis of 10 cases of microscopic polyangiitis (MPA)

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Conflict of interest: None

Objective: MPA often develops in elderly patients. The number of these patients will be increased in upcoming aging society. We analyzed 10 cases of these patients with MPA within recent one year. **Method:** An observation period is one year from June, 2015 to May, 2016. We analyzed 10 patients with MPA according to the diagnostic criteria of the Ministry of Health and Welfare for a diagnosis in 1998. **Results:** Ten patients were diagnosed with the criteria of MPA. The sex differences were all women. Average age 77.9±7.2 (±SD). Three cases had the disturbances of both pulmonary and kidney. MPO-ANCA were 90% positive and PR3-ANCA were 40% positive among the patients. **Discussion:** The previous report indicated that the ratio of males to females was approximately 1:1 and the distribution of age was 55 to 74 years in elderly people. However, recent our data showed all the patients were females. RemIT-JAV study indicated MPO-ANCA was 97.4% positive and PR3-ANCA was 45.5% positive in MPA, and that in the GPA MPO-ANCA was 54.6% positive. Our data concerning with the positive ratio of ANCA was corresponded to RemIT-JAV study. **Conclusion:** Our recent report indicated elderly patients were all females different from previous data from RemIT-JAV study.

P2-206

A case of recurrent granulomatosis with polyangitis with tracheobronchial nodules

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Conflict of interest: None

A 67-years-old woman was admitted with pharyngodynia, left otitis media, left mucosal hyperemia and occult hematuria. The patient was seropositive PR3-ANCA (336EU) and needle renal biopsy revealed cellular crescentic glomerulonephritis. Thus, we diagnosed it as a systematic form of granulomatosis with polyangitis (GPA). Treatment with corticosteroid (PSL) and cyclophosphamide (CY) led to remission and a lower titer of PR3-ANCA (10.9EU), and then PSL was tapered to 10mg/day. However, after that she had bloody phlegm and PR3-ANCA level increased to 30.9EU. We suspected of recurrent GPA and alveolar hemorrhage, then performed bronchoscopy which revealed a nodule of left mainstem bronchus and bleeding of this nodule. Transbronchial biopsy identified granuloma with giant cell. These findings led to a diagnosis of relapse of GPA. She was given rituximab therapy, and then showed remission. Although this is recurrent case, it suggests that biopsy from the bronchus is useful for diagnosis of GPA.

P2-207

A patient showing RPGN associated with alveolar hemorrhage with dual positivity for anti-GBM antibody and MPO-ANCA

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Conflict of interest: None

A 70-year-old man admitted to our hospital because of fever, malaise and systemic edema for one month. Laboratory tests indicated that this patient had anemia (Hb 8.2 g/dL), renal dysfunction (s-Cre developed 1.89 mg/dL to 10.3 mg/dL for a month), and anti-GBM antibody and MPO-ANCA. We diagnosed him as rapidly progressive glomerulonephritis (RPGN). Metylpredonisolone 500 mg/day pulse therapy and predonisolone 40 mg/day had been started. However, alveolar hemorrhage was observed at the 16th disease day. Although, twice plasma exchanges improved alveolar hemorrhage, kidney function didn't improve and hemodialysis was continuously required. Respiratory condition gradually became worse, and he died at the 43rd disease day. Pathological analysis after his death showed that 70% of glomeruli had fibrotic crescent, and linear IgG deposit was detected at GBM. Moreover, fibrous extracelluar matrix was detected around lung small vessels, and the linear deposition of IgG was observed in lung capillary and alveolar wall. We reported herein the clinical course and pathological findings of a RPGN patient with alveolar hemorrhage, who was both positive for anti-GBM antibody and MPO-ANCA. with some literature reviews.

P2-208

Granulomatosis with polyangiitis limited to the sinus, preceded by eosinophilic pneumonia and diagnosed by repeated rhinosinus biopsy

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Conflict of interest: None

[Introduction] The positivity rate of ANCA is low in the patients with GPA limited to the upper respiratory tract. Even though the rhinosinus biopsy is important, its positivity rate is not high. Previous reports about appropriate biopsy procedures are scarce. We report a case of GPA limited to the sinus, preceded by eosinophilic pneumonia and diagnosed by repeated biopsy. [Case] 76 year-old man with dyspnea was diagnosed as eosinophilic pneumonia. High dose PSL was started and respiratory symptoms improved. During PSL tapering, nasal congestion appeared. His nasal membranes were extremely thickened without purulent rhinorrhea. CT scan revealed mucosal edema with bone erosion. Neither lung nor kidney symptoms manifested, and ANCA was negative. The nasal mucosal biopsy under local anesthesia, and with the endoscopic sinus surgery, the biopsy of several sinus sites was performed, but it showed

only nonspecific inflammation. The 3rd nasal mucosal biopsy was done and inflammatory granulomatous vasculitis with giant cells was observed. GPA was diagnosed. [Clinical significance] The eosinophilic pneumonia can precede not only EGPA but also GPA. The rhinosinus lesions in GPA may be skip lesions, and repeated biopsy may improve the definite diagnosis rate of sinus limited type GPA.

P2-209

A case of microscopic polyangiitis (MPA) with a high titer MPO-ANCA in pleural effusion

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Conflict of interest: None

A 65-year-old male had begun to experience numbness and weakness in the peripheral portion of both lower limbs in September 2015. He was admitted to our hospital because of appetite loss, general fatigue and dyspnea in November. On admission, he had a slight fever and numbness in both upper and lower limbs. Laboratory data showed WBC 19100/μl and CRP 15.25mg/dl. EMG showed multiple mononeuropathy. The level of serum MPO-ANCA was elevated (45.3 EU). Chest CT showed pleural effusion without interstitial pneumoniae. Level of MPO-ANCA in pleural effusion was markedly elevated (144 EU). Based on the presence of MPO-ANCA positivity and peripheral neuropathy, he was diagnosed with microscopic polyangiitis (MPA) with pleuritis. He was treated with prednisolone 40 mg/day and azathioprine 25 mg/day. His general condition immediately improved. Three weeks later, the level of MPO-ANCA in serum decreased (1.3 EU) and the pleural effusion disappeared. This was a unique case of MPA accompanied by pleuritis with a high titer MPO-ANCA in pleural effusion

P2-210

A case of microscopic polyangiitis with skin lesions treated appropriately by pathological assessment

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Conflict of interest: None

A 68-year-old male showed leg ulcers two years before coming to our hospital. Dermatologist diagnosed him as microscopic polyangiitis (MPA), because of pathologic findings and MPO-ANCA positive. The treatment with prednisolone (PSL) improved his symptoms and PSL was reduced gradually. But leg ulcers were not yet fully recovered and renal dysfunction appeared about seven months later. Because his disease activity was evaluated that grew worse, azathioprine and increased PSL improved his condition. After three months, he was transferred to our hospital for rehabilitation. We detected new skin lesions at his legs, so we suspected his disease activity grew worse and underwent skin biopsy. Although skin biopsy specimens didn't show vasculitis, atypical mycobacteria were detected. His skin lesions were improved not with antituberculous drugs but reduction of immunosuppression. In many cases of MPA, skin lesions are only organ involvement. In such cases, we must assess disease activity by the skin lesions. But some cases show infection is responsible for the skin lesions and we should consider that treatment is different for MPA. So we consider pathological examination is useful not only for diagnosis but also assessment of disease activity and determination of treatment strategy.

P2-211

A case of ANCA-associated vasculitis (AAV) developed in the course of systemic lupus erythematosus (SLE)

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Conflict of interest: None

It is rare to be complicated with AAV in SLE, but some cases have been reported. We report an autopsy case of AAV developed in the course of SLE. A 40-yrs female was diagnosed as SLE with discoid rash, arthritis, thrombocytopenia, antinuclear antibody positive, anti-Sm antibody positive in 2007. We performed high-dose steroid therapy. At the point of 12.5 mg of PSL, discoid rash and thrombocytopenia flared up, and we have maintained combination with tacrolimus. Although lower-extremity edema had developed from June 2014, she declined visiting hospital. On September 10, she was transported our hospital for severe dyspnea and clouded consciousness. On admission, she had severe edema, pleural effusion and ascites, pancytopenia, renal dysfunction and we performed steroid pulse therapy, plasmapheresis, hemodiafiltration under ventilation as severe lupus nephritis. Triggered by massive bowel bleeding, she dead by the multiple organ failure on the 32nd day of hospitalization. We performed autopsy under the agreement of the family. The autopsy findings showed that the glomerulus accepted deposition of IgG and C3, but there was severe necrotizing crescentic glomerulonephritis. Lupus nephritis and AAV were thought to be coexistent based on MPO-ANCA positive.

P2-212

A case report of ANCA associated vasculitis revealed by pleuritis

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Conflict of interest: None

<Presentation of case> A 69-year-old man with a history of alcohol cirrhosis and type 2 diabetes mellitus presented to our outpatient clinic with shortness of breath and weight loss that had started 2 month ago. Right pleural effusion was detected incidentally which was exudative. C-ANCA was 15.0 U/ml. There was no other sign of ANCA associated vasculitis at that time, so we carefully observed him. One month later he developed mild fever, sore throat and cough. Urine sediment showed red blood cell cast and granular cast. Creatinine was slightly impaired from his baseline. CRP was abruptly increased to 5.27 mg/dl. A kidney biopsy revealed a few fibrotic crescent formation. We started treatment with as ANCA associated vasculitis. Subsequent normalization of the creatinine and CRP level was obtained. A pleural biopsy showed only non specific inflammation. <Discussion & conclusion> Pleural effusion is a rare respiratory manifestation in c-ANCA associated vasculitis. We report this case with some literature review.

P2-213

A case of EGPA diagnosed with myocarditis and cardiogenic shock

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Conflict of interest: None

【Case】The patient is a 77 yo female with 20 years history of bronchial asthma. She had been well until 2 weeks prior to admission when she noticed weakness of right upper and lower extremities. She was admitted to her neighbor hospital for cerebral infarction. Laboratory tests taken at the time of admission revealed leukocytosis (19600/μl) with eosinophilia (69%) of unknown reasons. After admission, the patient also developed chest pain and cardiogenic shock, and was transferred to our hospital for intensive care. Although ANCA tests were negative, neurological examination at initial evaluation disclosed mononeuritis multiplex. Coronary angiography denied ischemic heart disease, and myocardial biopsy was done which showed myocarditis with infiltration of eosinophils. Based on findings above, diagnosis of eosinophilic granulomatous polyangitis (EGPA) was made, and methylprednisolone 60 mg / day was started. Her eosinophils decreased after initial dose of steroid,

and ejection fraction improved from 10% to 40% at day 10.【conclusion】We experienced a case of EGPA who presented with myocarditis and cardiogenic shock. Cloe Comarmond et al reported that 16.4% of EGPA patients have cardiac involvement. EPGA should be suspected in case of fulminant myocarditis with eosinophilia.

P2-214

Investigation of 4 case of Eosinophilic Granulomatosis with Polyangitis (EGPA) that caused acute Mononeuropathy multiplex with tissue biopsy

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Conflict of interest: None

【Object】To report of 4cases of EGPA that caused acute mononeuropathy multiplex with biopsy【Method】Case1, a 46-year-old man. Asthma since age45. Impossible to walk in40 days. Abnormal sensation of limbs and limb muscle atrophy. Decrease in limbs SNAP and CMAP by NCS. Eosin5060/μl, MPO-ANCA -, sural nerve tissue shedding of myelinated fibers. Case2, a 75-year-old female. Asthma since age50. Bedridden by abnormal sensation in14 days. NAP not evoked with NCS, eosin23700/μl, MPO-ANCA -, myelinated fibers in sural nerve. Muscle biopsy was performed from signal change part of MRI but no vasculitis finding. Case3, a 73-year-old female. There is sinusitis. Abnormal sensation and drop feet in 20 days. NAP not evoked, Eosin2150/μl, MPO-ANCA -, myelinated fibers in sural nerve. Case4, a 63-year-old female. Asthma since age50. Bedridden with abnormal sensation and muscle weakness in 2months. Eosin9950/μl, MPO-ANCA +, NAP not evoked, skin patch showed eosinophil infiltration around the blood vessel and fibrin deposits on the vessel wall.【Result】In 4cases, symptom progression stopped by steroid, but ADL was unchanged. Immunoglobulin therapy did no improvement in NCS.【Conclusion】Skin biopsy was useful, not neuromuscular biopsy. Mononeuropathy multiplex has decrease in ADL, early treatment is useful.

P2-215

A case of eosinophilic granulomatosis with polyangitis (EGPA) accompanied by anterior ischemic optic neuropathy

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Conflict of interest: None

A 61-year-old woman with 3-year history of bronchial asthma was hospitalized due to acalculous cholecystitis and was clinically diagnosed as eosinophilic granulomatosis with polyangitis (EGPA) from numbness at her arms and legs, erythema at her lower legs, eosinophilia and positive MPO-ANCA. High dose glucocorticoid (GC) including steroid pulse therapy was started and the abdominal pain improved. However, along with tapering GC, purpura-like eruptions appeared at her thighs and forearms and the numbness of her limbs worsened, requiring her 2nd hospitalization. On the 10th hospital day, blurred vision and the defect of the nasal visual field in her right eye occurred and the diagnosis of anterior ischemic optic neuropathy (AION) was made. Although the possibility of EGPA complicated with giant cell arteritis cannot be excluded as the biopsy of temporal artery could not be performed, the AION can be considered one of the manifestations of EGPA in this case showing a clinical feature typical as EGPA. Because EGPA is known to involve variety of sizes of vessels including medium-sized artery and the cases of EGPA accompanied by AION including our another case have been reported, the possibility of the development of AION should be in mind even in a case of EGPA.

P2-216

Intractable polyarteritis nodosa with Brodie abscess like findings on magnetic resonance imaging

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Conflict of interest: None

A 64-year-old man visited his primary care physician in July 2011 with swelling and pain in his ankles. He had right testicular tenderness, edema in lower legs, ulcers on both toes. Serum CRP levels was 17.8 mg/dL and urinalysis results were normal. Rheumatoid factor and ANCA were negative. Enhanced MR imaging revealed a testicular tumor-like lesion and slight contrast enhancement in the left anterior and posterior tibial muscles. Skin and testicular biopsy showed fibrinoid necrosis of medium- and small-sized vessels, indicative of polyarteritis nodosa (PAN). In January 2012, PSL (70 mg/day) and MTX (8 mg/week) were initiated to induce remission. Although the leg pain and swelling improved temporarily, his symptoms relapsed in June 2012. T2-weighted MR image with fat suppression showed high intensity area in right distal tibia with peripheral bone marrow edema, suspecting Brodie abscess. Bacterial pathogens were not identified in repeated needle aspiration and culture. On diagnosis as relapse of PAN, cyclophosphamide, rituximab, or tacrolimus were used concomitantly but disease was intractable. Four years after the first remission induction treatment, treatment with infliximab (IFX) was started in March 2016 and remission has been maintained by administering IFX every 8 weeks.

P2-217

Two cases of polyarteritis nodosa (PAN) diagnosed by angiography

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Conflict of interest: None

[Introduction] PAN is a rare disease, and often has difficulty in diagnosis. We report two cases of PAN diagnosed by angiography in our hospital. [Case 1] A 69 - year - old man. He was under postoperative follow-up of valvular heart disease, but he got fever, cough and had pleural effusion. CT scan reveals multiple hepatic arterial aneurysms accompanied by hemorrhage. We suspected PAN and performed abdominal angiography, multiple aneurysms were found in the hepatic, renal and colon arteries. In accordance with the diagnostic criteria of 2006, we diagnosed as suspected case of PAN, We started treatment with steroid pulse and cyclophosphamide. He has been well. [Case 2] An 80-year-old man who had been healthy all his life. He got fever, abdominal pain, and admitted our hospital. And one week later, he developed multiple organ failure. We suspected PAN and performed abdominal angiography, we found multiple aneurysms of hepatic artery and renal artery. As suspected cases of PAN, we started steroid pulse and plasma exchange therapy. But he died of multiple organ dysfunction. [Conclusion] We have experienced two cases of PAN diagnosed by angiography. PAN is reported as 1 year survival rate of 50% in case of no treatment. So early indication of angiography is important for the diagnosis

P2-218

A case of cutaneous polyarteritis nodosa diagnosed by mammotome breast biopsy

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Conflict of interest: None

[Case] A 72-year-old woman was diagnosed with localized polyarteritis nodosa of the breast. The patient presented with breast pain, breast lump, slight fever, and general fatigue for a month. She was consulted to our department. The lump of right breast was 10mm in diameter, and with associated erythema. Laboratory test showed elevated levels of C-reactive protein and erythrocyte sedimentation, but not autoantibody positivity. Breast cnacer was denied with mammography and ultrasonography. Mammotome breast biopsy revealed medium and small-sized arteritis. Invasion of histiocytes was also observed and diagnosed as polyarteritis nodosa. There were no major organ lesions, and she was diagnosed as cutaneous polyarteritis nodosa localized to the breast. Prednisolone therapy begun and her symptoms disappeared. [Conclusion] This is rare case of polyarteritis nodosa. As it may be necessary to distinguish from malignant tumors, biopsy is considered important for diagnosis and treatment.

P2-219

Two cases of refractory skin ulcer complicated with polyarteritis nodosa (PAN) successfully treated with adalimumab (ADA)

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Conflict of interest: None

We report two cases of PAN successfully treated with adalimumab. [Case 1] A 51-year-old man who diagnosed with PAN 2 years ago. Treatments with prednisolone (PSL), intravenous cyclophosphamide (IVCY), methotrexate (MTX), azathioprine (AZA), and etanercept (ETN) were unsuccessful. His ulcers improved by additional treatment with ADA. [Case 2] A 40-year-old man who diagnosed with PAN about 20 years ago. Treatments with betamethasone (BT), IVCY, MTX, mycophenolate mofetil (MMF), rituximab (RTX), ETN and intravenous immunoglobulin (IVIg) were unsuccessful. His ulcers also improved by additional treatment with ADA. It is possible that ADA administration is useful treatment for refractory skin ulcer complicated with PAN.

P2-220

A case of the polyarteritis nodosa that complicated trochlear nerve paralysis

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Conflict of interest: None

A 71 years old woman presented with polyarthritis and fever. She consulted this hospital and became the hospitalization. In a medical examination, MCP joints and PIP joints showed multiple joint swelling. And CRP, RF and the anti CCp antibody were positive. Because peripheral joints showed synovitis by the joint ultrasonography, RA was strongly suggested. However, we considered other inflammatory disorder because a febrile symptom and tenderness of both gastrocnemius were detected. In 3DCTA, the renal and splenic artery showed microaneurysm. Also, vasculitis with fibrinoid necrosis was detected in the gastrocnemial biopsy that accepted a muscle ache. Polyarteritis nodosa (PN) was diagnosed than the above. A diplopia developed between the hospitalization close inspections. Because there was no abnormality in MRI and MRA, mononeuropathy with PN was suggested. After 40 mg/day of PSL administration, the inflammatory reaction, the arthralgia and the muscle ache were relieved immediately. Also, the diplopia disappeared in around three weeks. As for the case of the trochlear nerve paralysis with the vasculitis, several cases are reported in GPA. We report the merger of polyarteritis nodosa and the trochlear nerve disorder as a very rare and valuable case.

P2-221

Death due to rupture of abdominal aneurysm in a patient with polycystic kidney disease, despite treatment for suspected polyangiitis nodosa: A case report

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Conflict of interest: None

[Case] An 85-year-old male was admitted with lethargy, dyspnea, and hemoptysis for 3 days. Vital signs were nearly normal, but bilateral wheezes and pitting edema of his legs were noted. Laboratory tests showed creatinine 13.49 mg/dL, C-reactive protein 1.68 mg/dL, urinary protein 3+, and urinary occult blood 2+. Computed tomography (CT) revealed bilateral ground-glass opacity and cysts in kidneys. We suspected microscopic polyangiitis and administered methylprednisolone 1 g/d for 3 days, followed by prednisolone 60 mg/d. Urine output gradually increased, but the patient complained of abdominal pain on the 15th hospital day. Enhanced CT showed extravasation from the splenic artery, and angiography showed a bead-like aneurysm; transcutaneous arterial embolization was performed. However, he rebled and died that night. [Pathology] Microscopic examination revealed disruption of the tunica media and a pseudoaneurysm. Vasculitis was not detected. [Discussion] We considered polyangiitis nodosa following angiography. However, pathology did not detect findings of vasculitis. We surmised that rupture of an aneurysm in association with polycystic kidney disease caused his death. This pathologic condition must be considered when polyangiitis nodosa is suspected.

P2-222

A case of necrotizing vasculitis in the liver

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Conflict of interest: None

Necrotizing vasculitis is rare in the liver. We here report a case of necrotizing vasculitis in the liver. A 38 year-old man was introduced to our hospital, because he was suspected to have vasculitis. The patient was well until he felt abdominal pain 2 months before admission in our hospital. He visited the previous hospital where CT scan revealed gallbladder wall thickening and patchy enhanced lesions in the liver. In the diagnosis of cholecystitis, cholecystectomy and liver biopsy were performed. In the liver biopsy samples, vasculitis was found and referred to our hospital. On the admission, the patient complained, abdominal pain. He did not present fever, skin rash, and peripheral nerve symptoms. Lab tests were normal except elevation of CRP levels and ALP autoantibodies including ANCA were negative. Abdominal angiography showed no abnormalities. The liver biopsy samples revealed necrotizing vasculitis with the destruction of the elastic layer of the small artery. Based on these findings, the patient was diagnosed as having liver restricted vasculitis, which was considered as isolated organ limited vasculitis or a part of MPA with no evident vasculitis in other organs.

P2-223

Tocilizumab might be effective for polyarteritis nodosa complicated with rheumatoid arthritis

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Conflict of interest: None

[Case] Forty-three-year-old female patient had suffered from spontaneous pain of both lower thighs and polyarthralgia from 4 months before the first presentation to our hospital. Subsequently livedo reticularis and dysesthesia had appeared on both lower thighs and her weight had decreased by 8 kg during the 4 months. Therefore she was introduced to our hospital. The patient was diagnosed as RA with polyarthralgia and laboratory data (CRP 9.22 mg/dl, ESR 128 mm/h, RF 26 u/ml). At the same time, she was pathologically diagnosed as polyarteritis nodosa (PAN) by skin biopsy. PSL (50 mg/day) was administrated. Physical and laboratory findings improved promptly. PSL was gradually decreased to 9 mg/day in combination with etanercept. However, new subcutaneous nodules appeared at left upper arm, left thigh and both lower thighs. So the dose of

PSL was raised to 20 mg/day and etanercept was changed to tocilizumab. Subcutaneous nodules disappeared promptly then. Though the amount of PSL was decreased to 9 mg/day within one month, the remission of PAN was maintained with tocilizumab. [Clinical meaning] The effectiveness of biologics for PAN has not yet been established. This case suggests that tocilizumab might be effective for induction and maintenance of remission of PAN.

P2-224

The impact of pulmonary involvement on treatment of rheumatoid arthritis

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Conflict of interest: None

Object: To examine the effect of the pulmonary involvement on treatment of the patients with rheumatoid arthritis (RA). Method: Subject were outpatients in Tokyo Metropolitan Komagome Hospital division of systemic immunological diseases from September1 -31 2016. Suevey items were age, sex, duration of RA, type of pulmonary involvement, drugs, serum level of RF, anti CCP antibody, CRP and ESR. Result:330 RA patients were recruited (male=70. female=260 ratio=0.269). Mean age was 69±12y.o. Disease duration was 140±123 months. RA with pulmonary involvement was 113 (male=29, female=84. ratio=0.345). RA only patients was 217 (male=41, female=176, ratio=0.23). Pulmonary involvement included interstitial pneumonia (N=39), organizing pneumonia (N=11), airway diseases (N=29), old tuberculosis (N=13), nontuberculous mycobacteria (N=11), pleurisy (N=2). Pulmonary involvement group had more male patients, positivity and power of RF and anti CCP antibody was high, frequency of corticosteroids and ST use were high, MTX was less prescribed and major biologics DMARD was abatacept (ABT). Conclusion: RA patients with pulmonary involvements had high titer of anti-CCP andibody and were less prescribed drugs which may injure lungs and more used ABT.

P2-225

Mortality of lung disease in rheumatoid arthritis : data from the Japanese diagnosis procedure combination database

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Conflict of interest: None

Lung disease is one of main cause of mortality in rheumatoid arthritis. This study analyzed statistics in lung disease of rheumatoid arthritis using the Japanese diagnosis procedure combination (DPC) database. Data were collected between July 2007 and March 2014 and included patient information on diagnoses coded of rheumatoid arthritis. A total of 375,539 patient (73% female) records were available. Mean age was 66.5. The mortality rate was 3.8%. Data were classified by reasons for hospital admission, the mortality rate was calculated for each reason. The rate was 11.0% with lung disease, 7.1% infection, 5.8% cardiovascular disease, 5.8% neoplasm. Among lung diseases, the mortality rate of interstitial lung disease was 16.0%, lung disease caused by extrinsic factor including drugs 14.6%, pneumonia 9.2%. Multivariate logistic regression analysis was performed to define risk factor for mortality of lung disease. Male, older age, Carlson comorbidity index≧2, using no drug were associated with the mortality.

P2-226

Survey of RA patients' consciousness for infectious disease risk

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Conflict of interest: None

[Objective] Knowledge and consciousness of RA patients for infectious disease were surveyed. [Patients and methods] 120 patients (20 male and 100 female, average 64.9 years old) who were receiving RA treatment were surveyed by the questionnaire about infectious disease which was made originally. The questionnaire contains susceptibility to infection totally or specifically, and typical symptom of the pneumonia. [Results] Patients who recognized the name of the RA drugs which they took was 92%. Patients who recognized susceptibility to infection was 78%. Patients who knew the risk of pneumonia were approximately 50%, and patients who knew the risk of hepatitis B, tuberculosis and fungal infection was 10-20%. There were few patients who knew the typical symptom of each disease, and the examination items for the infection screening. [Conclusion] It is essential for RA patients to recognize the immunosuppressive state of themselves and the possible symptom of the adverse events. Patients didn't know the risk of the infection as well as the name of RA drugs which they took. Face to face patient education by the medical staff is necessary to educate the specific and individual risk of infection for the safer RA treatment.

P2-227

Risk factor of cytomegalovirus infection in rheumatic disease patients treated with moderate to high dose prednisolone

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Conflict of interest: None

[Objective] The purpose of this study is to investigate the risk factor of cytomegalovirus (CMV) infection in rheumatic disease (RD) patients treated with more over moderate dose PSL (0.5mg/kg/day). [Method] One hundred forty-eight patients who have treated with moderate to high dose PSL between April 2012 to March 2015 were enrolled, and the clinical and laboratory data were analyzed. [Results] The dominant underlying diseases were angiitis (n=38), SLE (n=35), PM/DM (n=27) and RA (n=17). Fifty-seven patients were treated with pulsed methyl-PSL, 93 patients with immunosuppressive drugs. CMV antigenemia test was examined for 422 cases, 32 patients were diagnosed with CMV infection. The median interval to onset was 28 days. By ROC analysis, a level of $5/10^4$ WBCs was determined to be the optimal threshold value (sensitivity:81.2%, specificity:66.9%). Treatment IVCY, concomitant comorbidity of diabetes mellitus and elevation of serum AST levels at week 2 after the administration of PSL were identified as significant risk factors for CMV infection. [Conclusion] CMV antigenemia screening test may be important for RD patients treated with more over moderate dose PSL, especially in cases with IVCY, concomitate diabetes mellitus and liver disorder.

P2-228

Consideration of the advantage of in-hospital measurement of beta-D-glucan in our hospital

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Conflict of interest: None

[Objectives and methods] With the rise of recent advancement of medicine, opportunistic infection increasingly pose a severe problem. Our clinical laboratory made up the transition from outsourcing to in-hospital measurement of beta-D-glucan (BDG), known as a biomarker of invasive fungal infections and pneumocystis pneumonia (PCP), in July 2014. We investigated the trend of number of samples of BDG before and after introduction of in-hospital measurement and clinical background in

each cases. [Results] The number of samples of BDG increased from 1023 to 1232 tests per year after introduction of in-hospital measurement. From July 2014 to July 2015, 429 samples have ordered from the Department of Rheumatology and about 91% of these samples were from patients prescribed immunosuppressive drugs. 15.4% were positive including 7 cases of PCP and 5 cases of mycotic diseases. The average of serum level of BDG in group considered as false positive was significantly lower than the level in PCP and mycosis. All PCP patients were cured with early initiation of effective treatment. [Conclusion] Introduction of In-hospital measurement of BDG was beneficial to reduce laboratory turnaround time and to lead to early diagnosis and intervention of PCP and mycosis.

P2-229

Clinical characteristics and outcome of Pneumocystis pneumonia with collagen vascular disease in our department for the past 10 years

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Conflict of interest: None

Objectives: To examine the clinical characteristics and outcome of *Pneumocystis* pneumonia (PCP) in our department over the past 10 years. Methods: We review patients with PCP and concomitant collagen vascular disease (CVD), who admitted to our hospital between '06 and '16. Diagnosis of PCP was established by clinical history, imaging findings, β-D-glucan, KL-6, and PCR examinations of sputum. Results: The 32 patients (19 women), aged 45 to 89 (mean 71.1) were enrolled. The CVD of 32 patients consisted of rheumatoid arthritis (RA) in 15 cases and non-RA in 17: MPA in 9, DM/PM in 3, SLE in 2, and GPA, SSc, GCA in 1. In the RA cases, 13 cases (87%) used MTX and 4 (27%) used biologics. In the non-RA cases, the average dose of prednisolone used at onset of PCP was 0.5 mg/kg. 75% of the patients were above 65 years old, and 53% of the cases had past history of pulmonary disease. While 16 cases (50%) survived PCP, the fatal cases showed low albuminemia and high A-aDO_2. Prophylactic treatment with SMX-TMP was used in two cases. Conclusion: Although newly developed treatment such as biologics and immunosuppressants became available for CVD, further study on the risk factor, pyophylaxis, and treatment of infections seemed indispensable to improve the outcome.

P2-230

A case of polymyalgia rheumatic that developed pneumocystis pneumonia during receiving low dose of steroids

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Conflict of interest: None

A 79-old-man. Arthralgia and muscle pain of his whole body appeared in March X. He was admitted to our hospital and diagnosed with polymyalgia rheumatica. He also had exacerbation of diabetes mellitus. After controlling for the treatment of diabetes, he was received prednisolone (PSL) 15 mg / day and the above findings improved markedly. PSL was tapered to 10 mg / day in May. After that he began to have shivering, palpitations and shortness of breath. Computed Tomography scans showed ground-glass opacities in the lung field. He was diagnosed with pneumocystis pneumonia (PCP), based on detection of *Pneumocystis jirovecii* DNA in sputum and high serum levels of β-D-glucan. He was treated with sulfamethoxazole-trimethoprim mixture and high doses of steroids, and improved. Generally, risk factors for PCP in non-AIDS patients are known to receiving more than moderate doses of steroids. Although the scientific basis for PCP prevention is poor, preventions are often not done when using low doses of steroids. But there are some reports of PCP in patients receiving low doses of steroids. Even when using low doses of steroids, we should evaluate the patient's condition in a limited basis, and we use preventions or explain the possibility of PCP onset as necessary.

P2-231

Prognosis of Rhumatoid Arthritis patients complicated with deteriorated and hospitalized ideopathic pneumonia

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Conflict of interest: None

(Purpose) We exammined the prognosis of RA patients complicated with ideopathic pneumonia. serous illness patients with deteriorate and hospitalized and patients with natural course were compared. (Method) Among the RA patients with IP followed in our hospital from 2012 to 2016 Oct, two groups were set up.10 patinets were deteriorated and hospitalized and recieved steroid pulse therapy, 15 patiens have treated as an outpatient without serious illness. RA and IP illness duration, medication, IP condition was compared. several factors about RA and IP condition and medication at the final examination were also compared. (Conclusion) Two patients were dead in the serious IP group. But significant difference was not observed about an average dose and medicated percentage of TAC·MTX·PSL and compasite measure of RA DAS28·CRP·MMP3, indicated IP condition of KL-6 and ΔTSS.

P2-232

Two patients with rheumatoid arthritis who complicated NTM and further developed pneumothorax

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Conflict of interest: None

[Case 1] A 73-year-old man. RA onset in 2009. He was treated with DMARDS 3 agent and PSL 5 mg. Added ETN from 2011. Because of insufficient effect, changed from February 2013 to TCZ. Although respiratory symptoms were not observed, pneumothorax developed in April 2013. Cavitary lesions were found in the upper right lung field by CT, and M. intracellulare (Gaffky. 9) was observed from the lesion, which was considered to be pneumothorax by NTM. [Case 2] 74-year-old man. RA onset in 2000. TCZ was used, but diagnosed as NTM (M. intracellulare) July 2015, TCZ was canceled. He was treated with 1 mg of TAC and 7 mg of PSL, but developed pneumothorax in May 2016.【Progress of 2 cases】Both cases were treated with three antibiotic combination therapy and bronchoscopic embolization. It took a long-term hospitalization for about 6 months.【Discussion】Bio use for RA complicated NTM is out of contraindications of usage guidelines. NTM is also increasing in Japan, and it is expected that bio-use for RA complicated NTM will increase in the future. However, NTM has a higher pneumothorax merger rate than tuberculosis. The rate of pneumothorax incidence and therapeutic response in NTM-associated rheumatoid arthritis cases is unknown, and accumulation of cases is important.

P2-233

SAPHO syndrome-like presentation by disseminated nontuberculous mycobacteria (NTM) infection in a case with anti-IFNg autoantibody

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Conflict of interest: None

A 55-year-old man admitted to our hospital complaining of 2-month

history of fever and 4-week history of polyarthralgia and palmoplantar pustulosis. MRI scan and bone scintigraphy showed Th5-7 spondylitis and arthritis of bilateral sternoclavicular joints, sacroiliac joints, wrists and ankles. We diagnosed him as SAPHO syndrome and initiated prednisone (10mg/day) and TNFα inhibitor, which soon relieved his symptoms. After discharge, his symptoms recurred a week after every administration of TNFα inhibitor. He gradually developed right cervical lymphadenopathy and headache and was re-admitted 2 months after the discharge. The biopsies of the lymph node and bone marrow, and the positive cultures from the lymph node, sputum and blood lead to the diagnosis of disseminated NTM (M. intracellulare) which was complicated with cryptococcal meningitis. While he was HIV-negative, additional tests revealed he was anti-IFNγ autoantibody positive from the former admission. HIV infection is the leading cause of disseminated NTM; however, there are many case reports showing the association with anti-IFNγ autoantibody in Asia. This case report highlights that disseminated NTM can present with reactive pustular skin lesions, polyarthritis and spondylitis which can mimic SAPHO syndrome.

P2-234

Successful treatment of tocilizumab for a rheumatoid arthritis patient suffered from mycobacterium avium infection

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Conflict of interest: None

[Background] Biological agents are generally contraindicated to patients with rheumatoid arthritis (RA) suffered from nontuberculous mycobacteria infection. Recently it has been suggested that biological agents can be administered for RA patients complicated with mycobacterium avium complex (MAC) that has nodular or bronchiectasis lesions in lung. I report a case of RA with MAC successfully treated with tocilizumab (TCZ). [Case] A 74-year-old man with a six-year history of RA on methotrexate 14 mg weekly and prednisolone 6 mg daily. He was diagnosed as MAC infection at age 68 due to positive culture of MAC twice and bronchiectasis in lung. He was treated with clarithromycin, ethambutol, and rifampicin, but MAC was still positive after eight months after treatment. His RA activity had been high and TCZ treatment was started. Five months after TCZ treatment, his RA activity was improved and low disease activity or remission has been maintained for 19 months. MAC infection has been well controlled because pulmonologist examined his chest XP every month. Cultures of MAC has been negative for 13 months and XP findings has not been exacerbated. [Clinical significance] TCZ can be used safely for RA under strict control of MAC infection.

P2-235

A case of wrist tendon sheath synovitis due to nontuberculous mycobacteriosis with SLE

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Conflict of interest: None

We describe a case of wrist tendon sheath synovitis due to nontuberculous mycobacteriosis, which was complicated by systemic lupus erythematodes (SLE). The patient was a 64-year-old woman with SLE gradually developed swelling and pain on the left wrist without trauma. She was found to have synovitis on the palmar side of the left wrist in November 20XX and underwent synovectomy. Pathological examination of the synovial tissue extracted during surgery showed, only findings of noncaseating granuloma with Langerhans cells. *Mycobacterium intracellulare* were identified in PCR of the synovial tissue from the swollen wrist area, therefore, antibiotic therapy for 21 months with rifampin and clarithromycin improved the symptom. Swelling has not recurred in 21 months during the chemotherapy of NTM. After nine months of finishing the chemotherapy, she was found the swelling and pain of her left wrist again. Because she was diagnosed the relapse of wrist tendon sheath synovitis due to nontuberculous mycobacteriosis, she was started the medication. Synovitis due to nontuberculous mycobacteriosis is often difficult to diagnose and often recurred, because it presents with nonspecific clinical findings and similar to the arthritis of collagen diseases.

P2-236

Two cases of Nontuberculous Mycobacterial Spondylitis of autoimmune diseases treated by Vertebral Fixation

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Conflict of interest: None

Recently nontuberculous mycobacterial (NTM) infection has been reported as a complication of autoimmune diseases. We treated two cases of NTM spondylitis developed with DM and RA. **Case1.**67 year-old woman treated for DM had back pain and fever. Laboratory data and imaging suggested inflammatory reaction and collapsed L1 vertebral body, and the surrounding abscess compressed spinal canal. Needle biopsy showed the existence of M.avium. We treated for this spondylitis with CAM and anti-tuberculous drugs, but the infection did not get well, and then we performed anterior and posterior vertebral fixation. **Case2.**65 year-old woman treated for RA with ADA and MTX had back pain and fever. Laboratory data and imaging suggested inflammatory reation and abscess pooling around Th10 vertebral body. Needle biopsy showed the existence of M.intracellurare. We treated for this spondylitis with CAM and anti-tuberculous drugs, but abscess expanded. Then we performed posterior vertebral fixation and removal of her abscess. **Discussion** Because NTM spondylitis is very rare, we cannot diagnose it immediately. If we cannot heal their infection with chemotherapy, we should perform surgical treatment. We should know the fact that patients treated with immunosuppressive agents have high risk of NTM infection.

P2-237

Foscarnet improves both herpes zoster and cytomegarovirus antigenemia in patient with systemic lupus erythematosus: A case report

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Conflict of interest: None

A 22 year-old-woman was diagnosed as systemic lupus erythematosus (SLE) 8 years ago and started oral prednisolone (PSL) and azathioprine. Three months ago, she developed hemophagocytic syndrome accompanied with relapse of SLE, and improvement was obtained by combination therapy of mPSL pulse, cyclosporine and mycophenolate mofetil. During the course of therapy, cytomegalovirus (CMV) antigenemia was observed (C7 HRP 14/50000) and ganciclovir (GCV) was administered. Due to bone marrow suppression, which was suspected as a side effect of GCV, we changed from GCV to foscarnet (PFA) and CMV antigenemia was improved. She was admitted to our hospital with bullous rash from the vulva to the left thigh. Acyclovir (ACV) was started with diagnosis of disseminated herpes zoster. Three days after the administration, CMV antigenemia were observed (C7 HRP 5/50000). We changed from ACV to PFA for both herpes zoster and CMV antigenemia and improved it. Unlike herpes simplex virus and varicella-zoster virus, CMV has no thymidine kinase which is a virus-specific enzyme. Therefore, ACV is ineffective and GCV or PFA is effective to CMV. This case suggested that the selection of antiviral drugs in consideration of the mechanism of action is important when complications of viral infections.

P2-238

A case of MCTD with exacerbation of myositis triggered by cytomegalovirus (CMV) infection

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Conflict of interest: None

An 82 year old woman diagnosed with MCTD. Raynaud's symptoms were observed, and anti-U1-RNP antibody was recognized. Moreover MCTD could be diagnosed by poly arthritis, scleroderma etc. The administration of steroids was not carried out, only NSAIDs were carried. During the follow-up observation, a slight fever was observed, and it was difficult to ascend or descend the stairs, and the muscle weakness findings up to MMT4/5 in the proximal muscle of the lower extremity were observed. In the laboratory findinds were observed. CPK 221 (H) showed mild rise,aldolase 8.7 (H),myoglobin 140.5 (H) as myogenic enzyme were increased. Initially, considering deterioration of myositis of MCTD, it started from administration of PSL 20mg/day. Consequently, myositis have been improved..But CD4/CD8 ratio tended to decrease to 0.29 (L), and when the suspected merger of virus infection was suspected. So laboratory datas showed CMV IgG 123 (H), CMV IgM 1.59 (H), CMV p65 antigen positive, these dataes showed the possibility causing deterioration of myositis triggered by CMV infection.

P2-239

A case of successful in treating cytomegalovirus enteritis and encephalitis with abnormally high cytomegalovirus pp65 antigen during rheumatoid arthritis treatment

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Conflict of interest: None

A 82-years-old female patient. She was diagnosed with rheumatoid arthritis in 2002. In 2006, she was treated with prednisolone (PSL) and steroid joint injection. In November 2015, she transferred to internal medicine, and we started PSL10mg, Tacrolimus 1mg, Avatacept 500 mg, and steroid joint injection. In June 13th, 2016, she was hospitalized with suspicion of acute enteritis or cholecystitis. The cytomegalovirus (CMV) pp65 antigen (CMV-Ag) was 2241/2 slides (C10, C11 method), and we diagnosed with CMV enteritis. We started ganciclovir (GCV) 10mg/kg/day, and we administered immunoglobulin (high titer of CMV) for 3 days. She had got consciousness disturbance, and MRI showed periventricular inflammation, we diagnosed with CMV encephalitis. Gastrointestinal symptoms and consciousness status improved gradually, and CMV-Ag was 0 / 2 slides on July 4th. However, we continued to administer GCV because she had meaningless conversation. We confirmed negative of CMV-DNA quantification, and stopped GCV on August 2nd. Her meaningless conversation disappeared, and she was discharged. In immunosuppressed patients, CMV infection is an important complication affecting prognosis. We report a case of successful in treating CMV enteritis and encephalitis with abnormally high CMV-Ag.

P2-240

A case of Epstein-Barr virus-associated enteritis with hemorrhagic shock in a patient with rheumatoid arthritis

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Conflict of interest: None

【Object】We report a case of Epstein-Barr virus (EBV) -associated enteritis with hemorrhagic shock treated with rituximab (RTX) and surgery in a patient with rheumatoid arthritis (RA). 【Methods and Results】A 64 year-old man with RA was treated with prednisolone, methotrexate and infliximab. He complained of intermittent abdominal pain one month before admission, and the pain was becoming more severe. A few days after admission, a small-bowel perforation was found and surgically closed. *Listeria monocytogenes* was detected in blood culture, and he was treated with antibiotics. The abdominal pain did not ameliorate, and hematochezia followed it. Ganciclovir was used for presumed cytomegalovirus infection, but hematochezia continued, resulting in hemorrhagic shock. Copies of EBV DNA of blood and ileocecal tissue samples were detected by Real Time PCR at high levels, and EBV-encoded small RNA was immunopathologically positive. Steroid pulse therapy was not effective, then RTX was used. The signs and symptoms of enteritis were getting better, but bleeding continued, then surgery was performed. The enteritis was led to complete remission. 【Conclusions】EBV-associated enteritis is a differential diagnosis in RA patients with abdominal pain, and RTX is an effective treatment option.

P2-241

The immunosuppression caused by the treatment for rheumatoid arthritis developed chikin pox in a patient having the immunity against varicella-zoster virus

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Conflict of interest: None

A seventy-six old woman was referred to our hospital because of high fever, generalized eruption, abnormal biomarkers indicating hepatocellular damage, and thrombocytopenia. She had been suffering from rheumatoid arthritis (RA) for ten years and was receiving methotrexate MTX (10mg/week) and prednisolone (5mg/day) at the presentation. Although she had acquired the immunity (positive IgG antibody and negative IgM antibody against varicella-zoster virus), she was diagnosed clinically as having chikin pox from the nature of her eruption. MTX was terminated and acyclovir was given to her for seven days. Then, the biochemical makers and platelets normalized gradually. At day 10, her blister became into scabs and C-reactive protein became negative. The histopathological examination of her skin showed the denaturation of epidermis and intraepidermal bulla. The immunostaning for virus specific antigen showed the presence of varicella-zoster virus. We considered the immunosuppression caused by the treatment for RA developed chikin pox in a patient having the immunity against varicella-zoster virus. We would like to discuss the immunosuppressive aspects of the treatment for RA.

P2-242

A case of acute hepatitis C in a patient with rheumatoid arthritis

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Conflict of interest: None

We report a case of a 68-year-old man who had been treated with MTX for RA in our hospital since January 2016. Because his disease activity was uncontrolled, he had received infliximab (IFX) treatment from April. IFX therapy was effective in his RA, but his treatment was stopped by infusion reaction of IFX at July. On September 1, he was admitted to our hospital for fatigue and jaundice. In laboratory data, AST, ALT, and T-Bil were elevated and he was diagnosed acute hepatitis. However we confirmed that HCVAb were negative before the administration of IFX, this antibody and HCV-RNA was positive on admission. Therefore he was suspicious acute hepatitis by HCV. He was treated with a combination of glucocorticoid and IFN β to hepatitis C, and then his condition was improved. Most patients infected with HCV are asymptomatic, and HCV infection is often persistent, suggesting that HCV has low antigenicity, and inhibits host immune response. In our case, we considered that the development of his hepatitis C related to withdrawal of IFX therapy because immune system suppressed by IFX is possible to proceeding to recovery phase. 【Conclusion】We should think that Acute hepatitis on RA patients may be caused by HCV infection besides drug induced or HBV

reactivation.

P2-243

A Case of Hepatitis E Virus Infection accompanied with Rheumatoid Arthritis

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Conflict of interest: None

A Case of Hepatitis E Virus Infection accompanied with Rheumatoid Arthritis A 64-year-old woman with rheumatoid arthritis (RA) had been treated solely with prednisolone (PSL) 5 mg/day for 22 years. In addition, Salazosulfapyridine (SASP) and methotrexate (MTX) have been administered since 1999 and 2003 respectively, which resulted in RA being a low disease activity. She started complaining about fatigue and appetite loss 4 months prior to admission. The abdominal ultrasonography and CT examination did not show any conclusive results. On the other hand, the laboratory data showed that liver transaminase and biliary enzymes were high (GOT 94 IU/L, GPT 167 IU/l, ALP 606 IU/L, γGTP 111 IU/L). After 4 weeks, the liver transaminase and biliary enzymes were abnormally higher (GOT/GPT=142/172). Over the past 3 years, she had taken MTX 10mg/week, and no new medication was received. On her laboratory data, the results for hepatitis B and C infections showed negative. She was placed on bed rest, and her liver dysfunction was improved. The HEV-IgA test was positive, so hepatitis E was eventually diagnosed. We should take hepatitis E into consideration when liver dysfunction is found in individuals under immunosuppression.

P2-244

Nocardia bacteremia and lung abscesses in a patient with SLE during induction therapy for lupus nephritis with MMF and glucocorticoids

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Conflict of interest: None

We report a case of nocardiosis in a patient with systemic lupus erythematosus (SLE) during induction therapy for lupus nephritis with MMF and glucocorticoids. A 15-year-old woman was diagnosed SLE in 1977. She had been treated with prednisolone (PSL). When she was 54 years old, in March 2016, she develops proteinuria. Renal biopsy specimen revealed lupus nephritis type III (A/C) + V. We started to treat her by induction therapy with methylprednisolone pulse followed by PSL 30mg/day and MMF 3g/day. After three months, she was admitted again because of multiple lung masses and high levels of C reaction protein (CRP). She was diagnosed pulmonary nocardiosis and nocardia bacteremia. Then, she was treated with imipenem-cilastatin and trimethoprim-sulfamethoxazole followed by oral amoxicillin-clavulanate. Her general condition and lung pulmonary nocardiosis were improved. Nocardia is a pathogen that can cause in immunocompromised hosts. While some reports of nocardia infection affected of organ transplantation recipient with MMF has been shown, there are only few reports of nocardia infection in a patient with SLE during induction therapy for lupus nephritis with MMF and glucocorticoids.

P2-245

A case of 64 years old woman *Nocardia brasiliensis* infection during treatment of alveolar hemorrhage in systemic lupus erythematosus

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Conflict of interest: None

A 64 years old woman, who had taken prednisone 30mg for systemic lupus erythematosus, was admitted complaining fever, dyspnea on exertion and infiltrative shadow. The bronchoalveolar lavage revealed alveolar hemorrhage, so pulse steroid therapy and intravenous cyclophosphamide were started on the 7th hospital day. Her symptom and infiltrative shadow were improved. But on the 52th day, fever and disturbance of consciousness occurred. Cerebrospinal fluid examination revealed the amount of neutrophil and protein increased and head MRI revealed multiple cerebral infarctions and aneurysm. We suspected infectious endocarditis and started antibiotics. 4 sets of blood cultures were negative. On the 59th day, subcutaneous abscess occurred and the result of gram and kinyoun acid fast stating revealed beaded acid bacilli, which suggested nocardia infection. The result of culture was Nocardia brasiliensis. We administered sulfamethoxazole-trimethoprim. On the 66th day, she died of cerebral hemorrhage. Nocardia often causes pneumonia, cutaneous infection and brain abscess in immunocompromised patients. Nocardia bacteremia is rarely documented. If blood culture is negative, it's important to check lung involvement and existence of abscess and suspect nocardia infection with gram stain.

P2-246

A case of clinically amyopathic dermatomyositis (CADM) accompanied with disseminated nocardiosis

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Conflict of interest: None

[Case] A 63-year old Japanese woman [Chief complain] cough, dyspnea on exertion, skin rash on precordia, back of the hands, and front of the knee. [History of present illness] Three weeks before admission, the patient had fever elevation, dry cough, dyspnea on exertion, and skin rash on precordia, back of the hands, and front of the knee. She prescribed a course of antibiotics and NSAIDs, while was not effective. Laboratory data revealed leukocytosis, elevation of serum CRP and ferritin level, ESR, however, serum level of CK, aldolase, AST, and ALT were not elevated. Her rash was typical for dermatomyositis. We diagnosed her as clinically amyopathic dermatomyositis and started of treatment with steroid and immunosuppressive agents. Fever and rash improved gradually, but chest CT showed mediastinal emphysema and cavitation in left inferior lobe. Then, the culture test of bronchoalveolar fluid revealed Nocardia farcinica. Brain MRI showed brain abscess. Then we started treatment of antibiotics. [Summary] We report a case of clinically amyopathic dermatomyositis (CADM) accompanied with disseminated nocardiosis.

P2-247

Parvovirus B19 infection with ACPA positivity and organized pneumonia

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Conflict of interest: None

A 40-year old woman with no past medical history presented for workup of slight fever and migratory arthralgia appeared before 3 weeks ago. At the examination, she had right wrist, knee, ankle pain. With ultrasonography, there were active synovitis, and with chest CT, there were a consolidation with airbronchogram at lower lung field. Because of positive test for parvovirus B19 IgM antibody, we treated her with NSAIDs and low dose DMARDs. arthritis and lung consolidation resolved spontaneously, and ACPA titer decreased. It is well known that parvovirus B19 is associated with RF, anti phospholipid antibody, and anti nuclear antibody, but there are few reports that showed the association between parvovirus and ACPA. This case might showed the relationship between parvovirus infection and ACPA positivity.

P2-248

Three cases of autoimmune diseases with parvovirus B19 infection

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Conflict of interest: None

We experienced three cases of autoimmune diseases with parvovirus B19 (PVB19) infection. First, 32year-old woman, who had arthralgia, developed fatigue, neck lymphadenopathy and fever and diagnosed systemic lupus erythematosus. She had elevated serum titer of PVB19 and positive PVB19 DNA-PCR in bone marrow. Although she treated with prednisolone, she developed CNS lupus one year later. She took methylprednisolone (mPSL) pulse therapy with immune globulin (IVIG), then got a negative PVB19. Second, 36year-old woman, who had itchy and photophobia, developed arthralgia and purpuric eruption and diagnosed dermatomyositis because of Gottron's sign with muscle symptom. She had elevated titer of PVB19 and positive PVB19 DNA-PCR in serum. She took mPSL pulse therapy with IVIG, then her PVB19 disappeared after one year. Finally, we had 60year old woman, who diagnosed Adult onset Still disease, with positive PVB19 DNA-PCR in her bone marrow. Although she took mPSL pulse therapy, her symptoms were not improved and developed acute liver damage. We treated her with mPSL pulse therapy with IVIG and cyclophosphamide pulse. Viral infection is the one of pathogenesis of autoimmune diseases. We philologically report the relationship between autoimmune diseases and PVB19 infection with our cases.

P2-249

A case of bacterial abscessed lymphadenitis with normal levels of C-reactive protein during the treatment for systemic lupus erythematosus with prednisolone, mycophenolate mofetil (MMF) and tacrolimus

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Conflict of interest: None

A 16-year-old man having systemic lupus erythematosus (SLE), was admitted in our hospital in 2016. He was firstly diagnosed SLE two years ago and he frequently experienced flares of SLE for his neglect of the therapy. In admission, he had a swelling of right supraclavicular lymph nodes. After the treatment of SLE with a multi-targeted immunosuppressive therapy including prednisolone (PSL) 60 mg, tacrolimus (Tac) 3 mg and mycophenolate mofetil (MMF) 1.5 g, his serological markers such as an increase in anti-ds-DNA antibodies and a decrease in complement (CH50) were improved, although the lymph nodes became more swelled and painful with neither fever nor elevation of CRP levels. To examine the cause of lymph node swelling, lymph node biopsy and its culture were done and we made a diagnosis with Streptococcus pyogens lymphadenitis. After he was treated with the suitable antibiotics and became rapidly well. Even if there were neither fever nor an increase in CRP level in lupus patients treated with the multi-targeted therapy, a diagnosis of bacterial infection may be controversial and possible in differential diagnosis of lymphadenopathy.

P2-250

A case of successful treatment with multidisciplinary therapy for necrotizing subcutaneous panniculitis by serratia marcescens in systemic lupus erythematosus

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Conflict of interest: None

25-year-old female was admitted to our hospital because of high fever, butterfly erythema, pitting edema, low complement titer, high antinuclear antibody titer and pericarditis. She was diagnosed as systemic lupus erythematosus. The treatment of prednisolone (PSL;1mg/kg per day) was undergone, but her symptoms are worse during steroid taper. She was treated by a steroid pulse therapy, followed PSL and tacrolimus. Although continuing therapy, she had a high fever, vomiting and tenderness of left lower leg. Then, she became a state of shock soon. She was treated with a ventilator, and her left leg was opened to full-thickness, treated with extensive surgical debridement. Serratia marcescens was detected in blood culture and skin tissue's culture. She was diagnosed necrotizing subcutaneous panniculitis with sepsis. She was continued to intensive care, but it was difficult to control the infection because of the extensive skin surgery. Therefore she underwent with left hip disarticulation and flap angioplasty. Then, she was treated with antibiotics, immunosuppressive agent, skin cleaning, and rehabilitation for a long time. Now, she can walk with prosthetic legs. We report it with a review of the literature.

P2-251

Purulent arthritis of the wrist and knee joint observed in a patient with RA concomitant with CKD under the biotherapy and hemodialysis

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Conflict of interest: None

Biotherapy in the RA patient with comorbidities and complications is common. Analysis of risk and minute management are needed in each patients.【case report】A 59 year old men with history of RA (11 years) and CKD (10 years) was introduced to our hospital for inflammation of the right wrist and knee joints. The superficial and localized infection around the shunt for hemodialysis (HD) placed in left forearm was also observed. Biotherapy (monthly TCZ div) and night HD (3 times a week) were performed at the previous clinic. Diagnosis of acute purulent arthritis of the joints was made based on the clinical features, laboratory data and gram positive coccus revealed from the joint fluid. Under the administration of VCM, open synovectomy was performed. MSSA was proved from the culture of the blood from artery and the joint fluid 3 days after administration. From that result ABPC/SBT was started changed from VCM and continued for 17 days. Immediate improvement of the both arthritis was achieved. The patient discharged from hospital after 25 days and biotherapy with TCZ reconvene after 60 days. Function of the joints were maintained with no relapse after 150 days.【conclusion】Close observation is needed for the HD shunt of the RA patients under biotherapy.

P2-252

Two cases of rheumatoid arthritis involving facial swelling from odontogenic infections

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Conflict of interest: None

Objective: Two rheumatoid arthritis (RA) cases with sudden facial swellings and different diagnoses and courses are reported. **Method**: Two patients with odontogenic infections secondary to RA and similar early symptoms were examined to review points to note for non-dentists in treating RA based on the outcomes. **Results**: The first patient was admitted for rehabilitation of disuse syndrome after pneumonia treatment. The second patient was admitted for detailed tests and treatment of increased inflammatory response. Both developed acute facial swelling and were referred to an oral surgery at another hospital. **Conclusion**: The first patient was diagnosed as a combination of right odontogenic maxillary sinusitis and pneumonia, and was successfully treated by antibiotic infusion. The second patient was diagnosed as a cervicofacial bone and soft tissue abscess; underwent emergency surgery in an oral surgery, placed on a ventilator for a time after the surgery, and numbness extending from the right cheek to the lower jaw remained. **Clinical significance**: The deterioration in these two cases might have been avoidable by regular dental check-ups regardless of symptoms and consultation with a dentist for

the presence of periodontitis as part of the differential diagnosis of inflammatory response.

P2-253

A case of upper limb necrotizing fasciitis in a patient with rheumatoid arthritis

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Conflict of interest: None

[Purpose] We experienced the upper limb necrotizing fasciitis (NF) in a patient with rheumatoid arthritis (RA). [Object] A 57 y. o. woman.12 years disease duration, Steinblocker classification StageIV, ClassII. No familial history. She had a diagnosis of RA at the age of 40 y. o.. Etanercept was started at the age of 49 y. o.. Her disease turned worse at the age of 57 y. o.. She had a fever, polyarthralgia, the flare and skin ulcer formed on her upper limb. We had a diagnosis of cellulitis and we gave antibiotic. Soon she had a thrombocytopenia. Malignant rheumatoid arthritis was denied. We thought that she had a DIC. The recombinant human thrombomodulin, steroid, platelet blood transfusion were not effective. Immunoglobulin was effective. We performed an incision, debridement for upper limb NF. After the immunoglobulin dosage, her physical condition and the wound of her upper limb was improved. We operated the split thickness skin grafting after negative pressure wound therapy. She recovered in ADL before the onset. [Conclusion] This case suffered from it with thrombocytopenia in a timing of surgical treatment. The reports of the NF in RA patient during biological treatment appeared. We thought that it was important that we considered the NF for the cellulitis-like symptom in RA patient.

P2-254

Legal-clinical mutual comprehension and issues relating to rheumatoid arthritis treatment guidelines

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Conflict of interest: None

Rapid progress is being made with rheumatoid arthritis treatment, and its therapeutic efficacy has improved dramatically. However, serious adverse effects sometimes occur, and healthcare personnel must therefore pay attention to preventing medical errors and malpractice claims. Guidelines for use in clinics and hospitals have been prepared, with the aim of standardizing treatment, and many physicians judge these guidelines to constitute medical treatment policy. These guidelines have also been used as evidence in relation to medical errors and malpractice claims. Since the Case of Fukushima Prefectural Ono Hospital in 2009, treatment guidelines have increasingly been taken to constitute medical treatment policy; however, generally in judicial proceedings, treatment guidelines are often judged to constitute standards, and it is therefore essential to increase the mutual understanding of healthcare and legal personnel. In this paper, we report results from a questionnaire-based survey of physicians involved with rheumatoid arthritis treatment about their awareness of treatment guidelines and measures to ensure that treatment is performed safely and analyze legal cases in the past.

P2-255

Questionnaire survey about patients' community

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Conflict of interest: None

[Object] In order to support patients' activities to exchange information each other among patients with rheumatoid arthritis, we conducted a questionnaire survey. [Methods] Under the cooperation of 41 rheumatologists in Aichi prefecture, we collected the answers of self-administered questionnaires from 449 patients aged 20-79 year. [Result] Total of 3.3% had participated in the Japan Rheumatism Friendship Association and a 5.9% had joined other patients' communities. Except for the one patient out of 38 who had participated in the patients' community expressed their activities favorable. Twenty percent of the patients answered that they had seen some web sites which RA patients offered some information based on their own experiences, and 77% of them admitted such information useful. [Conclusions] Activities among RA patients to exchange information are limited in Aichi prefecture so far. However, those who had participated in such activities found relatively high degree of satisfaction.

P2-256

Effective use of an interview sheet and establishment of a training system for nurses involved in the care of patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] To enable nurses to provide sufficient patient care, and observe and assess patients by using the interview sheet. [Methods] Fifty-eight nurses were trained to use the interview sheet. After the interview, self-assessment and assessment by others were conducted. [Results] The mean interview time was 15.1 min. Of the 58 nurses, 45 and 13, and 19 and 39 were "able to" and "not be able to" assess themselves and others, respectively. Among the 45 nurses who assessed themselves, 30 (67%) were not able to assess others. This suggests that they could not perform assessment and nursing intervention despite detecting anxiety. The 19 nurses who assessed others provided nursing intervention to patients, with collaboration with other professionals being the most frequently used (n=13), followed by advice to families. [Conclusion] The interview sheet allowed detection of patient anxiety in a 10-min interview. In this study, patient anxiety could be detected in a 15-min interview. The nurses who were satisfied with anxiety detection and those who tried to resolve the detected anxiety used different measures after the interview. The interview sheet is a tool for collaboration among professionals and establishing a medical care team.

P2-257

The outcome of early treatment for rheumatoid arthritis using a cooperative network between clinics and our hospital

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Conflict of interest: None

The aim of this study was to evaluate the outcomes and problems of early treatment for rheumatoid patients referred from clinics in our area [Editor1]. (Patients and Methods) From January 2014 to June 2016, 22 patients (4 men and 18 women), referred from orthopedic clinics were evaluated. Thirteen patients were suspected of having early rheumatoid arthritis (RA) and the remaining 9 were treated for early RA within one year. (Results) Mean C-reactive protein (CRP) decreased from 2.1 mg/dl to 0.1 mg/dl after treatment. The disease activity decreased, and the mean DAS28 at the latest visit was 2.7 vs 4.6 (first visit). Three patients improved and were referred to a primary clinic. (Discussion) The symptoms of RA include limb pain, which leads patients to visit the orthopedic clinic initially. It is easy to refer the patients to the specialist for RA using the network; this enables early treatment. However, problems remain, including the difficulty of treating patients with medical problems at orthopedic clinics. It is important to create opportunities for information exchange in RA cases to produce effective treatment outcomes.

P2-258

An attitude survey on RA treatment of clinicians in northeastern Osaka (2nd. report)

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Conflict of interest: None

Purpose: Kitakawachi region in northeastern Osaka has a population of 1.2 million people. In this region, the majority of examinations and medical treatments for rheumatoid arthritis (RA) are performed in clinics. We conducted a sentiment survey to build a collaborative system for continuous and effective RA medical examination. **Objectives/Method:** The survey was distributed to 380 facilities, including internal medicine and orthopedic surgery departments of hospitals and clinics which follow RA patients. **Results:** Answers were obtained from 108 facilities (28.4%). Thirteen percents of facilities answered to Sero-negative cases been introduced to professional facilities. On the other hand, 26% facilities concluded RA treatment by itself. About 40% facilities use the 2010 ACR/EULAR diagnostic criteria, however 33% did not know this criteria. Furthermore, 45% did not know T2T. Forty-four % set treatment target in remission or low disease activity. Not only from the treatment of RA such as MTX and biological agents, but it is necessary to run education campaign of strategy of RA treatment in more depth extensively.

P2-259

Surveillance of local medical network for rheumatoid arthritis

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Conflict of interest: None

[Objectives] We established the institute of Rheumatology to treat rheumatic disease by medication and surgery. We conducted a survey about rheumatoid arthritis (RA) to perform good cooperation with other medical clinics. [Methods] We surveyed about correspondence of RA, MTX dosage, biological treatment, rehabilitation, and request for us using questionnaire. [Results] 45 responses were obtained. Orthopedics was 67%, physician was 22% and others was 11%. Rheumatologist was 22% certified JCR and 24% certified JOA. There were 30% carried out diagnosis and treatment, 50% consulting for us high disease activity, 11% asked me to make a diagnosis. The clinics that use MTX less than 8mg and up to 16mg were each 40%. Certified rheumatologist tended to use high MTX dosage. 71% were possible to treat biologics. Half of them correspond only subcutaneous injection. The rate of corresponding intravenous treatment was 70% in the hospital and 18% in the clinic. Outpatient rehabilitation is 51%, home-visit rehabilitation is 33%. Requests for us were consulting of uncontrolled patients, diagnosis and corresponding to adverse events. [Conclusion] Result of this surveillance, there were some difference in corresponding RA. The most common request was consulting of uncontrolled patients.

P2-260

Opinion survey for patient referral system in patients with rheumatoid arthritis

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Conflict of interest: None

Objectives: Patient referral system between family doctor and specialized hospital is used in the purpose of encouraging differentiation of medical care institutions. In the present study we investigated how patients with rheumatoid arthritis (RA) think about the referral system. **Methods:** We performed questionnaire survey about patient referral system at public lecture for patients with RA. **Results:** Among total 300 attendants 85 RA patients answered the questionnaire. Twenty-three (27%) patients answered that they were willing to use referral system. Among them, the number of patients treated with methotrexate (MTX) was 18 (73%), which was greater than that of patients treated with biologic agents (5 (27%)). They wrote that the reason were too long time for visiting hospital or waiting medical examination. On the other hand, 18 (21%) patients answered that they did not hope to use referral system. Among them, the number of the patients treated with MTX was not different from that of patients treated with biologic agents. They also wrote that the reason was absence of rheumatologists in neighborhood. **Conclusions:** Our study suggested that MTX-treated patients whose disease activity was stable were willing to use referral system. It is desired that family doctors experience MTX use.

P2-261

Importance of cooperation between hospital and dispensing pharmacy in drug administration guidance for rheumatoid arthritis patients

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Conflict of interest: None

Purpose: In many cases, drug administration guidance (DAG) was done by pharmacist in dispending pharmacy (PhDP). Recently cooperation between hospital and DP has been recognized important because the PhDP should understand therapeutic strategy in order to provide effective and safe therapy in patient care. In this study, we performed questioner for both patients and PhDP in order to improve DAG. Methods: We performed questioners for patients (n=295) about understanding for drug, and the ones for PhDP (n=62) about contents of DAG. Results: Many patients answered they could not understand precaution statement during taking medicine, could not appropriately deal with symptom for side effect. While PhDP answered they did not give guidance for those subjects. Therefore, we held workshop about therapeutic strategy by MD for PhDP and created manual for them. Conclusions: Information held by PhDP is little because they got it only from patients. From this questioner study, we understood which contents would be important to improve DAG by PhDP. In addition, these results helped us create manual for DAG. These results indicate that cooperation between hospital and PhDP is further necessary in the feature.

P2-262

Living and physical conditions in rheumatoid arthritis patients 5 years after the Great East Japan Earthquake

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Conflict of interest: None

Objective: We examined the status of RA patients 5 years post-earthquake. Patients and methods: A questionnaire survey was conducted to assess pain on visual analogue scale (VAS), and living and physical conditions 3 and 5 years post-earthquake in patients with RA. Results: The VAS scores of patients whose houses were completely or partially destroyed, as well as residents in intact houses, returned to the pre-earthquake values 6 months post-earthquake and were maintained at the same level at 3 and 5 years. About 80% of patients whose houses were completely destroyed had moved to another house or lived in a temporary

house at 3 years. However, at 5 years, about 60% of these patients had returned to their own house or were living in a reconstruction house, and about 40% had moved to another house. Of those whose houses were partially or not destroyed, 90% were living in their own house 3 and 5 years post-earthquake. For patients whose houses were completely destroyed, physical problems such as anxiety, insomnia, and malaise were found in about 80% at 3 years and about 60% at 5 years. Discussion:Health disorders persist in many patients. Psychological support, in addition to RA treatment, should be continued.

P2-263

An attitude survey among nurses about oral health of patients with rheumatoid arthritis

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Conflict of interest: None

{Objective} When we provide the optimal nursing of patients with rheumatoid arthritis (RA), we have to discern the importance of oral health in quality of life (QOL). This is the interventional study which aimed to determined the effect of workshop among nurses about oral health. {Method} We examined 22 nurses who were engaged in nursing of patients with RA. We converted oral health impact profile (OHIP-14) into VAS-scaled form according to the degree of necessity of every article of it. Test subjects filled out converted OHIP-14 before and after the workshop about oral health. {Result} VAS-scaled values of necessity about all articles of OHIP-14 increased after workshop with significant difference. When we classified articles with seven categories, the highest value of VAS scale was found at “physical pain” category (81.8), then “physical disability”(64.1) and “functional limitation”(63.7) categories followed before the workshop. After workshop the highest value was found at “physical pain” category (95.8), then “physical disability”(92.9) and “handicap”(90.5) categories followed. {Conclusion} The workshop about oral health was significantly effective to promote understanding the necessity of oral health in the course of nursing of patients with RA.

P2-264

Weak point in the ability for practices that “The Certified Nurses by Japan Rheumatoid Foundation” recognized by an instrument developed to assess clinical core competency as rheumatology nursing

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Conflict of interest: None

[Methods] Developed questionnaires was 20 items (each item’s point is five). It was sent by mail to 600 RA caregiver nurses who were selected randomly out of 1800 certified and registered nurses listed on the Japan Rheumatism Foundation Web site and of these, 227 (38%) gave valid responses. 72% were outpatient, rheumatology nursing experience was 7 years (±4.6). [Ethical considerations] The study was approved by my university’s ethics Committee. [Results] Respondents’ responses revealed that the top 3 practices at which the registered RA nurses were not good were “oral condition assessment and oral care knowledge and techniques (mean2.449)”, and “comprehension of body condition by reading Xray image (particularly, judgement of interstitial pneumonia, lung cancer, and atelectasis) (m2.48)”, “foot condition assessment and foot care knowledge and technique (m 2.537).” On the contrary, the top 3 practices they felt they could do well were “collaboration with doctors (m 3.824)”, “having good communication with a patient (mean 3.796)”, and “compassionate and kindly support (m 3.740).” [Conclusions] Japanese nurses are aware of their lack of competence on oral and foot care provision for RA patients and Xray image reading, and that such competence needs to be built up.

P2-265

Role of Care Nurse for Rheumatoid Arthritis in Team Medical Care

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Conflict of interest: None

Purpose:It was important to improve patient’s adherence for therapy to achieve low disease activity, or remission. In this study, we analyzed role of guidance for self-injection (SI)of bDMARDs. Methods:For patient taken SI therapy, guidance for SI was performed by care nurse for rheumatoid arthritis (CNRA). Questionnaire was done to examine anxiety of patient for disease or SI, understanding of disease and so on. Results:Before guidance, patients had anxiety for side effect of bDMARDs, effect of bDMARDs itself, procedure for SI, expense for therapy, and showed fear for SI. After the guidance, they satisfied easiness of SI, changed image of SI, relieved from burden of therapy, decreased doctor’s visit, and family understood disease. Satisfactory rate for the guidance was 66.4%. While, patients complained burden of cost, concern for family, and difficulty for storage or disposal of waste. Several patiens complained difficulty of judgement of SI in poor physical condition or difficulty dealing with trouble in SI. Rate of SI was improved from 69.9% to 88.2% by guidance based on patient’s circumstance. Conclusions:In order to achieve improved adherence for therapy, it is suggested that careful guidance for SI by CNRA takes important role to resolve anxiety or trouble of patients.

P2-266

The specific role of rheumatology care nurses of our medical centre in the management of rheumatoid arthritis

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Conflict of interest: None

[Purpose] While treatment of rheumatoid arthritis has been progressing dramatically, treatment-related co-morbidities sometimes disturb the patients’ safety and QOL. The importance of rheumatology care nurses’ role has been increasing. The present study is to clarify what roles the rheumatology care nurses should be supposed to assume. [Methods] Medical charts and nursing records of RA patients of our Centre who were treated with methotrexate (MTX) and/or Biologic DMARDs (Biologics) from January to September in 2016 were retrospectively reviewed. [Results] Eighty-eight patients (F 72, M16) with mean age of 68 were enrolled. The needs complained from the patients were categorized into 5 parts listed below. 1) 24 cases of drug compliance (biologics 12, MTX 6, steroids 6), 2) 21 of emergency responses, 3) 11 of consultation for decision making, 4) 7 of mental healthcare, and 5) 5 of self-care for articular function. During the monitored period, there were 4 serious adverse events which required admission (phregmon, interstitial lung disease, neutropenia, leg injury plus pneumonia, each. All patients were improved and discharged. [Conclusion] The present study found out 5 important categories which the rheumatology care nurses should play a role.

P2-267

Self-management in female patients with rheumatoid arthritis (RA)

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Conflict of interest: None

[Objectivs] To clarify the factors which influence self-management in patients with rheumatoid arthritis (RA). [Methods] The total of 145 female patients, who were diagnosed as having RA, were subjected to be analyzed relationships between QOL (SF-8), a degree of satisfaction (VAS), self-efficacy (GSES), activities of daily living (mHAQ), awareness of stresses (SDS), and self-management. [Results] There was an association between the awareness of stresses and the self-efficacy. There were also associations between the awareness of stresses, QOL, the degree of satisfaction, and mHAQ. Self-management was associated with the age, the symptoms, the awareness of stresses, and the preparation to the stresses. [Conclusion] We suggested that nursing supports were necessary so that the RA patients could be aware of the awareness of stresses and select the appropriate self-cares.

P2-268

Is biologics harmful for childbearing?

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Conflict of interest: None

Background: The safety of using biologics for RA patients before pregnancy is still controversial. Method: Analyzing the outcome of pregnancy of RA patients in our division who were treated by Biologics when pregnant. Result: There are eight cases. Mean age when pregnant was 30.2±5.0 years old. ETN was used for six cases, and TCZ and ABT was used for one case, respectively. The mean weight of baby when born was 2787.6±230.6g. No cases have miscarriage, and none of them have major deformity.

P2-269

The importance of pre-pregnancy counseling in Systemic lupus erythematosus

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Conflict of interest: None

【Objectives】In pregnancy with SLE, maintaining low disease activity before and during pregnancy is crucial for good outcomes for mother and child. This study aimed to investigate whether pre-pregnancy counseling leads to what result in pregnancy outcome.【Method】In our hospital, since 2013, we provide rheumatic disease patients who would like to become pregnant with adequate treatment and education, as well as aiming for better pregnancy outcomes. We compared pregnancy outcomes in 15 cases with pre-pregnancy counseling and 58 cases with no pre-pregnanacy counseling.【Result】The mean age was 32.1±8.9 years. There were 13 live births (86.6%), 2 miscarriages (14.4%), no stillbirth with pre-pregnancy counseling. On the other hand, there were 39 live births (63.7%), 9 miscarriages (17%), 2 stillbirths (3.4%) with no counseling. Patients with pre-pregnancy counseling had decreased lupus activities after abortion compared with patients with no counseling (SLEDAI:0.67vs 2.98, P=0.001). And also neonatal birth weight with counseling is higher than the other patients (BW:2833g vs 2490g, P=0.004).【Conclusion】In pregnancy complicated with SLE, it is essential that having made a pregnancy plan become get better result in activity of SLE after abortion and neonatal birth weight.

P2-270

Pregnancy in women who have Raynaud's phenomenon with systemic lupus erythematosus: Case Series

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Conflict of interest: None

【Object】Pregnancy hypertension syndrome (PIH) occurs more frequently in SLE. PIH is circulatory insufficiency due to vasospasm, and we focused on Raynaud's phenomenon.【Methods】Among of SLE pregnant patients at Showa University Hospital between April 2008 and October 2016, we studied the pregnancy course of four who had Raynaud's phenomenon before pregnancy.【Results】(Case1) She was treated with PSL10mg, aspirin, heparin10000units/day due to APS. She developed PIH at 35th weeks and deliveried at 37th weeks. (Case2) She was treated with PSL10mg during pregnancy. Exacerbation of SLE and fetal growth delay occurred around 20th weeks, andshe was stillborn at 23th weeks. (Case3) She was treated with PSL10mg. Exacerbation of SLE has occurred from 30th weeks, PIH started from 35th weeks, she deliveried on 38th weeks. (Case4) She was treated with PSL10mg and TAC3mg. SLE worsened from 24th weeks, urine protein increased at 37th weeks. She delivered 38th weeks. Raynaud's phenomenon were disappeared in all cases.【Discussion】Patients who had Raynaud's phenomenon before pregnancy had Raynaud's phenomenon disappeared during pregnancy and tendency to cause PIH and exacerbation of SLE. We thought Raynaud's phenomenon improve due to vasodiatoraction of luteal hormon.

P2-271

~The deep remission may paradoxically induce dropout of T2T treatment~ The analysis of the rheumatoid arthritis patients' background factors who suspended outpatient service in the rheumatology clinic

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Conflict of interest: None

Method)we extracted the rheumatoid arthritis patients who visited out rheumatology clinic, from 1st October 2015 to 1st October 2016. In the whole 875 patients,56 patients interrupted outpatient service in the last 6 months. We analyzed theses patients background to define the primary factors for interrupted outpatient service. Based on the medical chart, the tangible reasons were recorded in 42 patients and residual 14 patients had no clear reason. we called each of the 14 patients, we could contact 5 patients and asked the reasons why they didn't visit our clinic. Results)All 5 patients were reached deep DAS-CRP remission,3 patients remained remission without any treatment and 2 patients remained with medication from the non rheumatology clinic. Discussion)The 8 outof the all 14 dropouts were in deep DAS-CRP remission (1.48 ±0.26) on the last visit, and deep DAS-CRP remission maybe the triggering factor for the interruption of outpatient servic. The paradoxical result leads us to consider more skills and tools to prevent dropout.

P2-272

Sarcopenia accompanied by rheumatoid arthritis is predictable by home body composition analyzer

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Conflict of interest: None

[Purpose] Rheumatoid arthritis (RA) often accompanies sarcopenia due to joint destruction and inflammation. Appendicular skeletal mass index (ASMI) used for its diagnosis can be calculated from body composition analyzer (BCA) for professional use, but not from BCA for home (BCA-H) not providing muscle mass in each part of body. We investigated how we can predict ASMI from BCA-H. [Methods] 50 patients enrolled in CHIKARA study were measured 125 times by both BCA. Muscle mass obtained from BCA-H, adjusted by body height, was defined as Y. We investigated the correlation between Y and ASMI (X). [Results] 10 males and 40 females were included. They had mean disease duration of 6.7 years, DAS28-ESR 3.44, HAQ 0.375, CRP 0.08 and MMP3 67.3. R value between X and Y was 0.847 ($P<0.001$) by Spearman correlation analysis. Y can be predicted by 1.41X+5.95 in male and 1.46X+5.24 in female. Diagnosis criteria for sarcopenia includes X (kg/m^2) less than 7.0 in male and 5.7 in female, which deserves Y (kg/m^2) less than 15.82, 13.56 respectively. Diagnosis accuracy using each criteria was 0.693 (95%CI 0.541-0.844) by kappa coefficient. [Conclusions] Y calculated from BCA-H showed strong correlation to X, and there was high reproducibility. Therefore, sarcopenia accompanied by RA is predictable by

BCA-H.

P2-273

Sonographic evaluation of the lower limb skeletal muscle mass in patients with rheumatoid arthritis

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Conflict of interest: None

Objective. *Sarcopenia* has been defined as the aging-related loss of muscle mass and strength that occurs with advancing age. The aim of this study was to evaluate the relevance of the sonographic assessment of the lower limb skeletal muscle mass in patients with rheumatoid arthritis (RA). **Method**. Six patients with RA who underwent a ultrasonography (US) examination of the joint for synovitis screening, and 7 control group were enrolled in this study. We studied a total of 26 lower limbs of 13 participants who underwent US examinations. To assess skeletal muscle mass, the four limbs skeletal muscle index (SMI) using a bioelectrical impedance analysis (BIA), the skeletal muscle cross-sectional area by computed tomography (CT) at the third lumbar vertebra (CTMI), and muscle thickness of the quadriceps femoris (QMT) by US were evaluated. **Results.** There were no significant differences in age and BMI between control and RA groups. CTMI and QMT were significantly decreased patients with RA compared with the control groups. The QMT showed a significant correlation with SMI (r = 0.980) and the CTMI (r = 0.628). **Conclusions.** These results suggest that sonographic examinations are useful for the screening of *sarcopenia*.

P2-274

Occult malignant tumors detected by screening tests in the patients with rheumatoid arthritis in being referred to our hospital

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Conflict of interest: None

[Objectives] The malignant neoplasm has been the leading cause of death in Japan since 1981. Paraneoplastic syndrome is a cause of flare-up in RA. We investigated malignant tumors detected by screening tests in the patients with RA who were referred to our hospital. [Methods] The patients with RA from 2002 to 2015 were analyzed. Screening examinations included a blood and urine analysis and computed tomography (CT) scanning. [Results] Occult malignant tumors have been found by screening test in nine patients with RA. The mean age at the time of finding a malignant tumor was 69.6 year-old (52-83). The mean follow-up period after operation for malignant tumors was for 3.7 years (0.3-10). There were six lung cancers, one breast cancer, one bladder cancer, and one renal cancer. All cases were detected by CT scanning. Radical surgeries were performed in 5 cases. They have no recurrence in the last follow-up. A case of renal cancer has already suffered multiple organ metastasis and died after four months. Symptom of arthritis was disappeared one month in a case of lung and bladder cancer and nine month in a case of breast cancer after the surgery of malignant tumors. [Conclusion] Occult malignant tumors may accelerate their arthritis as a paraneoplastic syndrome in the patients with RA.

P2-275

A case of persistent inflammatory knee joint monoarthritis treated with intravenous Infliximab infusion

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Conflict of interest: None

【Case】The case was 64 years old woman who had suffered from persistent inflammatory knee joint monoarthritis from 2005. She was treated with conservative therapy with intra articular injection of hyaluronic acid at the other hospital and admitted our hospital by rucurrent knee joint hydrops. Laboratory test showed the negative value of Rheumatoid factor, ACPA, and antinuclear antibody and slight elevation of CRP. At 2010, the aspirated joint fluid reached 100ml and at 2011, it reached 150ml. At 2012, tonsillotomy was performed but the symptom continued. By administration of MTX or oral steroid and intra-articular injection of steroid suppressed the retension of joint fluid for several months, but the symptom relapsed. At September 2015, after administration of Infliximab (3mg/kg) hydrops of knee joint resolved. At June 2016, hydrops of knee joint relapsed and 50ml of joint fluid was aspirated. After increasing the dose of Infliximab to 6mg/kg, hydrops of knee joint resolved and the remission continued.【Discussion and Conclusion】Intravenous Infliximab treatment was effective for the inflammatory knee monoarthrits.

P2-276

The efficacy of Tocilizumab (TCZ) monotherapy for Polymyalgia rheumatica (PMR)

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Conflict of interest: None

Objectives: To assess the efficacy and safety of TCZ monotherapy for PMR. Method: 13 PMR patients were enrolled. TCZ was administered biweekly for the first 2 months and every 4 weeks for subsequent 40 weeks (15 infusions total). VAS, EUL, ESR was prospectively measured every 4 weeks and was evaluated at week 24,52 and 78. Remission was defined as VAS <10, EUL=0 and normal ESR. Baseline patient characteristics revealed various comorbidities in 9 of the patients. 2 patients discontinued TCZ because of insufficient efficacy at week 4 and 12. One patient discontinued TCZ due to lung abnormal shadow at week 8. Of 13 patients, 10 completed 15 infusions. At week 24,2 patients achieved remission, other 7 patients at week 52 and the other one patient at week 78. CSs was administered in 2 cases because of pemphigoid and flare of PMR. At week 78, 5 patients remained remission. ESR raised slightly abnormal in 3 patients at week 78 without any symptoms. Serum IL-6 level revealed significant decrease at 24, 52 and 78 week after temporal increase 4 weeks after first infusion in 3 patients. There were no serious adverse events for 78 weeks of study period. Conclusions:TCZ monotherapy may be a good alternative therapy to CSs for the elderly with various comorbidities.

P2-277

A case of TAFRO syndrome with supranuclear disoraders of facial nerve

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Conflict of interest: None

A 62 year-old woman was admitted our hospital in April, 2016. She had fever, generalized edema, lymphoadenopathy, and pleural effusion. Blood exams showed thrombocytopenia (1.8 X 10^4/ml). Creatinine levels were 6.2 mg/dl. Patholgical examination of lymph node showed hyperplasia of lymphoid follicle and infiltrated plasma cells, which was consistent with the typical pathological findings in Castleman's disease. Jaw jerk reflex, sensory abnormality of trigeminal and facial nerves were observed. She was diagnosed with TAFRO syndrome having supraneuclear disorder. Tocilizumab (TCZ) and cyclosporin A (CyA) were administrated as an initial therapy. After administration of TCZ and CyA, fever, generalized edema, lymphoadenopathy, and pleural effusion were improved. After these treatments, serum creatinine levels were decreased to 0.81 mg/dl. Platelet counts was 12.6 X 10^4/ml. Four months later of the initial

treatments, sensory abnormalities of facial nerves were palliated. Peripheral nerve involvements were well known in patients with TAFRO syndrome. We described here the first case of TAFRO syndrome with supraneuclear disorder. Although supraneuclear disorder was improved after administration of TCZ and CyA, TAFRO syndrome is very rare disorders. The further study will be necessary.

P2-278

Rosai-Dorfman disease (RDD) mimicking Osteomyelitis in a patient with Mixed connective tissue disease (MCTD)

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Conflict of interest: None

A 47-year-old woman with a 4-year history of MCTD which was well controlled by prednisolone 2.5 mg/day and tacrolimus 2 mg/day develped a 1-month history of local swelling, pain and heat over her right forearm before admission. Findings consistent with osteomyelitis were observed in MRI examination of her right forearm in our hospital. Although she received intravenous antibiotics (ceftriaxone and levofloxacin) after admission to our hospital, there was no significant improvement. Additionally a low-grade fever developed and the level of C-reactive protein slightly increased. She also noticed two hard subcutaneous nodules on her chest and left scapula. FDG-PET revealed abnormal uptakes in her chest, left scapula, right kidney nodule, some bones and near her heart. Immunohistochemical stainings of her left scapula's nodule and right ulna showed positive for S100 and CD68 and negative for CD1a, showing emperipolesis. We diagnosed her with RDD based on these findings. After diagnosis, a dose of prednisolone was increased to 7.5 mg/day and tacrolimus was discontinued, and she showed neither inflammations nor developments of new nodules until now.

P2-279

Elbow lung metastatic carcinoma treated as rheumatoid synovitis for three years; A case report

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Conflict of interest: None

[Introduction] Joint metastasis is very rare. Prognosis is poor, with a mean survival term of less than six months. We report the case of a right elbow joint metastasis from a lung squamous cell carcinoma in an 83-year-old male. He was treated with salazosulfapyridine as rheumatoid arthritis for 3 years. Case Presentation [Past History] Dementia, Angina pectoris, Hypertension, Chronic heart failure, Duodenal Ulcer, Chronic Kidney Disease, osteomyelitis of right foot [Past Surgical History] Amputation of right leg at 79 y.o. [Present History] At 80 years old, he came hospital as polyarthritis with right elbow pain. RF 4, ACPA 1.1, CRP 7.34 mg/dl, MMP-3 480.4, WBC 4,600, ALP 299. Tumor markers were in normal range. As a seronegative rheumatoid arthritis, Salazosulfapyridine was started. Symptom was improved and CRP level was decreased. At 83 years old, he was suffered from joint pain. Switched medication to tacrolimus. After 30 days from then, His pain was in relief except Right Elbow joint. Open biopsy has done. Squamous cell carcinoma was found. Palliative care team was stepped in. He was died after 2 months. [Differential Diagnosis] Paraneoplastic syndrome. Infection, malignant tumor. [Clinical Point] atypical rare case because of slow developing lung cancer.

P2-280

Hashimoto encephalopathy associated with respiratory failure and fibromyalgia: A case report

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Conflict of interest: None

38-year-old woman. 4 months before admission goiter. 3months before admission first visit our hospital with sore throat and malaise. Euthyroidism, anti-thyroglobulin antibody 582.6 IU / ml, TPO antibody 231.2 IU / ml, goiter, Hashimoto's disease was diagnosed and admitted to ours hospital due to proximal muscle weakness. CK normal, CRP<0.01, IgG 2008mg/dl, anti-Jo-1, anti-AChR antibody negative, BGA pH7.39, $PCO_2$40.2, $PO_2$75.0, %VC74, FEV1.0%87. NCV normal, EMG action potential low. No inflammatory no atrophy of muscle MRI. Head and neck MRI, Ga scintigraphy, CSF cell count and protein normal. Muscle biopsy mild lymphocytic infiltration around blood vessels, no vasculitis and muscle atrophy. Bone marrow, skin biopsy normal. On the 6th hospital day during sleep SpO_2 and % VC reduced to 80 and 58, BiPAP was started during night. Slow α, spike & wave in EEG, encephalopathy was diagnosed. On the 19th hospital day, apnea worsened so BiPAP used all day. Methylprednisolone started. Systemic severe pain appeared. Analgesic invalid, paroxetine effective, and was diagnosed fibromyalgia. Oral prednisolone was started. Steroid therapy was effective for refractory fibromyalgia, and pain and change of anti-TPO antibody titers was parallel.

P2-281

A case of Weber-Christian Disease with abdominal panniculitis

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Conflict of interest: None

A 32-year-old female was admitted to our hospital because of persistent fever, erythema and sclerosis of skin in April, 2016. She had been diagnosed as erythema nodosum (EN) in 2013, and received transient corticosteroid therapy, resulting in remission. However, in January, 2016, she had a developed fever erythema of abdomen and extremities, and sclerosis of skin. The diagnosis of EN exacerbation, had been made, and 10mg/day of prednisolone (PSL) had been restarted. On admission, CT scan revealed heterogeneous concentration of subcutaneous tissue, which is consistent with panniculitis. Also, bilateral axillary and paraaortic lymph node swelling was observed. Laboratory test showed elevated value of LDH, interleukin-2R, a ferritin. There were no obvious findings of malignancy. The biopsied specimen of the erythema revealed lobular panniculitis. We made a definite diagnosis of Weber-Christian disease. Since her symptoms were resolved without additional treatment, she was followed up with the administration of PSL. Weber-Christian disease is considered as non-suppurative panniculitis of unknown etiology. Our present case shows an atypical clinical course, and provides a new insight to understand the mechanism of the disease.

P2-282

A case of elderly RA patients with cognitive dysfunction who treated and care with ultrasonography by RA expert nurse

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Conflict of interest: None

76-year old woman hospitalized to our hospital by gait disturbance due to *Rheumatoid Arthritis (RA).* She was diagnosed with RA since 3 months ago. She was initiated with NSAIDs and MTX, but stopped because she had been appeared lung institial pneumonia. She admitted to our hospital because gait disturbance. She recognized multiple lacunar infarctions in the head MRI at the time of admission, and MMSE of 17/30 indicated cognitive dysfunction. Her physical findings showed active arthritis but she did not recognize their pain. DAS 28-CRP 3.14 (MDA), ultrasonography showed highly active synovitis. However Pt VAS showed 0 mm. A discrepancy of between DAS28-CRP, ultrasonography and Pt VAS might be suggested by cognitive dysfunction. She was scheduled to treat with a biologics, but she could not understand her need for treatment. The RA expert care nurse repeatedly performed ultrasonography on the bedside and explained while watching the screen together,

gradually gaining understanding of the treatment and introducing the biological preparation. We reported the usefulness of ultrasonography to treat and care for elderly RA patients with cognitive dysfunction. In our hospital, RA expert care nurse of Sonographer of Japan College of Rheumatology) use ultrasonography as a tool for day care.

P2-283

Multidisciplinary treatment to a female patient with impaired activity of daily living, due to severe multiple tophi and chronic gouty arthritis

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Conflict of interest: None

Tophus is one of severe complication of chronic gout. It is very rare to see patients with visible tophi in Japan since management of gout and hyperuricemia is now well-recognized. We have treated rare case of 70 years-old female patients who had multiple tophi on her upper and lower extremities, and her tophi on both heels were melted, causing severe impairment of daily living. She had been treated with NSAIDs for gouty arthritis, however, chronic kidney disease (CKD) due to NSAIDs use or/ and gouty nephropathy due to hyperuricemia made it very difficult to manage her gouty arthritis and tophi by urate-lowering treatment (ULT). We surgically removed melted nodules on heels. Physical therapy was performed to improved her limited range of motion of legs, and strengthening of lower extremities. Colchicine prophylaxis and increased dose of ULT, and decreased diuretics also resolve her chronic gouty arthritis. There has been no gouty flare for three months after the surgery. [Clinical significance] Multidisciplinary approach was needed to treat our rare case of severe chronic gout with multiple tophi.

P2-284

A rare case of the adult parechovirus type 3 infectious disease that is complicated with significant myalgia and muscle weakness

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Conflict of interest: None

[Case] 39 years old, a man. [Chief complaints] fever, myalgia, muscle weakness [Present history] On September 15, 2016, the patient's eldest son had a high fever and his second son had fever and abdominal pain on 19th. The patient had a high fever and orchidalgia on 27th, visited the urology department on 28th. Laboratory data showed WBC 6400/μl, CRP 1.875mg/dl, suggesting viral didymitis. Thereafter, he developed a muscular pain of both thighs inside on 29th and hospitalized on 30th because shifting from a supine position to a standing position became difficult. [Clinical course after admission] there were sharp pain in both sides femoral region at hospitalization and rising and postural change were difficult. The laboratory findings showed that CK 1026IU/l, AST 65 IU/l, LD 338 IU/l, Mb 39 ng/ml and platelet 71,000/μl. There were no abnormal findings in the muscle CT. His symptom and the laboratory findings were relieved by use of rest, infusion, NSAIDs

P2-285

Biologic agent therapy of rheumatoid arthritis in the elderly for the last 10 years: Results from Japanese multicenter registry

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Conflict of interest: None

Objectives Of the treatment of rheumatoid arthritis (RA), biologic agent therapies are chosen, if disease activity remains moderate or high despite csDMARDs therapy. In the elderly, with comorbidity and their less spare ability, safety is often concerned in the choice of biologic agent. We investigated the tendency to choose biologic agent and compared baseline characteristics in the elderly for the last 10 years. 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 year by, and baseline disease activity and concomitant MTX among TNF inhibiters, tocilizumab (TCZ), and abatacept (ABT). Drug continuation rates were compared among TNF inhibiters, TCZ, and ABT. Results From 2005 to 2010, etarnercept (ETN) was used the most. After the advent of ABT, ABT was used the most. Baseline disease activity slightly decreased as a whole (DAS28-CRP; 4.88 to 4.44). Despite baseline disease activity of TNF inhibitors decreased (DAS28-CRP; 4.88 to 4.37), that of TCZ increased (DAS28-CRP; 4.94 to 6.24). In 2011-2014, baseline disease activity of TCZ (5.85) was higher than that of TNF inhibiters (5.11) ($p<0.05$). 2 years drug continuation rates due to all unfavorable causes; ABT was 92.4%, better than that of TNF inhibitors 87.1% and TCZ 69.2%($p<0.05$). 2 years drug continuation rates due to adverse events; TCZ was 80. 8%, lower than that of TNF inhibitors 94.6% and ABT 96.2%($p<0.05$). Conclusion ETN was used most before the advent of ABT. After the advent of ABT, ABT was used most. This selection was made for speculation that ABT is lower risk than other biological agents. Baseline disease activity slightly decreased showing that tight control management became also popular among elderly.

P2-286

Trend of atypical femoral fractures in rheumatic patients in the highly super aging area of North Japan

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Conflict of interest: None

Background: A number of recent case reports and series have identified atypical fractures of the femoral shaft. Atypical femoral fractures (AFFs) with lack of trauma or less-energy have been reported to relate using of the bisphosphonates (BPs) and glucocorticoids (GCs) for a long time, affecting collagen diseases. Objective: We have analyzed the atypical femoral fractures (AFFs) in rheumatic patients of our hospitals in the highly super aging area of North Japan. Methods: We investigated retrospectively all cases of AFF summarized by ASBMR Task Force 2013 including affected rheumatic disease patients in our hospital from 2009 to 2014. Results: We have seven cases twelve AFFs in our hospital from 2009 to 2014. The rheumatic patients with AFFs were seven femurs in four women in that periods. Three cases have bilateral AFFs. The mean age of them was 54.9 year-old. As comorbid conditions, one patient of systematic lupus erythematosus, dermatomyositis and rheumatoid arthritis was bilateral, one polyarteritis nodosa was lateral AFF. Mean femoral neck angle was 131 degrees and femoral shaft angle was 5.1 degree. Two patients with AFF had prodromal pain (29%). All patients received BPs and prednisolone (PSL). Mean duration of receiving those drugs was 5.7 years and 6.2 years, respectively. Mean dosage of PSL was 17.9 mg/day (10-30). The surgery using intramedullary nail fixation were performed in six cases eleven AFFs. One patient has treated conservatively. Teriparatide and therapy of low-intensity pulsed ultrasound was induced for all cases. Mean duration of post-operative observation was 28 months (12-70). At the latest follow-up, six femurs were observed the sign of union at fracture site on X-ray or computed tomography of them, but not one femur. Mean duration of union of the fracture site was 12 months in six femurs. Conclusion: Seven AFFs were observed in 2009-14 in rheumatic patients of our hospital in the highly super aging area of North Japan.

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Serum level of syndecan-4 and its correlation with clinical parameters in rheumatoid arthritis patients

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sity First Hospital, Beijing, China

Conflict of interest: None

Objectives: To detect serum level of syndecan-4 in RA patients and investigate its correlation with RA clinical parameters. Methods: The concentration of serum syndecan-4 was assayed by enzyme-linked immunosorbent assay (ELISA). 43 patients' serum samples from our RA cohort study between 2014 and 2016, and 20 age- and gender-matched osteoarthritis (OA) patients' serum samples were collected and analyzed. Compared the serum syndecan-4 levels in RA patients with DAS28≥3.2 and DAS28<3.2 by Wilcoxon signed rank test. The relationships between serum syndecan-4 levels and RA clinical parameters (DAS28, rheumatoid factor (RF), erythrocyte sedimentation rate, C-reactive protein, etc.) were analyzed. Results: Baseline serum syndecan-4 levels of RA patients were significantly higher than the matched OA patients (1101.56 pg/mL vs 281.41 pg/mL, p<0.001). In RA patients who had sera both at the point of DAS28≥3.2 and DAS28<3.2 (n=13), we found that the former syndecan-4 levels were higher than the latter (1666.22 pg/mL vs 1378.34 pg/mL, p=0.65). The levels of serum syndecan-4 and RF were significantly and positively correlated in RA patients (r=0.696, p=0.008). Furthermore, there is a tendency that serum syndecan-4 levels were higher in the RF-positive (n=31) than in the RF-negative (n=12) RA patients (1344.43 pg/mL vs 971.27 pg/mL, p=0.078). Conclusions: Serum syndecan-4 concentration significantly higher in RA patients, and it is positively correlated with RF. Syndecan-4 may play an important role in the pathogenesis of RA.

P2-288

Ultrasound of the wrist in low disease rheumatoid arthritis patients: Intercarpal joint is more sensitive than radio-carpal and distal radio-ulnar joint

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Conflict of interest: None

Background: Comprehensive evaluation, including multiple recesses of all accessible peripheral joints, may be overly time-consuming in daily practice and in conducting clinical trials. **Objectives:** This study aimed to investigate synovitis activity at wrist joint at different levels by ultrasonography (US) assessment of patients with rheumatoid arthritis (RA) and to determine simplified method of monitoring these patients and to search the lesser time consuming and can be used in clinical practice method. **Methods:** Gray scale synovial hypertrophy (SH) and power Doppler (PD)ultrasound were performed on the dorsal radio-scaphoid, inter-carpal and radio-ulnar joints of dominant wrists[1]. One way ANOVA with multiple comparison were performed for each joint. **Results:** A total of 38 patients with RA and affection of the wrist joint underwent a standardized PD examination assessing three positions in their wrist. The mean SH is 1.08±0.487 at radio-carpal joints, 1.08±0.487 at inter-carpal joints, and 0.45±0.602 at radio-carpal joints with significant higher at radio-carpal and inter-carpal joints than radio-ulnar joints. The mean PD is 0.08±0.273 at radio-carpal joints, 0.79±0.577 at inter-carpal joints, and 0.16±0.437 at radio-carpal joints with significant higher at inter-carpal joints (Fig 1). Overall inter-carpal joint is more sensitive than the other joints. (Table 1) **Conclusions:** A standardized ultrasound examination of inter-carpal joint in patients with RA may be used as a measure of disease activity. More studies are needed to examine by PD US to obtain the best validity of Doppler measurements.

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Diagnostic test accuracy of ultrasonography for synovitis in rheumatoid arthritis: systematic review and meta-analysis

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Conflict of interest: None

Objective. To evaluate diagnostic test accuracy of ultrasonography (US) compared with magnetic resonance imaging (MRI) for the detection of synovitis in rheumatoid arthritis (RA) patients. **Methods.** A systematic literature search was performed in the Pubmed, EMBASE, the Cochrane Library, and Web of Science Core Collection. Studies evaluating diagnostic test accuracy of US for synovitis detected by MRI as the reference standard for wrist, metacarpophalangeal (MCP), proximal interphalangeal (PIP), and knee joints were included. To assess the overall accuracy, we calculated the diagnostic odds ratio (DOR) using a DerSimonian-Laird random-model and area under the hierarchical summary receiver operating characteristics (AUC) using Holling's proportional hazard models. The summary estimate of the sensitivity and the specificity were obtained using the bivariate model. **Results.** Fourteen of 601 identified articles were included in the review. The DOR was 9.8 (95%CI 4.2-22, I^2 = 2%), 24 (95%CI 10-57, I^2 = 16%), 23 (95%CI 6.5-84, I^2 = 19%), 4.1 (95%CI 0.78-22, I^2 = 0%) and AUC was 0.79, 0.89, 0.91, 0.70, for wrist, MCP, PIP, and knee joints, respectively. The summary estimate of sensitivity and specificity were 0.73 (95%CI 0.57-0.85)/0.73 (95%CI 0.41-0.91), 0.68 (95%CI 0.48-0.83)/0.94 (95%CI 0.86-0.97), 0.71 (95%CI 0.33-0.93)/0.94 (95%CI 0.89-0.97), and 0.91 (95%CI 0.56-0.99)/0.60 (95%CI 0.20-0.90) for wrist, MCP, PIP, and knee joints, respectively. **Conclusion.** US is a valid and reproducible technique for detecting synovitis in the wrist and finger joints. It may be considered for routine use as part of the standard diagnostic tool in RA.

P2-290

What is the predictive factor for good response to tocilizumab in rheumatoid arthritis?

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Conflict of interest: None

【Objectives】To compare continuation rates (CR) of tocilizumab (TCZ) by the responsiveness to the therapy and to identify a predictive factor for good response (GR) to TCZ in rheumatoid arthritis (RA). 【Methods】Patient with RA who newly started receiving TCZ after April 2008 in our hospital, were included in the study. We collected patient records, medication histories, laboratory data, and clinical parameters longitudinally after starting TCZ. Statistical analyses were performed using the chi-square test, binomial logistic regression analysis, Kaplan-Meier method, and the log-rank test. 【Results】Ninety-two patients with RA were included in the study. The mean age and disease duration at baseline were 60 ± 13.5 years and 8.7 ± 8.0 years, respectively. The seroprevalence of the anti-citrullinated protein antibody and the rheumatoid factor were 95.4% and 95.7%, respectively. The rate of methotrexate and prednisolone at baseline were 45.7% and 64.1%, respectively. TCZ was administered as the first biologic in 42 patients. DAS28 (ESR) and CDAI revealed high disease activity at baseline (5.2 ± 1.5 and 25.4 ± 14.1, respectively). The mean continuation rate of all patients was 42.1 ± 4.0 months. The mean CR was significantly higher in patients who achieved GR in EULAR response criteria at 6 months after starting TCZ, than the others (54.0 ± 6.0 months vs 29.0 ± 5.3 months, p = 0.004). By multivariate statistical analysis, we identified the two predictive factors for achieving GR at 6 months after starting TCZ, the low number of using previous biologics and the low CDAI at baseline (p = 0.018, odds ratio (OR) = 0.386, and p = 0.011, OR = 0.944, respectively). 【Conclusion】RA patients who achieved GR at 6months after starting TCZ showed higher CR than the others. This study also suggests that the low number of biologics usage and the low CDAI at baseline are the predictive factors for GR.

P2-291

Clinical and hematological effects of tocilizumab on serum hepcidin, anemia response and disease activity in patients with active rheumatoid arthritis

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Conflict of interest: None

Objective. The purpose of this study is to evaluate the clinical and hematological effects of tocilizumab in active rheumatoid arthritis (RA) patients. **Methods.** Fourteen patients with active RA were enrolled in this study. The patients received tocilizumab 8mg/kg intravenously every four weeks for 6 months. Disease activity, anemia-related factors including serum hepcidin-25, and hematological parameters were monitored at baseline and at 1, 3, and 6 months after the initiation of treatment. **Results**. Significant reductions in tender joint count, swollen joint count, visual analogue scale, erythrocyte sedimentation rate, C-reactive protein plus reductions in a 28-joint disease activity score were seen within one month after the first tocilizumab treatment. These effects lasted throughout the six-month study period. In addition, significant improvements in anemia-related factors such as hepcidin-25, ferritin, iron, hemoglobin, red blood cell counts and mean corpuscular volume were observed during the treatment period. Moreover, hematological parameters were improved reductions in counts for leukocytes, monocytes, neutrophils, and platelets. The lymphocyte counts and their subset numbers were unchanged. Changes in hepcidin levels significantly correlated with changes in C-reactive protein, erythrocyte sedimentation rate, ferritin, hemoglobin and counts for red blood cells, leukocytes and neutrophils during the treatment period. **Conclusions**. This study demonstrates that tocilizumab significantly and meaningfully reduces disease burden in patients with active RA patients. In addition, tocilizumab diminishes the levels of inflammatory anemia in the patients by inhibiting hepcidin production. These clinical data provide evidence of a favorable outcome from the tocilizumab in RA.

P2-292

Concordance between ultrasound joint synovitis and clinical joint assessments by patients or physicians in rheumatoid arthritis

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Conflict of interest: None

Objective: Ultrasonography (US) has been prevalently used as a valid and objective modality for joint examination in patients with rheumatoid arthritis (RA). This study aimed to examine and compare the concordance between joint symptom, tenderness, or swelling and US synovitis. Methods: Fifty patients with RA (84% female; median age, 69 years; disease duration, 2.4 years; disease activity score of 28 joints, 3.84) completed the self-evaluation of joint symptoms including pain and considerable stiffness in the (proximal) interphalangeal, metacarpophalangeal, wrist, elbow, shoulder, knee, and ankle joints. These joints were also subjected to physical examination by a physician to evaluate for the presence of tenderness and/or swelling, and to US examination for the presence of synovitis defined as gray-scale score ≥2 or power Doppler signal score ≥1. Results: In a total of 1492 evaluated joints, symptoms, tenderness, and swelling were observed in 288 (19.3%), 182 (12.2%), and 220 (14.7%) joints, respectively, and US synovitis was observed in 317 (21.2%) joints. The overall concordance rate with US synovitis was the least for joint tenderness ($\kappa = 0.30$) when compared with joint symptoms ($\kappa = 0.39$) or swelling ($\kappa = 0.43$). Furthermore, in the composite activity measure DAS28, the substitution of tender joint count (TJC), but not swollen joint count (SJC), by US synovitis joint count or even by patient joint count (PtJC) altered DAS28 scores to some extent (r^2=0.80 and 0.82, respectively, for TJC, and r^2=0.97 and 0.96, respectively, for SJC). Conclusion: Joint swelling showed the best concordance with US synovitis, followed by patient-reported joint symptoms and then joint tenderness. Patient-reported joint symptoms may be a better clinical assessment than the examination for tenderness, leading to the improvement in DAS28 evaluation for disease activity.

P2-293

Analysis of pathogenic CD4+ T cell subsets and their transcription factors expression in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To characterize CD4+T cell subsets by cell surface markers and to analyze their expression of transcription factors in the patients of rheumatoid arthritis (RA). [Methods] We collected CD4+T cells isolated from peripheral blood mononuclear cells (PBMC) and synovial fluid mononuclear cells (SFMC) of naïve RA patients and healthy control (HC), and performed the analyses by flow cytometry. 1) The rate of helper T (Th) cell subsets classified from the cell surface markers (CD45RA, CXCR5, CXCR3, CCR6) and their expression of transcription factors (T-bet, GATA3, RORγt) in PBMC (RA N=14, HC N=9) and SFMC (RA N=3) were examined. 2) At 24 weeks after treatment, RA (N=3) were analyzed in PBMC in the same way described 1). [Results] 1) The rate of CXCR5-CD45RA-CXCR3-CCR6+ type 17 helper T (Th17) cells was significantly lower, and the expression of CCR6 and RORγt in Th17 cells was significantly higher in RA than that in HC (MFI of CCR6; RA 9048±1507, HC 5099±679.4, P=0.040. RORγt+ cells (%): RA 15.0±2.52, HC 4.32±0.46, P<0.01). In RA, the rate of Th17 cells in SFBC was higher than that in PBMC. 2) The expression of CCR6 and RORγt in Th17 cells in RA at 24 weeks after the therapeutic intervention was significantly decreased compared with that before treatments (MFI of CCR6; before treatments 10383±352.1, after treatments 4891±789.4, P<0.01. RORγt+ cells (%): before treatments 16.0±2.76, after treatment 5.67±0.80, P=0.023). [Conclusions] Our data suggested the high expression of CCR6 and RORγt of Th17 cells in contributes to migration of Th17 cells to inflamed joints, and might be related with the pathology of RA.

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Design characteristics of the CORRONA Japan-Rheumatoid Arthritis Registry

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Conflict of interest: Yes

Objectives: The primary objective is to prospectively study the comparative safety and effectiveness of newer classes and dosages of nonbiologic DMARDs, biologic DMARDs and targeted synthetic therapies approved for Rheumatoid Arthritis (RA) in a real world patient population in Japan. Secondary objectives include analyzing the epidemiology of RA health outcomes, comorbidities, and current treatment practices. **Methods:** Prospective, multicenter, non-interventional, observational study for patients with RA who are newly prescribed from 4 drug cohorts including: 1) methotrexate; 2) anti-TNF biologic DMARDs (adalimumab, certolizumab, etanercept, golimumab, infliximab, or approved anti-TNF biosimilars); 3) non-TNF biologic DMARDs (abatacept and tocilizumab),

and 4) JAK inhibitors (tofacitinib) at the time of enrollment into the registry by physicians. Target enrollment is 2,000 subjects with 500 per cohort. Baseline and follow-up data on patient demographics, medical history, disease duration, severity and activity, laboratory results, comorbidities, hospitalizations, and targeted safety events are obtained via physician and patient questionnaires. **Results:** 50 sites are anticipated to participate with 34 sites ethics committee (EC) approved at the time of abstract submission consisting of 23% clinics, 29% private mid to large-sized hospitals, 21% private academic hospitals, 15% national academic hospitals and 12% national/ local governmental hospitals. **Conclusion:** The Corrona Japan-RA Registry will provide real-world evidence on the comparative effectiveness and safety of recently approved RA therapies in Japan.

P2-295

MRI of bilateral hands prevents clinicians from failing to detect joint damage of patients with rheumatoid arthritis compared to scanning unilateral hand

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Conflict of interest: Yes

【**Object**】To compare the ability to detect joint damage of patients with rheumatoid arthritis (RA) between MRI of unilateral hand (unilateral approach) and that of bilateral hands (bilateral approach). 【**Methods**】 Thirty-one RA patients participated in this prospective study and received intravenous abatacept treatment for 12 months. MRI of bilateral hands was performed at baseline and Month 12. Images were scored for synovitis, osteitis, erosion, and joint space narrowing (JSN) according to the Rheumatoid Arthritis MRI Scoring System. Score of unilateral hand was defined as score of hand with higher synovitis score at baseline. A definite progression in the MRI score was defined as a change in the score greater than the smallest detectable change (SDC) cut-off. 【**Results**】The proportion of patients with progressive synovitis, osteitis, erosion, and JSN scores in "unilateral approach" and "bilateral approach" were 3% versus 13%, 0% versus 3%, 19% versus 19%, 13% versus 13%, respectively. We found no statistical significant differences in ability to detect progression of any MRI scores between "unilateral approach" and "bilateral approach". In "unilateral approach", however, there were 3 cases in which the progressions of synovitis in the opposite hands could not be detected and 1 case in which the progression of osteitis in the opposite hand could not be detected. 【**Conclusion**】MRI of bilateral hands revealed higher number of patients who showed progressive synovitis and osteitis scores compared to MRI of bilateral hands. Scanning bilateral hand is highly recommended when MRI is performed in clinical practice where clinicians are not allowed to overlook the progression of joint damage.

P2-296

The effect of 10-year infliximab drug survival on general health status in Japanese patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] This study was designed to identify 10-year infliximab (IFX) drug survival rates and the effect of successive 10-year IFX use on general health status in Japanese patients with rheumatoid arthritis (RA). [Methods] We retrospectively analyzed 1-year, 5-year, and 10-year drug survival rates for IFX and identified predictive factors of drug survival for IFX at each time setting. We also examined the effects of successive 10-year use of IFX (IFX-single:n=20) on patients' general health status. Blood markers such as WBC, RBC, platelet, hemoglobin, total protein, CRP, ESR, SAA, and MMP-3 in addition to CDAI, SDAI, DAS28-CRP and DAS28-ESR were compared with RA patients who first used IFX and switched their medication to other biological agents and continued their use for more than 10 years (IFX-switch:n=10). [Results] The drug survival rates for IFX are as follows: 1-year, 74% [39/53]; 5-year, 53% [28/53]; 10-year, 38% [20/53]. Logistic regression analysis revealed that low mHAQ measured before IFX usage became the statistically significant predictive factor for 1-year and 5-year IFX drug survival (1-year: [OR] =0.44, [CI95%] 0.25-0.76; 5-year: [OR] =0.54, [CI95%] 0.32-0.91), though only age became the predictive factor for 10-year IFX drug survival ([OR] =0.925, [CI95%] 0.867-0.987). The IFX-single group showed significantly improved total protein levels (p=0.01) and had a trend to reduce serum MMP-3 levels (p=0.097) when compared with the IFX-switch group, though there were no significant differences with WBC, RBC, platelet, hemoglobin, CRP, SAA, CDAI, SDAI, DAS28-CRP and DAS28-ESR between groups. [Conclusions] The 10-year drug survival rate for IFX was 38% in Japanese patients with RA and only age became the predictive factor of 10-year drug survival for IFX use. In addition, the successive 10-year use of IFX significantly improved total protein levels and had a trend to ameliorate MMP-3 elevation, as compared with 10-year multiple biologic agents usage.

P2-297

The impact of typhoons on inflammation in rheumatoid arthritis: true or myth?

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Conflict of interest: None

[Objectives] In clinical settings, many patients with rheumatoid arthritis (RA) have felt worsening disease activities when air pressure decreases and it is speculated that typhoons may affect inflammation in RA. However, to our best knowledge, there is no report investigating the influence of typhoons on blood inflammatory markers and disease activity indexes among patients with RA. This study was designed to examine whether typhoons can aggravate inflammation among patients with RA. [Methods] From August 9th to 12th in 2014, a large typhoon hit Kyoto, the most historic city in Japan and left disastrous damage. The air pressures during that period were recorded as follows: August 9th(999.1 hPa), 10th(986.2 hPa), 11th(994.3 hPa), 12th(998.6 hPa). Our hospital, located in Kyoto was also damaged by the typhoon. On August 12th, we open our out-patient clinic for thirty-five RA patients and measured blood inflammatory markers and clinical parameters such as CRP, ESR, SAA, MMP-3, grip strength, visual analogue scale (VAS), SJC, TJC, CDAI, SDAI, DAS28-CRP and DAS28-ESR. We retrospectively compared them with those measured when the last and the next visit. The last and the next visit were all within three months before/after the typhoon hit. [Results] One-way repeated analysis of variance followed by Bonferroni/Dunn post hoc revealed that the typhoon significantly elevated VAS (p=0.04: from 14±17 (last visit) to 19±21 (typhoon)) and reduced grip strength (P<0.01: from 194±83 mmHg (last visit) to 186±81 mmHg (typhoon)). In contrast, CRP (p=0.23), ESR (p=0.27), SAA (p=0.31), MMP-3 (p=0.15), SJC (p=0.50), TJC (p=0.77), CDAI (p=0.53), SDAI (p=0.46), DAS28-CRP (p=0.69) and DAS28-ESR (p=0.97) were not significantly increased with the typhoon coming. [Conclusions] Any blood inflammatory markers were not elevated by the typhoon passing, though grip strength and VAS were influenced.

P2-298

Filgotinib, a selective JAK1 inhibitor, shows similar PK and PD profiles in Japanese and Caucasian healthy subjects

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Conflict of interest: Yes

Objectives: Compare the PK, PD and safety of filgotinib between Japanese and Caucasian healthy subjects after repeated dosing of 200 mg filgotinib; compare the bioavailability of the Phase 3 tablet formulation relative to the Phase 2 formulation; assess the impact of food on formula-

tion. **Methods:** The PK of filgotinib was evaluated in 10 Japanese (1st and 2nd generation residing outside Japan for less than 5 years) and 10 Caucasian healthy subjects receiving once daily 200 mg filgotinib or placebo for 10 days. The overall PD effect was assessed in whole blood using *ex vivo* IL-6 induced phosphorylation of STAT1 (pSTAT1) as biomarker for JAK1 activity. In separate studies the PK of filgotinib after single 200 mg dose as different solid dosage formulations in healthy subjects and patients with rheumatoid arthritis (RA) were compared and the influence of food evaluated. **Results:** Overall exposures for filgotinib were similar in Japanese and Caucasians. In both ethnic groups, IL-6 induced pSTAT1 was decreased over the entire 24 hour post-dosing period, with maximum inhibition observed between 1 and 5 hours post dose. The different solid dosage formulations tested in healthy subjects and in RA patients resulted in comparable exposure with no clinically relevant food effect. The dose of 200 mg filgotinib was generally safe and well tolerated. **Conclusions:** Filgotinib showed comparable PK, PD and safety profiles in Japanese and Caucasian healthy subjects and comparable bioavailability with different oral solid formulations in healthy subjects and RA patients. The similarity in the PK and PD response suggests that there are no relevant differences among the ethnic groups in drug metabolism or JAK1 inhibition. These data support that filgotinib as the Phase 3 tablet may be administered at similar doses in Japanese and Caucasian RA patients.

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Clinical data confirm that filgotinib, a selective JAK1 inhibitor, has a low potential for drug-drug interactions and can be safely co-administered in RA subjects

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Conflict of interest: Yes

Objectives: Explore potential drug-drug interactions of filgotinib *in vitro* and in humans. **Methods:** Inhibition or induction of drug-metabolizing enzymes [CYP450, UGT] and drug transporters (Pgp, BCRP, BSEP, OATs, OCTs, OATP1B1/B3) were studied using human materials with reference substrates as suitable. *In vitro* conclusions on interaction potential with CYP3A4 were confirmed by evaluating the effects of filgotinib (200 mg QD) on midazolam (2 mg). Furthermore, the interaction with methotrexate, a drug commonly administered to RA patients and partially eliminated in urine by OATs was investigated in RA patients treated with up to 300 mg QD filgotinib. Lastly, the effect of acid reducing agents and P-gp inhibitor on filgotinib (200 mg) was assessed. **Results:** *In vitro* studies showed that filgotinib metabolism is mediated by carboxylesterases (CES). *In vitro*, filgotinib does not induce CYPs nor inhibit CYPs, UGT1A1, UGT2B7 and drug transporters, except minor effects on OCT2. In healthy subjects, midazolam pharmacokinetics were not impacted by filgotinib (5% increase in midazolam AUC). No clinically relevant effect of ARA (16% [famotidine] to 27% [omeprazole] decrease in filgotinib C_{max} only) or of itraconazole, potent P-gp inhibitor (64% increase in filgotinib C_{max} only) was observed. In RA patients, neither C_{max}, nor AUC of methotrexate was influenced by the co-administration of filgotinib. **Conclusions:** The clinical data show a lack of relevant drug interactions by filgotinib with CYP3A4 substrates, either through inhibition or induction of CYP3A4 activity, as well as with OATs transporters via methotrexate elimination. In addition, ARA and P-gp inhibitor do not interact with filgotinib. All together with the *in vitro* data on CYP450s, UGTs and key drug transporters, support that filgotinib can be co-administered with drugs usually administered to RA patients without dose adjustment.

P2-300

The long-term results of the total knee arthroplasty for rheumatoid arthritis in term of the quality of life

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Conflict of interest: None

[Object] To evaluate the long-term results of the total knee arthroplasty for rheumatoid arthritis in term of the quality of life. [Patients and Methods] Study participants consisted of patients who received a primary TKA between July 1999 and May 2006. Of the remaining 66 patients (72 knees), 58 cases (63 knees) were female. The average age at time of surgery was 62.5-year-old. The average RA duration was 12.5 years. All cases were assessed as more erosive subset. Evaluation methods included the use of the JOA score for objective evaluation, and the Japanese version of the WOMAC and version 1.2 of the Japanese Short Form 36 (SF-36) for the patient-derived outcomes. Examination points were Pre-operation and 3, 12 and 24 months after surgery. X-ray finding and complication were also evaluated. **[**Results] In the JOA evaluation, the post-operative score increased at 3-months and continued to increase for 24 months. Especially, pain and ability to walk on level ground showed considerable improvement. The WOMAC pain and function evaluation rose at 3 months, which then gradually improved at 12 months but got worse slightly in latest follow-up period. The SF-36 consists of 8 health components. Regarding physical health, there was significant improvement after 3 months and continued improvement over 12 months. The emotional health score, there was no clear improvement after 3 months, significant improvement was observed after 12-months. However, all 8 components got worse in latest follow-up period. Falling rete was more significant in SF-36 rather than WOMAC. In X-ray finding, there were 10 cases which had clear zone in ether component but no instability. About complication, deep infection occurred in one case but it was cured without leaving components. Femoral supracondylar fracture occurred in three cases and osteosynthesis was performed. [Conclusion] QOL of RA patients improved after receiving TKA in short term but got worse gradually in long term, especially in SF-36.

P2-301

The influence of aging on comprehensive disease remission in rheumatoid arthritis patient

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Conflict of interest: None

[Objective] Influence of aging on comprehensive disease remission (CDR) in rheumatoid arthritis patient in investigated from clinical data. [Methods] 299 RA patients who are treated for more than 4 years, were enrolled. Patient was classified for onset age. In these, EORA is no less than 65-year-old at onset, and YORA for the younger onset. YORA is separated for their age at endpoint, if it is no less than 65-year-old, YORA is classified as oYORA, and as yYORA for the younger. Patient was classified as CDR as three indices, in what 28-joint disease activity index with C-reactive protein (DAS28), modified health assessment questionnaire (mHAQ), and yearly progress of Sharp/van der Heijde Score (dSHS), were fulfilled remission. Number of CDR for each of the three age groups was counted, and their distribution, failure ratio (F-ratio) of each of CDR indices, and CDR for each age group were statistically evaluated with chi-square test. Statistical significance was set within 1%. [Results] Number for each age group counted 117, 81, and 82 for EORA, oYORA, and yYORA, respectively. Of these, remission was achieved 107, 67, 84 in EORA, while 85, 71, 66 in oYORA, and 65, 69, 55 in yYORA for DAS28, mHAQ, and dSHS respectively. F-ratio was 0.085, 0.427, 0.282 in EORA, 0.158, 0.297, 0.347 in oYORA, and 0.198, 0.148, 0.321 in yYORA, for DAS28, mHAQ, and dSHS respectively. EORA demonstrated significantly smaller F-ratio than the other, while oYORA demonstrated significantly smaller F-ratio than yYORA for DAS28. For mHAQ, EORA demonstrated significant larger F-ratio than the other, while oYORA demonstrated significant larger F-ratio than yYORA. For dSHS, there showed no significant difference between the three, and overall CDR F-ratio demonstrated no significant difference. [Conclusions] Elderly patient tend to decline activity in daily living, so that mHAQ is likely to fail, however, more easy to manage disease activity, as a result, tends to achieve remission in DAS28.

P2-302

The long-term efficacy of tocilizumab in refractory rheumatoid arthritis - A single-center cohort study

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Conflict of interest: None

Objectives: To evaluate the long-term efficacy of tocilizumab (TCZ) in patients with rheumatoid arthritis (RA) which are refractory to disease-modifying antirheumatic drugs (DMARDs) and tumor necrosis factor inhibitors (TNFi). Methods: We conducted a retrospective study of 38 patients who are inadequate responders to DMARDs and TNFi with high disease activity (DAS28-ESR > 5.1) and had been treated with TCZ during June 2012 to September 2016 for successive two years. We recorded demographic data and assessed disease activities of RA every three months by DAS28-ESR. We further evaluated the efficacy of TCZ in two groups, divided by the age of under 65 years (<65) and 65 years or more (≥65). Results: Under the 2-year treatment of TCZ, the average DAS28-ESR decreased from 6.9±0.5 to 3.3±0.7 (mean ± SD). According to EULAR response criteria, all patients achieved moderate response (DAS28-ESR < 5.1) at 2 years, among whom 13.2 and 50% achived remission and good response respectively. Neither remission (11.5% versus 16.7%; p=0.6) nor good response (46.2% versus 58.3%; p=0.7) had significant difference between the two groups. Conclusions: The current study yielded that the efficacy of TCZ in patients with refractory RA within 2 years regardless of the ages.

P2-303

Intravenous Infusion of Umbilical Cord Blood-Derived Mesenchymal Stem Cells in Rheumatoid Arthritis: A Phase 1, Proof-of-Concept Clinical Trial

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Conflict of interest: None

Object: The immunomodulatory actions of human umbilical cord blood (hUCB)-derived mesenchymal stem cells (MSCs) in rheumatoid arthritis (RA) have been studied extensively via in vitro or pre-clinical studies, yet few human trials have been conducted investigating the outcome of hUCB-derived MSC infusion. Methods: The CURE-iv trial was a phase 1, proof-of-concept clinical trial for RA patient with moderate disease activity despite treatment with methotrexate. Patients meeting the 2010 ACR/EULAR classification criteria and with a DAS28-ESR >3.2 were eligible for the trial. Subjects were each given a single intravenous infusion of 2.5 x 10^7, or 5 x 10^7, or 1 x 10^8 cells of hUCB-derived MSCs for 30 minutes; 3 patients in each cluster, with increment of cell numbers when there was no dose-limited adverse events. Clinical and safety parameters were monitored and followed after the infusion period (first 24 hours, 72 hours, 1 week, and 4 weeks). Serum cytokines at baseline and 24 hours after the infusion were analyzed. Results: Eleven RA patients were screened, 9 of which were enrolled from a single center. The mean age was 57.4 years, 78% being female, with a disease duration of 9.5 ± 8.7 years, and DAS28-ESR 4.53 ± 1.35. There was no ominous safety signal in all clusters up to 4 weeks after the infusion. One patient stated joint pain 60 min after the infusion (5 x 10^7 group), but it was thought to be unrelated to the investigational product. ESR and CRP changes at 4 weeks (n=9) were -7.89 ± 10.36 (p= 0.0517), and -0.37 ± 1.09 (p=0.3362). DAS28 and HAQ changes at 4 weeks were -1.60 ± 1.57 (p= 0.0159), and -0.15 ± 0.48 (p= 0.3706), respectively. One patient in the 1 x 10^8 group showed substantial decrease in all serum levels of IL-1beta, IL-6, IL-8, and TNF-alpha. Conclusions: This phase 1 clinical trial - a single dose intravenous infusion of hUCB-derived MSCs - for established RA patients was completed without any short-term safety concerns (NCT02221258).

P2-304

Semaphorin 4A was elevated in rheumatoid arthritis and correlate with production of rheumatoid factor and IgM

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Conflict of interest: None

Objective: Semaphorin 4A has been found to be involved in regulation of immune responses. The aim of this study was to investigate potential role of Semaphorin 4A in Rheumatoid arthritis. **Methods:** Blood samples were obtained from 93 patients with RA, 34 with SLE and 20 healthy controls. Expression of Semaphorin 4A mRNA in PBMC was measured by quantitative RT-PCR. Serum levels of Semaphorin 4A were analyzed by enzyme-linked immunosorbent assay. Clinical and laboratory characteristics of RA patients were performed and recorded. **Results:** Expression of Semaphorin 4A mRNA was higher in PBMC of RA patients than in SLE (P<0.01). Consistently, levels of serum Semaphorin 4A were significantly elevated in RA patients, compared with SLE and healthy controls (P<0.001, both). In subgroup analyses, serum Semaphorin 4A was higher in ACPA positive RA patients than ACPA negative controls (P<0.01). Moreover, it tends to be higher in active RA patients than patients in remission (P=0.05). No correlations were found between Semaphorin 4A levels and age, sex, disease duration, TJC, SJC, VAS, ESR, CRP, DAS28 as well as bone turnover markers CTX-I, osteocalcin and cathepsin K. Interestingly, Semaphorin 4A levels were positively correlated with RF titer (r=0.275, P<0.05) and IgM (r=0.287, P<0.05). **Conclusion:** These findings suggest that Semaphorin 4A might contribute to the active phase of RA and promote autoantibody production.

P2-305

Effect of Total hip arthroplasty on daily activity and disease activity in rheumatoid arthritis

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Conflict of interest: None

Objective: Total hip arthroplasty (THA) is a successful treatment for hip arthritis in rheumatoid arthritis (RA) patients. The purpose of this study was to investigate effect of total hip arthroplasty on daily activity and disease activity in RA patients. Method: 13 RA patients (16 hips) who underwent THA between 2010 and 2013 in our institution were enrolled in this study. Harris hip score (HHS), DAS-28 (CRP), and serum MMP-3 levels were assessed before and 1 year after THA. Result: 9 females (11hips) and 4 males (5 hips) with mean age of 69 years old were enrolled. Pain score, function score including limping and walking distance scores, activity score, and score for range of motion in HHS were significantly improved after THA. With decreasing of numbers of tenderness joints, serum CRP levels, and visualized analog scale, mean DAS-28 (CRP) was significantly improved after THA. Mean serum MMP-3 was also significantly decreased after THA. In a patient, periprothetic fracture was occurred during surgery but other complications were not seen during 1 year follow-up period. Conclusion: Arthritis in hip severely disabled daily activity in RA patients. THA improved hip pain, function, and inflammation that resulted in improvement of daily activity and disease activity in RA patients.

P2-306

A case in which multiple myeloma was manifested by discontinuing tocilizumab administered to rheumatoid arthritis

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Conflict of interest: None

A 85 - year - old woman had been pointed out IgA-κ type M proteinuria. Since 7 years ago, she was administered tacrolimus, prednisolone and tocilizumab for rheumatoid arthritis, and was admitted for the causes of anemia and renal dysfunction. Since joint symptoms were not observed, tocilizumab and tacrolimus were stopped. Two weeks after hospitalization, consciousness disturbance due to hypercalcemia occurred, and the same type of M protein as before was confirmed by immunoelectrophoresis examination. Bone marrow aspiration was not done. But, we have strongly suspected hypercalcemia was caused by multiple myeloma. M protein was observed before administration of tocilizumab, so in this case, multiple myeloma was accompanied by rheumatoid arthritis and it was suppressed by tocilizumab, and by stopping tocilizumab, multiple myeloma was manifested in hypercalcemia. It has been pointed out that tocilizumab, an IL-6 receptor antibody, inhibits the proliferation of multiple myeloma in basic studies. There is also a case report of rheumatoid arthritis and multiple myeloma both of which could be controlled by administration of tocilizumab. The tocilizumab use guidelines for rheumatoid arthritis suggest that it is desired to avoid tocilizumab administration to patients with previous malignancy or treatment, but as in this case of multiple myeloma accompanied by rheumatoid arthritis, administration of tocilizumab would provide therapeutic effects for both diseases.

P3-001

Establishment of autoinflammatory disease model in mice

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Conflict of interest: None

BACKGROUND. Recently, IL-1 is implicated in the pathogenesis of auto-inflammatory syndrome. To date, several animal rheumatoid arthritis models such as Collagen-Induced Arthritis/Adjuvant-Induced Arthritis (CIA/AIA) were established, however, no animal models for IL-1 diseases were reported. METHODS. We newly generated conditional transgenic mice of human IL-1 (IL-1 cTg), in which human IL-1α was driven under a Cre/loxP system, in a C57/BL6 background. We crossed the IL-1 cTg mice with inducible Cre mice, Mx1 Cre mice, to yield Mx1 Cre/IL-1 cTg mice. PolyIpolyC was administrated to 8-week old Mx1 Cre/IL-1 cTg mice, and the phenotypes were observed. Mx1 Cre/IL-1 cTg mice were also crossed with IL-6 knockout (IL-6 KO)mice or IL-17 knockout (IL-17KO)mice to yield Mx1 Cre/IL-1 cTg/IL-6 KO or Mx1 Cre/IL-1 cTg/IL-17 KO, respectively. RESULTS. Arthritis development was seen in all Mx1 Cre/IL-1 cTg mice one week after polyIpolyC administration. Elevated white blood cell counts, dermatitis, and splenomegaly were detected in these mice. Interestingly, these phenotypes were rescued in either Mx1 Cre/IL-1 cTg/IL-6 KO or Mx1 Cre/IL-1 cTg/IL-17 KO. CONCLUSION. We successfully generated a new IL-1 disease model, and show that either IL-6 or IL-17 may represent a therapeutic target to this disease.

P3-002

Exploration of the mechanisms of production with citrullinated proteins and ACPA in peptide GPI-induced arthritis

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Conflict of interest: None

[Object] To explore the pathogenic relevance of citrullinated proteins (Cit-P) and anti-citrullinated protein antibodies (ACPA) in peptide GPI-induced arthritis (pGIA). [Methods] 1) The titers of anti-pGPI antibodies and ACPA in sera were analysed by ELISA. 2) Cit-P expressions in joints and skins were examined by immunohistochemistry, those in sera were examined by Western blot analysis. 3) Cl-amidine (PAD inhibitor) was injected to pGIA. Clinical score, ACPA titers, Cit-P expressions and the level of proinflammatory cytokines in sera were assessed. [Results] 1) The titers of anti-pGPI antibodies and ACPA from pGIA were elevated from day14, and were significantly higher than those from control mice. 2) Cit-P was detected in joints on day14 and in skins on day7 from pGIA, whereas not detected from control mice. In sera, Cit-P was detected from pGIA at approximately 120 kD. 3) By Cl-amidine treatment, clinical score was significantly decreased, and ACPA titers tended to be lower. Cit-P in joints, skins and sera were clearly decreased, IL-6 level was significantly decreased. [Conclusions] Cit-P and ACPA were increased in pGIA, and the inhibition of PAD suppressed arthritis and Cit-P expressions. These results suggested that PAD was involved in the pathogenesis of autoimmune arthritis.

P3-003

Clinical effect can be predicted by RA synovial tissue grafted mice model

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Conflict of interest: None

Object: Many animal models have been used to evaluate the efficacy of antirheumatic compounds. However, in many cases, the clinical effects do not consistent with the results of animal model. This fact suggests that these animal models can not completely reflect human RA pathophysiology. In our study, we expected that synovial tissue grafted model can be used to predict the efficacy on RA synovial tissue. Methods: Synovial tissue from RA patients were subcutaneously implanted into severe combined immunodeficient mice (day 0). On day 7, plasma samples were collected and human cytokine derived from the implanted tissue was measured. Compounds which inhibit Janus kinase (JAK) or p38 mitogen-activated protein kinase (MAPK) were administrated for a week from day 8. To investigate the changes in human cytokine level, murine plasma were collected again on day 15. Results: JAK inhibitor, which efficacy is validated in RA treatment, suppressed human IL-6 induced by grafted tissue. On the other hand, p38 MAPK inhibitor which has failed to show enough clinical effect could not suppress human IL-6. Conclusions: Our result indicates that the therapeutic efficacy on RA synovial tissue could be predicted by using this model.

P3-004

Amelioration of rheumatoid arthritis-like disease by blocking of CD11b$^+$ cell-migration in a unique FcgRIIB-deficient mouse model

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Conflict of interest: None

[Object] Osteoclasts are derived from osteoclast precursors involved in peripheral monocytes and play an important role for bone destruction in rheumatoid arthritis. Here, we examined the effect of extravascular migration block of monocytes on the severity of arthritis. **[Methods]** Arthritis-prone FcgRIIB deficient B6 mice (designated KO1) were treated with rat anti-CD11b mAb (5C6), which blocks the migration of CD11b$^+$ cells including monocytes from vessels. **[Results]** Compared to non-treated KO1 mice, the development of RA was markedly suppressed in 5C6-treated mice associated with the lower serum levels of autoantibodies. The frequencies of CD69$^+$ and PNA$^+$ activated B cells and CD138$^+$ plasma cells in spleen were significantly decreased in 5C6-treated mice.

[Conclusion] 5C6 ameriorates joint inflammation and bone destruction in KO1 mice. 5C6 also suppress the activation of B cells with unknown mechanism. Detailed analysis is underway.

P3-005

Brain immunopathology of lupus-prone FcγRIIB$^{-/-}$Yaa mice – possible new neuropsychiatric lupus model

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Conflict of interest: None

Background: The entire pathophysiology of neuropsychiatric SLE (NPSLE) is still unclear, thus new animal models are important. Here we investigated the brain immune pathology of lupus-prone FcγRIIB$^{-/-}$Yaa mice in which deficiency of suppressive Fcγ receptor and dupulication of Toll-like receptor 7 potentiate autoimmunity. Methods: Brain immune pathology were analyzed by flow cytometry and immunohistochemistry in FcγRIIB$^{-/-}$Yaa mice at around 10 to 20 week-old. Congenic mice and other lupus model of NZBWF1 mice were also examined. Results: Flow cytometric analysis revealed increase in the number of microglial cells and myeloid lineage cells in the brains of FcγRIIB$^{-/-}$Yaa mice. MHC classIand class II expression were increased in those cells. In histopathology, MHC was also highly expressed in the vascular endothelium. Microglia and astrocytes were increased around them, suggesting chronic activation of glia. Though there was no clear accumulation of lymphocytes in the choroid plexus, focal increase were observed. These changes began around 10 weeks. Conclusion: Immunological changes were observed in the central nervous system of FcγRIIB$^{-/-}$Yaa mice even in early stage. This model will contribute to further understanding of NPSLE.

P3-006

The pathological role of IL-18Rα in the onset of nephritis of systemic lupus erythematosus (SLE) model mice

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Conflict of interest: None

[Objectives] IL-18 is a type of inflammatory cytokine produced from inflammatory cells like macrophages, and it has been reported that serum IL-18 is correlated with disease activity in humans and murine lupus, but the relation between IL-18Rα and the onset of lupus nephritis (LN) is unknown. We made IL-18Rα-deficient (K.O) SLE model mice cause renal ischemia/reperfusion injury (IRI) and evoke the LN, and examined a role of IL-18Rα. [Methods] Using SLE model mice (MRL-FAS^{lpr}) of the K.O group and the wild-type (WT) group, we evaluated the LN onset and disease activity by measurement of renal function, urinary albumin, serum anti-DNA-IgG antibody, histological analysis in acute and recovery phase after IRI. [Results] There was no significant difference between the K.O group and the WT group in serum BUN values in acute and recovery phase, and urinary albumin values over time. However, during recovery phase, serum anti-DNA-IgG antibody titer and the stage assessment of glomerular, tubular, perivascular infiltrates was significantly higher in the K.O group. [Conclusion] There were some differences in the LN onset and increase of disease activity between two groups in recovery phase. It was suggested that IL-18R influenced the LN onset, increase of disease activity due to ischemia.

P3-007

Interferon alpha causes SLE: double negative T (DNT) cell over-expressing PD-1 and Helios is responsible for the genesis of organ pathology in SLE

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Conflict of interest: None

Objective: We have successfully established an IFN alpha transgenic mice (IFN alpha Tg) that induces anti-dsDNA autoantibody and organ pathology such as glomerular disease akin to human SLE. In these mice, activated effector T cells were predominant, and CD3$^+$CD4$^-$CD8$^-$ double negative T (DNT) cells, responsible for glomerular organ injury, were expanded in the spleen. In the present study, we examined the phenotype of DNT cell in relation to the pathogenesis of SLE. **Methods:** CD3$^+$CD4$^-$CD8$^-$ DNT cell in spleen of IFN alpha Tg mice was detected and analyzed by using flow cytometry. **Results:** Splenic CD3$^+$CD4$^-$CD8$^-$ DNT cell of IFN alpha Tg mice expressed TCR beta and B220, whereas DNT cell was negative for pre-T cell receptor alpha, c-Kit and CD1d-tetramer. Further, PD-1 and Helios were highly expressed on DNT cell of IFN alpha Tg mice, in consistent with previous finding that PD-1$^+$Helios$^+$ DNT cells as autoreactive. **Conclusion:** IFN alpha augments DNT cell over-expressing PD-1 and Helios, and this DNT cell is responsible for the organ pathology as observed in SLE.

P3-008

Nrf2 is a critical target for the treatment of glucocorticoid-resistant lupus nephritis

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Conflict of interest: None

Objective: The aim of this study is to evaluate the anti-inflammatory effects of Nrf2 activators on human renal mesangial cells (HRMCs) and the development of lupus nephritis (LN) in mice. **Methods:** HRMCs were treated with Nrf2 activators and prednisolone. The expression levels of Nrf2 and its target genes were measured using qRT-PCR and ELISA. The anti-inflammatory effects of these compounds were assessed by measuring TNFα-induced cytokine secretion. Experimental LN was induced in BALB/c mice by a single intraperitoneal injection of pristane. The urine albumin-to-creatinine ratio was measured at 20 weeks after injection. Pathological changes as well as protein and mRNA expression levels were assessed in the kidney. Oral administration of Dimethyl fumarate (DMF) or prednisolone was initiated after pristane injection. **Results:** Nrf2 activators showed anti-inflammatory effects in HRMCs, whereas glucocorticoid (prednisolone) showed partial effects. Moreover, DMF ameliorated the development of kidney diseases in pristane-induced LN mice, whereas prednisolone did not have any effect. **Conclusion:** Nrf2 activators are potential therapeutic targets in glucocorticoid-resistant LN in humans.

P3-009

Deficient leptin signaling ameliorates sialoadenitis in MRL/lpr mice

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Conflict of interest: None

[Object] Leptin is secreted by adipocytes, the placenta, and the stomach. It not only controls appetite through leptin receptors in the hypothalamus, but also regulates immunity. In the present study, we investigate the potential role of leptin in sialoadenitis of MRL/lpr mice. [Methods] We produced leptin-deficient MRL/lpr mice. The effects of leptin deficiency on sialoadenitis were investigated in MRL/lpr mice. [Results] Submandibular sialoadenitis was suppressed in leptin-deficient MRL/lpr mice compared with leptin-intact MRL/lpr mice. [Conclusions] Leptin may promote the sialoadenitis in Sjogren's synderome. Blockade of leptin signaling may be of therapeutic benefit in Sjogren's syndrome.

P3-010

Role of allograft inflammatory factor-1 in bleomycin-induced lung fibrosis of mice

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Conflict of interest: None

Allograft inflammatory factor-1 (AIF-1) is a protein expressed by macrophages infiltrating the area around the coronary arteries in a rat ectopic cardiac allograft model. We previously reported that AIF-1 is associated with the pathogenesis of rheumatoid arthritis and skin fibrosis in sclerodermatous graft-versus-host disease mice. Here, we used an mouse model of bleomycin-induced lung fibrosis to analyze the expression of AIF-1 and examine its function in lung fibrosis. The results showed that AIF-1 was expressed on lung tissues, specifically macrophages, from mice with bleomycin-induced lung fibrosis. Recombinant AIF-1 increased the production of TGF-β which plays crucial roles in the mechanism of fibrosis, by mouse macrophage cell line RAW264.7. Recombinant AIF-1 also increased both the proliferation and migration of lung fibroblasts compared with control group. These results suggest that AIF-1 plays an important role in the mechanism underlying lung fibrosis, and may provide an attractive new therapeutic target.

P3-011

Anti-cyclic citrullinated protein antibody (ACPA) positivity in general population and follow-up results for ACPA positive

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Conflict of interest: None

[Object] To evaluate anti-cyclic citrullinated protein antibody positivity in the general population and to identify its prognosis. [Methods] Anti-cyclic citrullinated protein antibody (ACPA) were measured with immunochromatographic (IC) test in 3607 people who visited for health check from November 2014 to March 2016. For ACPA positive persons, consultation to rheumatology was recommended. Rheumatologist performed physical examination. Symptomatic examinees that do not fulfill classification criteria even if they have morning stiffness or joint pain were recommended to visit every 3 months. [Results] ACPA positivity with IC test was identified in 1.0%(n=37) of examinees. 64%(n=24) consulted to rheumatology department. They were confirmed ACPA positivity with CLEIA method. 58.3%(n=14) were CLEIA method positive. 4 examinees have already diagnosed as RA and 5 examinees have morning stiffness or joint pain, which did not fulfill classification criteria. Mean follow-up period of ACPA positive examinees with CLEIA and IC method was 10.5 month. One patient developed RA and she reached remission in 2 month after starting DMARDs. [Conclusion] Positivity of ACPA in general population was 1%. Regular follow-up of ACPA positive patient could lead prompt diagnosis and treatment.

P3-012

Higher avidity of IgG antibodies to human IgG1 or IgG4 hinge is accentuated in rheumatoid arthritis

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Conflict of interest: None

[Background and Purpose] Anti-hinge antibodies (AHA) are natural autoantibodies and have been demonstrated significantly higher in RA than other rheumatic diseases (non-RA). This study shows whether avidity of AHA is also higher in RA. [Patients & Methods] Tocilizumab and Natalizumab were used as a source of human IgG1 and IgG4 hinge antigen, respectively. Pepsin and MMP-3 were used as proteases for cleavage of IgG1 and IgG4 hinge region. IgG AHA in sera from patients with RA and non-RA and from healthy subjects was measured by ELISA. Avidity of IgG AHA was measured by inhibition ELISA using 3M-urea. [Results] All of the four IgG AHA levels were significantly elevated in RA. Avidity of four IgG AHA also showed significantly higher in RA by reflecting high IgG AHA levels. Even after adjustment to become almost the same IgG AHA level between RA and non-RA, the avidity showed significantly higher in RA. [Conclusion] IgG AHA in RA seems to be under control of affinity maturation similar to ACPA.

P3-013

The Clinical Significance of Anti-Cyclic Citrullinated Peptide Antibody Titers when Treating Rheumatoid Arthritis

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Conflict of interest: None

Purpose:The significance of anti-cyclic citrullinated peptide antibodies (ACPAs) as markers for evaluating the state of disease has not been established. We investigated ACPA changes over the course of treatment as well as correlations between ACPAs with parameters such as inflammation markers and disease activity. Methods:We investigated correlations between ACPAs and CRP, MMP-3, RF, IgG, IgM, DAS28 and mHAQ at baseline and after treatment in 149 rheumatoid disease patients. We investigated ACPA rate of change as well as how it correlated with other parameters in the 73 cases in which baseline levels of ACPAs were 100 U/mL or above. Results:Baseline ACPAs were found to correlate with RF, DAS28, CRP, IgG and IgM. However, after treatment, ACPA titers only correlated with MMP-3 and IgM. Parameters for which correlations were noted with ACPA rate of change were RF rate of change, DAS28 rate of change, IgG rate of change and IgM rate of change. When a group of cases in which ACPA levels decreased was compared with a group in which they increased, significant differences were noted for rates of change of RF, MMP-3, DAS28, CRP, IgG and IgM. Conclusions:While ACPAs are already known to be a disease marker, our results suggested that they could be useful as an index for evaluating the state of disease.

P3-014

Examination of Diseases other than Rheumatoid Arthritis in anti-CCP antibody-positive patient

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Conflict of interest: None

[Purpose] Anti-cyclic citrullinated peptide (CCP) antibody is a useful test for the diagnosis of Rheumatoid Arthritis (RA) with its high specificity of 96% and sensitivity of 67% reported in a recent study. However, clinician needs attention that some diseases other than RA are still included. [Method] We reviewed patients who measured anti-CCP antibody in our hospital between March/30/2010 and October/17/2016. We extracted patients with anti-CCP antibody positive without the diagnosis of RA. [Result] During the period, 1401 patients measured anti-CCP antibody, and 359 patients were positive. Among them, 333 patients (92.8%) were diagnosed as RA, 17 patients (4.7%) diagnosed as other diseases, and 9 patients (2.5%) did not reach diagnosis due to too short follow-up period. Diseases other than RA include 5 cases of osteoarthritis, 3 cases of polymyositis / dermatomyositis, 2 cases of Juvenile idiopathic arthritis, each one case of Sjogren syndrome, sacroiliac joint flame, tendon enthesitis, fibromyalgia, single wrist joint inflammation, suspect of scleroderma, and laboratory abnormality only. [Conclusion] Anti-CCP antibody positive patients include those who were diagnosed other than RA, with the variety of disease spectrum. Clinicians had better be careful in the daily practice.

P3-015

Significance of Anti-Mitochondrial Antibody Measurement in Connective Tissue Disease

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Conflict of interest: None

"Purpose" Primary biliary cholangitis (PBC) associated with autoimmune diseases. But anti - mitochondrial M2 antibody (AMA) is not sufficiently screened, we examined the necessity of examining AMA - measured cases in our hospital. " Method" We measured 239 cases of AMA measurement for the first time at our hospital and examined the positive rate of AMA in auto-antibody positive cases. Furthermore, hepatic fibrosis of AMA positive cases was examined. "Results" AMA was detected in 16% of all cases, 47% of which were positive for SS-A antibody (SSA), 43% positive for anti-centromere antibody (ACA), 7% positive for both SSA and ACA there were. AMA was detected in 16% of SSA positive cases and 41% of ACA positive cases. Serum ALP, γGTP and IgM were significantly higher in AMA-positive cases, but the mean and median were within the standard limits. In the study of hepatic fibrosis in AMA-positive cases, liver fibrosis index by real-time tissue elastography was 29% when it was 2.0 or more and 25% when the cut-off index of M2BPGi was 1.0 or more. "Conclusion" AMA was found in high rate in SSA, ACA positive cases. Liver fibrosis progression was estimated to be 20% or more, and it was thought that AMA measurement was necessary especially for SSA and ACA positive cases.

P3-016

Autoantibodies to Ki/SL are detected mainly in MCTD, overlap syndrome and polymyositis and frequently coexist with anti-U1RNP antibodies

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Conflict of interest: None

[Objective] Autoantibodies to Ki/SL have been reported in ~10% of patients with SLE, however, its clinical significance is not well established. We aimed to clarify clinical characteristics of patients with anti-Ki antibodies. [Methods] Autoantibodies in sera from 249 patients with systemic rheumatic diseases (26 PM 26, 47 DM, 20 CADM, 12 SLE, 82 SSc, 13 MCTD, 21 overlap syndrome, 28 others) were tested by ELISA and radioimmunoprecipitation (IP). Clinical features associated with anti-Ki were analyzed. [Results] Fourteen of 249 sera were anti-Ki positive; 13%(3/26) in PM but none in DM/CADM (0/67, p = 0.02), 8% in SLE, 3% in SSc, 23% in MCTD, 14% in overlap syndrome (3/21, all 3 were SLE-SSc overlap). Coexisting autoantibodies in 14 anti-Ki positive patients include anti-U1RNP (8), Sm (3), Ro52 (7), Ro60 (8), CENP-A/B (3), Su/Ago2 (3), RNA helicase A (2), OJ and EJ one each. Prevalence of anti-Ki among other antibody+ patients were 24%(8/33) in anti-U1RNP, 5% in anti-CENP-A/B (3/57), OJ 1/7 case, and EJ 1/9 case. Anti-Ki was not found in patients with anti-topoisomerase I (9), RNA polymerase III (8), MDA5 (18), or TIF1g (9). [Conclusion] anti-Ki antibodies are mainly found in MCTD, SLE-SSc overlap syndrome, PM and SLE and frequently coexist with anti-U1RNP antibodies.

P3-017

Anti-ribonuclease H2 is an immune biomarker for systemic lupus erythematosus

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Conflict of interest: None

Background: We previously reported that autoantibodies against chromatin assembly factor-1 (CAF-1), the proliferating cell nuclear antigen (PCNA)-binding protein, are specifically found in systemic lupus erythematosus (SLE). PCNA and its complex constituents elicit autoimmune responses in patients with SLE, suggesting that autoantibody diversification likely occurs due to epitope spreading. *Materials &* **Methods:** RNase H2 and CAF-1 immunoreactivity to recombinant antigens were evaluated by ELISA and further confirmed by immunoblot analysis using sera of patients with SLE or other systemic autoimmune diseases as well as healthy controls. **Results:** RNase H2 autoantibodies were detected in the sera of 33.9%(19/56) of SLE patients, and the frequency was significantly higher than the other systemic autoimmune diseases and healthy controls. Regression analysis also showed that serum anti-RNase H2 levels were strongly correlated to that of CAF-1 in SLE patients. **Conclusion:** Our data supports the use of RNase H2 autoantibodies as a serum biomarker for SLE diagnosis. Moreover, the strong correlation observed between RNase H2 and CAF-1 suggest that intermolecular epitope spreading may play a critical role in autoantibody production and diversification in SLE.

P3-018

The motor functions and the risk of osteoporotic fractures in RA patients with sarcopenia

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Conflict of interest: None

We investigated the motor functions and the risk of osteoporotic fractures in RA patients with sarcopenia. Method: Between September 2015 and September 2016, we investigated the femoral muscle in 117 RA patients who were measured with ultrasound scan. The cut-off value of the diagnosis of sarcopenia was 36mm in male and 34mm in female. In all of them the judgment of the locomotive syndrome by Japanese Orthopedic Assoc. method (Locomo test), bone mineral density measurement and the risk of osteoporotic fracture were investigated. Result: 76 patients were diagnosed as SarRA and 41 patients were non SarRA. In SarRA the average age was 73.4 years old and duration of RA was 15.6 years. In non SarRA the average age was 66.3 years old and duration of RA was 15.4 years. In Locomo test score SarRA was higher (26.5) than non SarRA (11.3). In T-score in femoral neck, SarRA was lower (-2.07) than non SarRA (-1.4). In the risk of osteoporotic fracture using FRAX, SarRA was higher (31.7%) than non SarRA (20.8%). The analysis excluding the influences of aging and sex using SPSS showed the same results. Conclusion: The RA patients with sarcopenia showed the low motor function, low bone mineral density and high risk of osteoporotic fracture compared with the RA patients without sarcopenia.

P3-019

The regulatory role of Allergin-1 in autoantibody production

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Conflict of interest: Yes

【**Objectives**】The purpose of this study is to clarify the role of Allergy inhibitory receptor-1 (Allergin-1) in autoantibody production.【**Methods**】1) WT and Allergin-1 deficient (Allergin-$1^{-/-}$) mice were treated with dead thymocytes. After dead thymocytes injection, the titer of anti-dsDNA and anti-Histone antibodies in serum was measured by ELISA. 2) WT and Allergin-$1^{-/-}$ peritoneal macrophages were co-cultured with stained apoptotic thymocytes. After 30 and 60 min, stained apoptotic thymocytes in macrophages were analyzed by flowcytometry. 3) WT and Allergin-$1^{-/-}$ peritoneal macrophages were stimulated by TLR7 ligands. After 48h, the production of IL-6, TNF-α and IL-1β in culture supernatant was measured by ELISA. 【**Results**】1) The titer of anti-dsDNA and anti-Histone antibodies was significantly higher in Allergin-$1^{-/-}$ mice compared with WT mice. 2) The phagocytic activities were significantly lower in

Allergin-1$^{-/-}$ macrophages than that in WT macrophages. 3) After TLR7 stimulation, IL-6, TNF-α and IL-1β productions were significantly increased in Allergin-1$^{-/-}$ macrophages compared with that in WT macrophages. 【**Conclusion**】 Allergin-1 might suppress autoantibodies production through the regulation of phagocytosis and inflammatory cytokine production in macrophages.

P3-020

Nailfold video capillaroscopy (NVC) is useful on diagnosis for scleroderma from Raynaud clinic in Tokyo Metropolitan Tama Medical Center

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Conflict of interest: None

Objectives: To evaluate the frequency of Giant capillaries in patients with non-scleroderma collagen diseases. Methods: Clinical data was obtained from our Raynaud clinic, where patients with Raynaud phenomenon were referred in suspicious with collagen diseases, from February to September 2016. All the patients were evaluated by NVC, blood test, and physical examination to diagnose collagen diseases including scleroderma based on ACR/EULAR scleroderma classification criteria 2013. NVC findings (microhaemorrhages, giant capillary and avascular area) were evaluated and classified into three patterns “early” “active” “late”. Results: Sensitivity and specificity of giant capillary in NVC for diagnosing scleroderma were 64.3% and 66.7%, respectively. Furthermore, those for diagnosing scleroderma spectrum disorders including undifferentiated connective tissue disease and dermatomyositis were 72.2% and 90.9%, respectively. As for NVC patterns, there were 3 cases with early and 4 cases with active pattern. One case with active NVC pattern suffered from polyarthritis, which needed to treat with tocilizumab. Conclusion: Our data suggests the presence of the giant capillary in patients with Raynaud phenomenon is the important finding for the diagnosis of scleroderma spectrum disorders.

P3-021

Prognostic value of Tpeak-Tend interval in patients with pulmonary hypertension associated with chronic rheumatic diseases

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Conflict of interest: None

[Background] The aim of this study was to examine the Tpeak-Tend (Tpe/corrected Tpe) interval, which is an indicator of transmural myocardial repolarization, measured non-invasively via electrocardiogram in patients with suspected pulmonary hypertension associated with chronic rheumatic diseases (CRD-PH). [Methods] Between March 2014 form August 2016, the study included 29 patients who suspected CRD-PH and underwent right heart catheterization (RHC), comprising 23 females and 6 males, with a mean age of 63.7 ± 12.2 years. We measured the Tpe interval using tail method from derivation V5. We calculated the QTc and corrected Tpe (cTpe) using Bazett’s formula. PH was definited mean pulmonary arterial pressure ≧ 25 mmHg by RHC. [Results] The study group was divided into two groups, CRD-PH patients (PH group) and non-CRD-PH patients (non-PH group). Not significantly, PH group had a higher level of cTpe than non-PH group (93.2 ± 31.8 ms vs 85.7 ± 13.5 ms, P=0.515). The cTpe cut-off values of 105 ms had sensivity, specificity, negative predictive value, and positive predictive value of 40.0%, 85.7%, 75.0%, and 57.1%, respectively for PH. [Conclusions] cTpe interval could be a useful method in PH diagnosis in patients with CRD-PH.

P3-022

Ultrasonographic evaluation of therapeutic response in biologic DMARDs switchers: Kyushu multicenter rheumatoid arthritis ultrasound prospective observational cohort in Japan

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Conflict of interest: None

Background; We have been prospectively investigated therapeutic efficacy by ultrasonography (US) after introduction of biologic (b) /targeted synthetic DMARDs in RA patients in Kyushu region, Japan from June, 2013. **Methods;** A total 246 RA patients were consecutively recruited. Disease activity was evaluated by both US scores and clinical composite measures every 3 months. Twenty-two joints including MCP, PIP and wrist joints of bilateral hands were assessed by grey-scale (GS) and power Dopper (PD). We evaluated sixty-nine bDMARDs switchers (TNF inhibitors, 24; TCZ, 28; ABT; 4) who completed the first 12 months observation period, in this study. **Results;** In overall, treatment continuation rates were 54% in TNF inhibitor group, 86% in TCZ group, and 76% in ABT group. DAS28-ESR significantly improved during 12 months. Total PD scores significantly improved during 12 months in TCZ and ABT groups but not TNF inhibitor group. **Conclusions;** In bDMARDs switchers, therapeutic response assessed by US may be better in TCZ and ABT group than in TNF inhibitor group. Residual synovitis could be detected by US in even if RA patients with low clinical disease activity. In addition to clinical evaluations, US assessment is considered to lead to accurate assessment of therapeutic response.

P3-023

Clinical implications of ultrasonography in monitoring disease activity of relapsing polychondritis: the assessment of auricular chondritis in 3 cases

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Conflict of interest: None

<Objective> To assess the clinical implications of ultrasonography (US) in monitoring disease activity of relapsing polychondritis (RP). **<Methods>** Three cases of a 78-year-old man with RP, a 74-year-old woman with RP associated with optic perineuritis and a 42-year-old woman with RP associated with uveitis were assessed by US before and after treatments. **<Results>** US of the auricle before treatment showed low-echoic swollen auricular cartilage with increased power Doppler signals (PDS) in all cases. US findings corresponded to the above-mentioned biopsy findings. After treatment with prednisolone combined with methotrexate, the auricular swelling completely resolved in all cases. Then, US findings also showed dramatic reductions in swelling of cartilage with the decrease in PDS. **<Disucussion>** US imaging can be used to differentiate between inflammation, vascular lesions, and tumors in the ear pinna. RP could be differentiated from the damage of repeated trauma (i.e. rugby) with producing subperichondrial serous effusion. As in the present cases, US imaging of the external ear and auricular cartilage in RP also facilitates evaluation of auricular lesions and monitoring of disease activity, especially when we consider the treatment response and the timing of drug tapering.

P3-024

A case of rheumatoid arthritis with Baker’s cyst treated using joint ultrasonography

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Conflict of interest: None

An elderly female who had suffered polyarthralgia was diagnosed as rheumatoid arthritis. The patient has been treated with loxoprofen: 180 mg, prednisolone: 10 mg and salazosulfapyridine: 1.0 g. She also suffered pain and swelling on the flexion side of her right lower leg, which was diagnosed as a Baker's cyst by leg MRI. Treatment with puncturing the cyst was attempted under the guidance using a joint ultrasonography. Puncture of the cyst collected a 70-ml yellowish and turbid synovial fluid, resulting in reduction of the cyst's size. However, since the pain and swelling of the right lower leg have recurred in two months, the puncture of the recurred cyst was re-performed under the joint ultrasonography. In addition, ligation of a connecting duct from the cyst to right knee-joint space and removal of the peripheral cysts were performed. Laboratory data were as follows: WBC: 10100/μl, CRP: 6.5 mg/dl, ESR: 40 mm/h, RF: 192 IU/ml, anti-CCP antibody: 83.2 U/ml, MMP-3: 156 ng/ml, and ANA: x40. Leg MRI exhibited high intensity area of the cyst without joint-cartilage defect and meniscus injury. The usefulness of joint-ultrasonography guidance for the puncture of Baker's cyst was discussed.

P3-025

Study of hand MRI taken within a year of rheumatoid arthritis onset ~ Where dose rheumatoid arthritis begin? ~

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Conflict of interest: None

[Methods] MRI was performed on the hands of patients with RA within a year of onset, and the distribution and frequency of arthrosynovitis, tenosynovitis, bone erosion, and bone marrow edema were assessed. [Subjects] Subjects were 19 patients aged 34-82 years (mean, 56.9 years) with RA within a year of onset, including 11 classified as Stage 1, 5 as Stage 2, 3 as Stage 3, and 0 as Stage 4, with a disease duration of 3-12 months (mean, 8.1 months). [Results] The rate of arthrosynovitis was as follows: distal radioulnar joint (84%), midcarpal-CM joint (79%), radiocarpal joint (63%), 2nd MCP joint (47%), 3rd MCP joint (32%), and 5th MCP joint (26%). The rate of flexor tenosynovitis was as follows: FDS/P (III) (63%), FDS/P (IV) (47%), and FDS/P (II) (42%). The rate of extensor tenosynovitis was as follows: ECU (26%) and ECR (26%). The rate of bone erosion was as follows: triquetrum (79%), capitate (68%), lunate (63%), navicular (53%), and 2nd metacarpal base (47%). The rate of bone marrow edema was as follows: triquetral (63%), capitate (47%), and navicular (42%). [Conclusion] The rate of synovitis was high in the wrist and the 2nd MCP joints by MRI in early RA. Bone erosion and bone marrow edema were frequently found in the carpals, such as the triquetrum and capitate.

P3-026

Efficacy of ultrasonography in sacroiliitis

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Conflict of interest: None

Objective: We investigated the efficacy of ultrasonography in sacroiliitis. **Subjects & Methods**: The sacroiliac joints of 44 patients complaining of lower-back pain (20 men and 24 women, mean age: 60.1 years) were examined with Gray scale and Power Doppler (DP) ultrasonography using LOGIQ-e system by GE™. **Results**: Details of the results are as follows: There were 18 cases of rheumatoid arthritis (RA), 12 cases of ankylosing spondylitis (AS), 5 cases each of fibromyalgia (FM), 3 lumbar spinal canal stenosis (LSCS), 3 cases of spondyloarthritis (SpA), and 1 case each of psoriatic arthropathy (PsA), polymyalgia rheumatic (PMR) and juvenile rheumatoid arthritis (JIA). Clear PD signals were detected in the sacroiliac joints of 24 patients (8 RA cases, 9 AS cases, 3 FM cases, 2 SpA cases and 1 case each of PMR and JIA). Numerous patients in whom PD signals were detected showed CRP positive values. **Conclusions**: This study showed that in some cases PD assessment can be effectively used for the detection and the evaluation of the treatment outcome in cases of sacroiliitis.

P3-027

A case of rheumatoid arthritis patient with bacterial pneumonia. The progress of her arthritis evaluated in the ultrasound

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Conflict of interest: None

A case is 66 years old woman. In 2011, swelling of the palmar and fingers, wrist stiffness appeared. In 2012, joint swellings of both fingers appeared, and laboratory tests showed RF positive and Anti Citrullinated Peptide Antibodies positive. Her condition was diagnosed as RA. SASP, MTX were initiated. The activity of synovitis was very high, ABT and PSL were add on. In July 2016, after TOF was initiated, she was admitted to our hospital. The disease activity of RA was moderate (DAS28CRP 2.86), and her clinical course was benign for 8 days. On the 9th day, pneumonia developed and stop the administration of TOF, started the antibiotic. At that time, though active synovitis by ultrasound (US)was observed. Along with the improvement of pneumonia, improvement of joint symptoms and synovitis was observed in the US. It is said that autoimmune disease including RA were infuluenced their clinical corse by viral infection or bacterial infection. Serum CRP level is in an unstable state by infection, US is useful in the evaluation of arthritis. In our hospital, ward nurses are qualified as a registered sonographer of Japan College of Rheumatology certification. And we can evaluate arthritis in RA patients at the bedside. It was possible to observe with US the course of arthritis caused by infection.

P3-028

Which enthesis scanning protocols are useful for diagnosis of spondyloarthritis by ultrasonography?

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Conflict of interest: None

[Object] This study was aimed to investigate which enthesis scanning protocols are useful for diagnosis of spondyloarthritis (SpA). **[Methods]** Patients with symptoms suggesting SpA (inflammatory back pain, arthritis of lower limbs, tenderness of enthesis and dactylitis) were enrolled. In 66 patients diagnosed with SpA and in 47 patients diagnosed with non-SpA, entheses as well as joint synovium and tendon sheaths were assessed by ultrasonography. **[Results]** The power Doppler (PD) signal of enthesis was the most useful finding for the diagnosis of SpA. In the scanning of exhaustive enthesis sites (average 26 sites), 97% patients of SpA and 21% of non-SpA showed a PD signal of enthesis. Diagnostic accuracy was highest when the scanning sites were limited to 16 sites: both sides of the collateral ligament of the finger, lateral epicondyle, quadriceps tendon, proximal/distal patellar ligament, lateral/medial collateral ligament of the knee and the Achilles tendon (sensitivity 92%; specificity 81%; accuracy 88%). **[Conclusion]** The examination of 16 enthesis sites by ultrasonography was useful for diagnosis of SpA with peripheral symptoms. It is also important to exclude other rheumatic diseases in clinical practice, because enthesitis in ultrasonography is not always specific for SpA.

P3-029

Investigation of gouty arthritis by joint ultrasonography (US)

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Conflict of interest: None

"Purpose and Method" Joint US is a noninvasive examination that can evaluate arthritis and uric acid deposition findings at gout attacks. In this report, we investigated double contour sign (DCS) and hyperechoic aggregate (HA), which are characteristic uric acid deposition findings in US and bone eriosion about 645 male patients. "Result" 11% of patients were without arthritis experience (N group), 29% of patients were first attack (1st group) and 60% of patients were with arthritis experience (His group). The first attack patient had arthritic sites of 72% 1 MTP, 18% of the ankle joint and 5% of the knee joint. We examined with 1 MTP of all patients (D: DCS only%, H: HA only%, B: both have%, A: one with%, E: bone erosion%). N group was D:45%, H:1%, B:0%, A:46%, E:1%. In 1st group, patients with 1MTP attack were D:29%, H:20%, B:38%, A:87%, E:29%, patients with attack except 1 MTP were D:20%, H:4%, B:0%, A:24%, E:0%. In the 1st group, patients without bone erosion of 1MTP were D:34%, H:20%, B:30%, A:84%,, with bone erosion of 1MTP were D: 3%H: 13%, B: 58%, A: 95%. "Conclusion" DCS was also found in 1 MTP joints without attack history, but almost no HA was observed. In 1st group with bone erosion, HA was observed significantly higher 71% to 50% than without bone erosion.

P3-030

Presence of ultrasound subclinical synovitis in patients with rheumatoid arthritis achieved in clinical remission

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Conflict of interest: None

[Objectives] Treatment for rheumatoid arthritis (RA) should aim to achieve clinical remission at first. The aim of this study was to investigate subclinical synovitis in patients with rheumatoid arthritis achieved in clinical remission using musculoskeletal ultrasound (MSKUS). [Methods] 72 patients in DAS28-ESR remission underwent MSKUS by five JCR registered sonographers were extracted. We evaluated the grade judgment of the gray scale (GS) and power doppler (PD), 26 synovial sites in 22 joints: bilateral first to fifth metacarpophalangeal (MCP) joints, first interphalangeal (IP) joint and second to fifth proximal-interphalangeal (PIP) joints and the wrists (radial, median and ulnar). [Results] Each 66 (91.7%), 45 (62.5%), 36 (50%) and 20 (27.8%) patients demonstrated residual synovitis (GS, PD≥1 and 2) in at least one joint. It was only 6 patients (8.3%) that did not show existence evidence in MSUKS. The rate of residual synovitis in each joints were MCP16.5%, PIP6.4% and wrist 41%(GS≥1) and MCP 2.2%, PIP 1.1% and wrist 18.3%(GS≥1). [Conclusion] PD≥2 remained for a quarter of all patients. It was thought that we required evaluation of the inflammatory synovitis in MSUKS periodically after the clinical remission achievement.

P3-031

Ultrasound findings of dactylitis in patients with spondyloarthritis

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Conflict of interest: None

[Object] To evaluate the ultrasound findings of dactylitis in patients with spondyloarthritis (SpA). **[Methods]** Sixty-three patients with SpA (57 with uSpA, 4 with PsA, 3 with IBD associated arthritis and 1 with AS) were enrolled. Ultrasound findings in patients with dactylitis defined as sausage-digit appearance (dactylitis group; n=26) were compared to those in patients without dactylitis (non-dactylitis group; n=37). Grey scale and PD signals of the finger and wrist joint, PD signal of the extensor and flexor tendon sheaths, and PD signals of the collateral ligament were assessed. **[Results**] There were no significant differences in clinical and laboratory findings between two groups. In ultrasound findings, the dactylitis group had PD signals of the collateral ligament (81%), the flexor (81%) and extensor (38%) tendon sheaths, and the MCP joint (27%). These findings were observed more frequently in the dactylitis group than in the non-dactylitis group ($p<0.01$). In logistic regression analysis, the PD signals of the collateral ligament and flexor tendons were independent contributors to a diagnosis of dactylitis in the ultrasound findings. [**Conclusion]** Ultrasound findings of dactylitis reflected the enthesitis, flexor tenosynovitis and synovitis of the fingers in SpA.

P3-032

Comparison of ultrasonographic synovitis and the physical findings (tenderness and swelling) of metatarsophalangeal joint in rheumatoid arthritis

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Conflict of interest: None

Introduction: Rheumatoid arthritis (RA) causes a variety of foot lesions, but the feet and ankles are not included in disease activity indices. The usefulness of joint ultrasonography in RA diagnosis and treatment have recently been reported. Many disease activity indices use tender joints and swollen joints, but few reports have examined the association between synovitis on joint ultrasonography. This study evaluated joint ultrasonography of the MTP joint and examined the results in conjunction with physical findings. **Subjects**: The subjects were 65 RA patients (82 feet). After interviewing subjects about any foot related complaints, pain and swelling were evaluated, and joint ultrasonography was performed. Grade 1 or higher on power Doppler ultrasonography was defined as synovitis. **Results**: The detection rates of pain, swelling, and synovitis in all 410 toes were 33.9%, 14.1%, and 13.4%, respectively. Forefoot-related complaints were cited in 13 feet, and pain was observed in all subjects. However, synovitis was only detected in 38.5%, and many cases had asymptomatic synovitis. **Discussion**: There was a high prevalence of asymptomatic synovitis, suggesting the utility of evaluating synovitis by joint ultrasonography.

P3-033

Images of Musculoskeletal ultrasound sonography findings in SAPHO syndrome

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Conflict of interest: None

(Case) In 2016, a 44-year-old man admitted to our department because of pain of lower extremities. He has suffered from pustulosis on his palm, sole and toe for 20 years. In 2013, he had a diagnosis of deep vein thrombosis because of pretibial edema. Afterward, aspirin and diuretics were administered to him, but his symptom wasn't alleviated. (Imaging) X-ray showed hyperostosis of tibia and fibula. Gadolinium-enhanced MRI showed extensive edema of plantar flexor tendon and contrast effect of calcaneus. Bone scintigraphy showed significant cortical accumulation of nuclide in bilateral tibia, fibula and calcaneus. Musculoskeletal ultrasound sonography (MSKUS) was performed. Gray scale mode revealed tibial surface irregularities, thickening of tibialis anterior muscle's tendon sheath with synovial effusion, synovium thickening of ankle and MTP joints, edema of deep subcutaneous fat, and enthesopathy of Achiles tendon. Power Doppler mode revealed significant blood flow signals in the same site of Gray scale's findings. Finally, he had a diagnosis of SAPHO syndrome and he was treated with prednisolone and methotrexate. (Discussion) MSKUS might be a useful tool for evaluating a local musculoskeletal inflammation in patients with SAPHO syndrome.

P3-034

Three cases of SAPHO syndrome in which ultrasound findings were useful for differential diagnosis

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Conflict of interest: None

[Object] In some cases, SAPHO syndrome would be difficult to diagnose. We report three cases in which ultrasound (US) findings were useful for differential diagnosis. [Case] 1: A 75 year old female, with left shoulder pain. She suspected septic arthritis of the left sternoclavicular joint, but antibiotics treatment was not effective. US showed proliferation of the synovitis and bone erosion in the left sternoclavicular joint. 2: A 64 year old female, with PIP joint pain of left middle finger. Because of anti-CCP antibody high-titer and CRP elevation, RA was suspected. US findings showed inflammation in the attachment of the extensor tendon at the middle phalanx of PIP joint. Moreover, US subclinical enthsitis was observed at the distal part of the patellar tendon and the lateral epicondyle of the humerus. Eruption in hand was diagnosed as palmoplantar pustulosis by biopsy of the skin. 3: A 17 year old female, with pain and swelling in the right clavicle. Bone tumor was suspected by MRI. As a result of biopsy, tumor was not detected. Proliferation of inflammatory tissue under the right subclavian periosteum was found in US examination. [Clinical Significance] US examination is useful for differential diagnosis in the cases of difficult to diagnose SAPHO syndrome.

P3-035

Efficacy of abatacept in patients with rheumatoid arthritis evaluated by ultrasound examination

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Conflict of interest: Yes

[Objective] The purpose of this study was to evaluate effectiveness of abatacept (ABT) for rheumatoid arthritis (RA) using ultrasound examination. [Methods] Fifty one patients with RA who had received ABT were enrolled. Patients underwent clinical, laboratory assessment and ultrasound examination at baseline, 24 and 36 weeks. Twenty-two joints (bilateral wrists, 1st-5th metacarpophalangeal joints, and 1st-5th proximal interphalangeal joints) were evaluated by a systematic multiplanar grey-scale (GS) and power Doppler (PD) examination. [Results] Mean age was 68.7 years old. Baseline disease activity score 28 (DAS28)-CRP was 3.66 ±0.42. Total PD score was significantly decreased from 11.3 at baseline to 5.0 at 24 weeks, and 3.5 at 36 weeks ($p<0.001$, <0.001 respectively). Total GS score was significantly decreased 15.6 at baseline to 12.7 at 24 weeks and 11.8 at 36 weeks ($P=0.025$, 0.005, respectively). Total PD score at 24 weeks was significantly decreased compared at 36 weeks ($p=0.006$), however, total GS score was not significantly decreased. Predictive factor which significantly decreased to PD score ≤ 1 at 36 weeks was DAS remission at 12 weeks. [Conclusion] Total PD score improved continuously after ABT therapy at 36 weeks.

P3-036

Detection of subclinical ultrasound synovitis in healthy subjects with anti-cyclic citrullinated peptide antibodies

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Conflict of interest: None

Background: Multiple studies have shown that rheumatoid arthritis (RA)-related autoantibodies, including anti-cyclic citrullinated peptide antibodies (ACPA), are present years prior to the onset or diagnosis of RA. Objectives: To evaluate the utility of synovial ultrasonography (US) in the preclinical healthy subjects with ACPA positive. Methods: Seven with positive ACPA among 3,977 participants for health screening underwent a complete clinical assessment. The US examinations were performed to detect and score signs of joint inflammation. Synovitis on gray-scale (GS) and power Doppler (PD) imaging were graded on a semiquantitative scale of 0–3. Results: The subjects were mainly female (85%), with a mean age of 53.1 years and a mean ACPA level of 373.0 U/ml. US-detected synovitis with a GS imaging score >1 and synovial PD signal score >0 were observed in five subjects. Out of these subjects, four developed RA requiring disease modifying anti-rheumatic drugs treatment within 6 months. The other two subjects, who had no US-detected synovitis, did not develop RA. Conclusions: The US synovial evaluation appears to be useful to detect subclinical synovitis in healthy subjects with ACPA.

P3-037

Comparison of ultrasound against clinical assessment in predicting structural damage in rheumatoid arthritis patients treated with biologics

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Conflict of interest: None

[Object] To clarify the advantages of ultrasound than clinical monitoring in rheumatoid arthritis patients treated with biologics. [Methods] We consecutively enrolled RA patients who started biologics. We assessed swollen and tender joints, ESR, CRP, and performed ultrasound examination for 40 joints blindly to clinical and laboratory information at baseline, 12, 24 and 52 weeks. Radiological progression was examined according to the modified Sharp score at baseline and 52 weeks. [Results] Joint deterioration were observed in 80/ 768 joints (10.4%). Baseline's clinical findings (pain, swelling, tenderness), US findings (GS, PD), and their persistent findings, showed predictive ability of Joint deterioration at 52 weeks. The most significant predictor was joints with PD both at baseline and 12 weeks (odds ratio 9.9, $p = 0.0016$). [Conclusions] US examination is indispensable in monitoring rheumatoid arthritis patients even if treated with biologics.

P3-038

Ultrasound findings in remission achieved RA patients treated with biologics

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Conflict of interest: None

Objective To know the subclinical inflammation in remission achieved RA patients, we evaluated the ultrasound findings in biologics treated RA patients with normalized CRP. Methods 48 RA patients that CRP decreased normal range (<0.3 mg/dl) by biologics (32 tocilizumab, 16 abatacept) were evaluated by ultrasound. We evaluated power doppler (PD) signals in 22 joints (both side MCP, PIP and wrist joints). In addition, we also evaluated the most painful joint that patient felt. Results RA patients with normalized CRP, remission rate of DAS28-CRP, DAS28-ESR, CDAI, HAQ, Boolean definition were 77%, 68%, 15%, 75% and 58% respectively. Patients who had PD signal positive joints in each remission criteria fulfilled were 35%, 37%, 0%, 36%, and 52% respectively. One third of DAS remission patients have PD signal positive joints suggesting, subclinical inflammation was remaining. However PD signal positive joints decreased in more strict cutoff of DAS28-CRP (36% in cutoff 2.0, 31% with 1.5, 0% with 1.0). Conclusion One third of DAS remission patients had PD signal positive joints. In contrast, patients who achieved CDAI remission had no PD signal positive joints. PD signals in ultrasound reveal subclinical inflammation in patients with clinical remission achieved but insufficient to drug free.

P3-039

The high doses golimumab bring better suppression of ultrasonographic synovial inflammation in patients with Rheumatoid arthritis

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Conflict of interest: Yes

[Object] The aim of this study was to compare the ultrasound findings between patients with rheumatoid arthritis (RA) treated by Golimumab 100mg and 50mg. [Methods] Fifty-two patients with RA treated by Golimumab were consecutively included. Ultrasound examination was performed in MCP joint, PIP joint, wrist, MTP joint, flexor and extensor tendon at finger and wrist level. [Results] In comparison between the dose of Golimumab at the time of ultrasound examination, disease activity was significantly higher in 100mg group (100mg, n=14: 3.6±1.0, 50mg, n=38: 2.2±0.8; p<0.01), but ultrasound findings were not different between 100mg and 50mg groups. In patients achieving remission, ultrasound findings were not different between 100mg and 50mg groups. [Conclusions] Even patients have high disease activity, Golimumab 100mg suppress the synovitis and tenosynovitis very well. In the condition where disease activity was sufficiently controlled, there was no difference in the synovitis findings of ultrasound at the dose of golimumab.

P3-040

Usability of ultrasound examination (US) to evaluate tenosynovitis and enthesitis of seronegative arthritis during treatment course

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Conflict of interest: None

[Background] US of joint is useful to evaluate efficacy of treatment during clinical course of rheumatoid arthritis (RA). For differential diagnosis of peripheral spondyloarthropathy (SpA) such as psoriatic arthritis (PsA) is sometimes difficult if it lacks skin lesion. PsA is characterized by dominant tenosynovitis, peritendinitis and enthesitis by US. [Purpose/Methods] To evaluate usefulness of US for seronegative arthritis other than RA, we have done US on seven PsA (three PsA, two SAPHO, two PPP) before/after treatment. [Results] US was performed above patients who were treated according to the 2012 EULAR recommendation. Representative cases were shown. Case-1: 77 y.o. female who had previous PPP, developed arthritis in her left 2,3 MCPs. US showed synovial thickening around extensor tendons and highly positive by power Doppler (PD). After 18 months with sulfasalazine, her tenosynovitis was disappeared. Case-2: 62 y.o. male who had dactylitis on toe with psoriasis on head and neck, developed polyarthritis on both wrists, knees, and fingers. US showed enthesitis on patella, and tenosynovitis on dorsal hands with moderate PD. After 6 months with MTX resolved tenosynovitis and enthesitis. [Conclusions] US of joints are quite usefull to follow-up peripheral SpA.

P3-041

FDG-PET findings in polymyalgia rheumatica

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Conflict of interest: None

Polymyalgia rheumatic (PMR) and elderly onset rheumatoid arthritis (EORA) have very similar clinical features and it is sometimes difficult to differentiate these two diseases. We studied the findings of 18-fluoradeoxyglucose positron emission tomography/computed tomography (FDG-PET) in PMR. Seven patients (male 3, female 4, average age 75.4 years old) were enrolled. Their serum CRP level was 4.72±1.66mg/dl, serum amyloid A342.7±238.0μg/ml, and MMP-3 213.8±175.2ng/ml. The uptake rate of FDG-PET in each joints were as follows; scapulohumeral joints 8/8, sternoclavicular joints 8/8, elbow joints 4/8, wrist joints 5/8, hip joints 4/8, ischial tuberosities 7/8, iliopectineal bursa 4/8, greater trochanters 5/8, spinous processes of cervical vertebras 3/8, spinous processes of thoracic vertebras 1/8, spinous processes of lumbar vertebras 6/8, knee joints 2/8, ankle joints 2/8. PMR is sometimes associated with large vessel vasculitis, but there were no abnormal uptake in large vessels in this study. Uptake of FDG in scapulohumeral joints, sternoclavicular joints and ischial tuberosities seems to be useful for the diagnosis of PMR. Uptake of FDG in processes of vertebras was found in not only PMR but also EORA, although less frequently, thus it needs careful analysis.

P3-042

The difference between swelling joints evaluated by a rheumatologist and joint ultrasonography scores in 65 RA patients

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Conflict of interest: None

We vertificated the difference between swelling joints evaluated by a expert rheumatologist and ultrasonography score in 65 RA patinents. [Background] mean age 61.6, disease duration 29.8 month, stage 1.72, 42 patients had no RA medicine. [Results] Concordance rate; MCP joints PDUS 76.3, GSUS 83.5%, PIP joints PDUS 88.0, GSUS 87.7%, Hand joints PDUS 70.0, GSUS 72.3%. Concordance rates were good in high grade PD/GS scores. [Discussion] The expert rheumatologist can not detect some subclinical synovitis in low grade PDUS/GSUS. Palmar blood flow and flexor/extensor tendosynovitis were main reasons why he evaluated swelling joints which don't have PD/GS positive in synovium. It is very important that rheumatologist check by joint ultrasonography at

clinical turning points of RA therapy.

P3-043

The inquest of evaluation about the advisability of biologics holidays in Rheumatoid Arthritis (RA) by ultrasonography

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Conflict of interest: None

Purpose: For the proper use of biologics in the practice of RA, we have inquested the prediction about advisability of drug holidays with musculoskeletal ultrasonography (MSUS). Method: There are 31 RA patients who have been stopped biologics according to the attending's evaluation without application criterion in the outpatient visit to the Juntendo University Hospital, we checked them every three months for a year by MSUS. Result: The restart of biologics regardless of the class is defined as exacerbation, without restart inclusive of enhanced treatment is as drug holidays on the other hand. The seven flared and other 24 maintained drug holidays for a year. Conclusion: The group of exacerbation tend is toward the DAS score in the start of drug holidays is not low, or the synovitis exist. The group of non-exacerbation tend is toward the DAS score is low. The combination between DAS score and MSUS indicate that prediction about advisability of drug holidays is more efficient. We want to inquest that new parameter except DAS score and MSUS, advisability of dose reduction and prolongation of interval, comparison between class by increasing patient numbers and follow-up period from now on.

P3-044

A study of the lesions of the Achilles heel bone enthesis in rheumatoid arthritis and spondyloarthritis

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Conflict of interest: None

[Object] Enthesitis in spondyloarthritis (SpA) is main characteristic of the condition. On the other hand, enthesitis of RA may be in a critical condition. I made a study of Achilles heel bone enthesis lesions in RA and SpA patients by ultrasoundsonography. [Methods] Enthesis ultrasound examinations were made between 2014 and 2016, in 72 RA patients,153 SpA patients in my clinic. Swellings of the Achilles tendon and bone erosions, calcifications were detected by B mode, and blood flow signals were studied by Power Doppler. [Results] RA showed swellings of 13% and bone erosions of 1%. calcifications of 21%, and blood flow signals of 0%, combined lesions of 10%, respectively. SpA showed swellings of 8%and bone erosions of 5%, calcifications of 20%, blood flow signals of 4%, and combined lesions of 15%, respectively. No significant abnormal findings were found in RA of 55% and in SpA of 48%. Although SpA showed calcifications and blood flow signal positive cases, 2%, calcifications and bone erosions positive cases, 2% of complex lesion patterns, RA showed no example with these complex lesion patterns. [Conclusions] RA might have the high-frequency lesions of enthesis as SpA. There might be the difference of the cause of enthesitis between RA and SpA.

P3-045

Clinical and pathological features of methotrexate-associated lymphoproliferative disorder occurring in the oral cavity of three patients with rheumatoid arthritis

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Conflict of interest: None

Methotrexate (MTX) is the primary drug used for the treatment of rheumatoid arthritis. MTX is one of the common cause of iatrogenic-associated lymphoproliferative disorders (LPD). Although approximately half of MTX-LPD cases occur in extranodal sites, the occurrence of MTX-LPD in the oral cavity is rare. Higher frequencies of Epstein-Barr virus positivity and better response to withdrawal of MTX have been reported in the intraoral lesion compared to other lesions. Recently, EBV-positive mucocutaneous ulcer (EBVMCU) has been proposed as a new clinicopathologic entity. We present MTX- LPD occurring in the oral cavity of three patients with rheumatoid arthritis. The ages of patients at the diagnosis of MTX-LPD ranged from 61 to 73 years, with a male:female ratio of 1:2. The primary site of LPD lesion was gingiva in the two patients and palate in the one patient. The duration of MTX administration ranged from 7 to 10 years. The two patients had achieved remission after discontinuation of MTX, and the one patient received standard chemotherapy. All patients sustained remission with no disease-associated deaths over a median follow-up period of 36 months.

P3-046

A retrospective study of the treatment without methotrxate for the patients with rheumatoid arthritis

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Conflict of interest: None

(Objectives) To identify efficacy and problem of treatment without methotrexate (MTX) in the patients with rheumatoid arthritis. (Methods) we divided enrolled 123 patients with rheumatoid arthritis into 3 groups: group A: patients treated without MTX (n=28), group B: patients treated with MTX (n=73), group C: patients who need MTX but treated without MTX (n=22) because of adverse effect or renal dysfunction. Clinical back ground, renal function, inflammatory data, disease activity and DMARDS were evaluated. (Results) MTX is used 59.3% of all patients in this study, average dose of MTX was 7.7mg / week in group B, CRP: group A:0.3mg/dl, group B: 0.6mg/dl, group C: 1.2mg/dl. ESR: group A:19mm/h, group B: 27mm/h, group C:41mm/h, DAS28-CRP: group A:2.1 group B:2.3, group C:3.0, DAS28-ESR: group A:2.6, group B:2.9, group C:3.8, CDAI: group A:5.8 group B: 7.1, group C:11.5, SDAI: group A: 6.1, group B:7.5, group C:12.6, e-GFR: group A: 61.9ml/min/1.73m^2 group B: 71.9ml/min/1.73m^2 group C: 57.5ml/min/1.73m^2, Biological DMARDS are used 3%(group A), 11%(group B), 59%(group C) (Conclusion) In group C, Both Inflammation and disease activity was highest. Although biological DMARDS are used most in group C, but disease activity of group C were not well controlled.

P3-047

What type of undifferntiaed arthritis do we need to use methotrexate?

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Conflict of interest: None

Background) 2010 ACR/EULAR classification criteria is very useful. However if the patients were not fullfilled with its classification criteria, we needed to treat the patients due to their high disease activity. Purpose) Undifferentiated arthiris (UA) who were not fullfilled with 2010 ACR / EULAR classification criteria, what type of UA we ought to use methotrexate? Methods) From 2011 to 2016, we investigated the methotrexate use patients who were not fullfilled with 2010 ACR / EULAR classification criteria. We devided some groups by cluster analysis. What type of clusters were effective by methotrexate?(effectiveness after methotrexate initiation after 24 weeks), in retrospectively. Result) 95 cases were detected. Clusters were classified into four groups. The most effective cluster was high marks (>3 points) swollen joints, tender joint count and the

synovitis period synovitis (1 point). On the other hand the lowest effectiveness cluster was high serological examination (>2 points) and low swollen joints, tender joints (<2 points). (Odds ratio: 7.66; p <0.01) Discussion) If we use methotrexate in patients who were not fullfilled with 2010 ACR/EULAR classification criteria, it is important that not only the number, but also compsite itself.

P3-048

The right dose of methotrexate therapy in rheumatoid arthritis

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Conflict of interest: None

Objective: Methotrexate (MTX) is the anchor drug for rheumatoid arthritis. It is not clear the right dose of methotrexate therapy. We investigate that the background of rheumatoid arthritis patients with adverse effect and remission by methotrexate therapy. Method: 134RA patients received RA therapy in our institution. 123 patients received MTX were evaluated based on:with adverse effect group (65 patients), without adverse effect group (58 patients).91patients completed at least 6 month of low desease activity (DAS28ESR) were evaluated based on:reduction or withdrawal of MTX with remission group (9 patients), the other group (82 patients). Rsult:In the adverse effect of methotrexate therapy, We recognized a significant difference in desease dulation (P=0.049). The significant difference was not found in age, methotrexate dose per weight or BMI, biologic DMARDs, corticosteroid. Conclusion:We recognised the advese effect of methotrexate therapy in RA with longer desease dulation.

P3-049

Comparison of methotrexate dose and clinical course between younger onset rheumatoid arthritis and elderly onset rheumatoid arthritis

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Conflict of interest: None

Objectives: We investigated the influence of starting age of methotrexate (MTX) to clinical course in EORA. **Methods:** Thirty eight MTX naïve RA patients who started MTX between Apr. 2014 and Apr. 2016, were assessed retrospectively, and were divided into two groups, younger onset RA (YORA): with disease onset <65 years and EORA: with disease onset ≥65 years or younger onset elderly RA. Initial dose of MTX and final dose of MTX, clinical disease activity index (CDAI), modified health assessment questionnaire (mHAQ) and adverse events (AEs) at final follow up were assessed. **Results:** The mean age of starting MTX was 53.2 years old in YORA and 73.2 in EORA. Although mean initial dose of MTX was significantly lower for EORA than YORA (4.6mg, 5.7mg, p<0.01), mean dose of MTX at final follow up was similar in EORA and YORA (8.9mg, 9.4mg, p=0.48). At final follow up, 14 patients achieved CDAI remission (8 and 6 in YORA and EORA) and 19 achieved low disease activity (9 and 10 in YORA and EORA). Mean point of mHAQ was 0.14 in YORA and 0.41 in EORA. Sever AEs were not observed in both group. **Conclusions:** There was no difference in the maintenance dose of MTX and clinical course between YORA and EORA, although initial dose of MTX was lower for EORA.

P3-050

Predictive factor of effectiveness of iguratimod therapy among rheumatoid arthritis patients

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Conflict of interest: None

[Objectives] To examine predictors of the efficacy of iguratimod (IGU) therapy in rheumatoid arthritis (RA). [Methods] We enrolled and classified all cases that received IGU therapy except for DAS28<3.2 in the initiation of IGU. Good or moderate responders in EULAR response criteria were responders, others were non-responders in this study. And parameters at baseline, 0 week and 4 week in each group was evaluated. [Results] 26 patients (22 females, mean age 65 yo, mean disease duration 136 months) were included. In responders (N=16, 14 cases with RF positivity), mean DAS28ESR at 24wks was 3.5 (vs 5.6 in non-responders, N=10, 9 cases with RF positivity). Univariable analysis showed ESR at 4wk, amount of change of ESR at 4 wk, rate of change of RF (ΔRF/0w RF) at 4wk. And multiple logicticregression showed ΔRF/0w RF at 4wk (mean in responders was -15%, vs 5% in non-responders). In according to ROC curve, cut off of ΔRF/0w RF was -9.2%(sensitivity 85%, specificity 78%). [Conclusion] In RF-positive RA patients with iguratimod therapy, ΔRF/0w RF was effective predictive factor.

P3-051

Efficacy at three years of daily clinical use of iguratimod in patients with rheumatoid arthritis

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Conflict of interest: None

Objective: The assessment about efficacy of the clinical use of iguratimod (IGU) has mainly been restricted to short-term outcome in patients with rheumatoid arthritis (RA). We performed a 3-year study on the efficacy of IGU. Methods: Thirty RA patients were enrolled in this study. The clinical course of RA was evaluated during 3 years. The patients who discontinued the IGU therapy were analyzed by the last observation carried forward method. Results: The survival rate at 3 years was 40%, and 8 patients discontinued the IGU therapies due to insufficient response, 2 due to adverse events and 8 based on their requests. The DAS28-CRP significantly decreased at 6 months, 1, 2 and 3 years compared with baseline. HAQ-DI did not decrease in this study. The low DAS28-CRP at 6 months was associated to the continuation of IGU. HAQ-DI and DAS28-CRP at baseline were significantly lower in the remission achievement group. A logistic regression analysis revealed the low DAS28-CRP at baseline was a significant factor contributing to the achievement of a clinical remission at 3 years. Conclusions:We assessed middle-term outcome of the clinical use of IGU therapy in RA patients. The most significant factor of clinical remission achievement at 3 years was the low DAS28-CRP at the initiation of IGU.

P3-052

Continuation rate of the Iguratimod with methotrexate therapy in patients with rheumatoid arthritis

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Conflict of interest: None

Objective: We investigated the efficacy and continuation rate of the Iguratimod (IGU) with methotrexate (MTX) therapy in patients with rheumatoid arthritis (RA). Methods: A total of 62 RA patients who were treated with IGU from September 2014 to March 2016 were observed. 23 patients treated with MTX (mean dose 7.9 mg/week). We evaluated the differences between the patients treated with and without MTX, clinical symptoms and laboratory test at baseline, 24 and 54 weeks, and continuation rate use of IGU. Results: DAS28-CRP decreased -1.35, with and without MTX were -1.45 and -1.22, at 54 weeks compared with that at baseline. Continuation rate of the patients who treated with IGU for 24 weeks were 74%, with and without MTX were 87% and 66%, had a significantly high rate in the combined with MTX. ($P^* < 0.05$) Conclusions: IGU with MTX therapy in patients with RA affect the efficacy and continuation rate.

P3-053

Long-term outcome of iguratimod in patients with rheumatoid arthritis in real-world clinical setting

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Conflict of interest: Yes

[Object] To investigate longterm outcome of igratimod (IGU) in patients with rheumatoid arthritis (RA). [Methods] 120 RA patients treated with IGU from April, 2013 to June, 2016 were included. Patients' characteristics, factors influencing to prescribing of IGU, drug continuation rates (Kaplan-Meier) were investigated. Time course of disease activity (DAS28-CRP & SDAI) was also investigated using 65 cases who passed 2 years after starting of IGU. [Results] Mean age 64.9 yo, Female 74.2%, Mean RA duration 10.0 y, MTX concomitant 50.0%. 82% of patients had factors influencing to prescribing IGU and intolerance of dose escalation of MTX was 1st reason (23.3%), old age over 80 y.o was 2nd reason (16.7%) and economical reason was 3rd (14.2%). Drug continuation rates were 71.1% at 1 year, 48.9% at 2 year and 43.1% at 3 year. Time course of disease activity (baseline-6 months-1 year-2 year) was 3.6-3.0-3.0-3.0 in DAS28-CRP. In 15 cases in remission of DAS28-CRP at 2 years, 2 were clasified with high disease activity and 9 were moderate disease activity at baseline. [Conclusions] Efficacy of IGU in RA patients who had intolerance of MTX dose escalation or usage of biologics was observed. Although drug continuation rates were decreased over time, IGU was very effective in some cases.

P3-054

Efficacy of iguratimod administration for the cases who stopped methotrexate

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Conflict of interest: None

Objective: We administrate iguratimod (IGU) for the cases who stopped methotrexate (MTX) due to maladaptation / side effects, or who did not show enough response to MTX / biologic agents (BIO). In this study, we focused on the cases that stopped MTX and evaluated the efficacy of IGU treatment. **Methods**: 55 cases that switched MTX to IGU were followed up more than 1 year. We evaluated the patients' background, disease activity. **Results**: 38 cases stopped MTX due to side effects. The causes of cancel were myelosuppression (17), MTX pneumonia (4), lymphoproliferative disease (3) et al. The average MTX dose and duration of MTX administration was 6.3mg/week and 5.1 years. Other 17 cases were stopped MTX due to aggravation of lung lesion (5), renal dysfunction (3) et al. DAS28-ESR (4) was decreased significantly from 4.53 (induction) to 3.63 (3 months) and 3.29 (6 months). 16 cases were treated together with BIO and maintained improvement even after administration of IGU. Two cases showed recurrence and resumed MTX. **Conclusion**: The IGU treatment is effective for cases who stopped MTX. It might be better to add IGU on MTX and stop MTX after the confirmation of the effect of IGU for the cases who received long term MTX treatment without the combination of BIO.

P3-055

Iguratimod successfully controlled RA in the aged patients

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Conflict of interest: None

By aging of population, safe and reasonable therapies for the aged RA patients have been expected. Effects of iguratimod for the aged RA patients have not been fully elucidated. We investigated the outcome of 87 iguratimod treated patients retrospectively, and compared the effects of iguratimod between over 65 year-old RA group and fewer than 65 year-old group at week 4, 12 and 24. DAS28-CRP of the aged group was higher than that of younger group before therapy. However, DAS28-CRP and MMP-3 levels of both groups improved at week 24, and DAS reached to the same levels. A case in the aged group dropped out by aspiration pneumonia and a case in the younger group by nausea. No remarkable increase of side effects in both groups was identified. Thus, the present results implicate iguratimod as a therapeutic choice for the aged RA patients.

P3-056

Effect of tapering conventional synthetic DMARDs or prednisone in RA patients after add-on iguratimod therapy

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Conflict of interest: None

Objective: The retrospective study aimed to examine the effect of tapering conventional synthetic DMARDs (csDMARDs) or prednisone (PSL) in rheumatoid arthritis (RA) patient after add-on iguratimod (IGU) therapy. Methods: One hundred forty-eight patients with RA with csDMARDs or PSL were additionally treated with IGU. Disease activity score (DAS) 28-erythrocyte sedimentation rate (ESR) and biological data were collected retrospectively from medical records. Results: The mean age was 63.2±12.8 years, mean disease duration was 10.0±10.4 years. The percentage of patients administered methotrexate (MTX), tacrolimus, salazosulfapyridine, PSL, biological DMARDs was 70.8%, 16.2%, 20.5%, 41.4%, 53.0%, respectively. For 24 weeks, 86.5% patients continued IGU treatment. DAS28-ESR significantly decreased from 3.30 to 2.79 at week 24 ($p < 0.0001$). In 12 patients (10.2%), MTX was tapered, and in 22 patients (19.0%) was PSL was tapered after 24 weeks. Conclusions: Additional IGU treatment is possible to tapering of csDMARDs or PSL in RA patients.

P3-057

The effectiveness and safety of iguratimod for the rheumatoid arthritis patients

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Conflict of interest: None

Objective:we evaluated the efficacy, safety of iguratimod (IGU) in RA with daily clinical use in our hospital. Method:38 patients were enrolled in this study, and the improvement in RA and safety during the 24weeks Results:DAS28-ESR at the time of the start was 4.6 ±1.0 and was 3.7±1.0 at24 weeks. DAS28-ESR was start 4.3±1.0 and was 3.6±1.0 with MTX at 24 weeks. and DAS28-ESR was start 5.3±0.7 and 3.8±1.2 at 24 weeks without MTX. A continuation rate in 24 weeks was 68% and was four gastrointestinal dysfunction. There were one case pneumonia, one urinary tract infection, but they improved all in hospitalization of about one week and was able to continue IGU. Conclusion:DAS28-ESR were decreased at 24 weeks later regardless of MTX combination presence by IGU use. I was used for a serious adverse event (SAE) for a long time in csDMARDs ofthe multiple drug during the contraction of a disease period, but there was not the SAE, and it was with a useful treatment choice.

P3-058

Effectiveness of Iguratimod at Our Outpatient Clinic

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Conflict of interest: None

Background: Use of iguratimod (IGU) as an antirheumatic began in September 2012 and its combined effect with other drugs such MTX has recently attracted attention. We investigated effectiveness of administering IGU. Methods: Of the consecutive 123 patients who began taking IGU at our department between September 2012 and September 2016, we examined 71 patients who took IGU continuously for >6 months. Subjects were divided into a remission group and a non-remission group based on their DAS28-CRP level after 6 months. Changes in the groups' DAS28-CRP and MMP-3 levels were examined. Results: Patients' mean age was 64 years, there were 17 men and 54 women, their mean disease duration was 131.9 months, and their mean IGU dosing period was 19.4 months. In the remission (n=40) and non-remission (n=31) groups, the mean DAS28-CRP before versus after IGU dosing was 2.68 versus 1.62 and 3.58 versus 3.22, respectively, and the mean change in the MMP-3 level was −76.42 ng/mL and +38.36 ng/mL, respectively. The respective disease durations were 117 and 151.7 months. Conclusions: IGU may have greater efficacy in patients with a low DAS before IGU dosing and in patients taking a combination of IGU and MTX. The MMP-3 level was improved in the remission group.

P3-059

Effects of iguratimod on protein profiles ofa chondrosarcoma cell line (OUMS27)

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Conflict of interest: None

[Object] Iguratimod is an anti-rheumatic drug, which has been reported to suppress production of inflammatory cytokines by inhibiting activation of NF-κB. However, precise mechanisms for the action is unclear. Further, effects of iguratimod on chondrocytes have been rarely reported. Thereby, we here comprehensively investigated an effect of iguratimod on a chondrosarcoma cell lineby proteomics. [Methods] A chondrosarcoma cell line (OUMS27) was cultured with 100 μg iguratimod for 24 hours and 7days. The OUMS27 cells without the treatment of iguratimod were used as a control. Then proteins extracted from the samples were separated by two dimensional gel electrophoresis. Protein spots with different production was subjected to mass spectrometry to be identified. [Results] 24 hours later, 11spots increased their intensity and 5spots decreased their intensity compared with the control. 7 days later, other 11spots also increased their intensity and other 10spots decreased their intensity. As protein spots that decreased their intensity by iguratimod, several pro-inflammatory factors were identifiedincluding hnRNP A2/B1. [Conclusions] We demonstrated that iguratimod affected protein profiles of chondrosarcoma cells. It was suggested that iguratimod suppress pro-inflammatory factors.

P3-060

The effectiveness of tacrolimus combined with biologic agent for rheumatoid arthritis

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Conflict of interest: None

[Object] To investigate the effectiveness of tacrolimus (TAC) combined with biologic agent for rheumatoid arthritis. [Patients and Methods] In the 403 patients who started to treat biologics between May, 2001 and August, 2015, 19 patients (men: two patients, women: 17 patients) who also took tacrolimus were included in this study. The average age at the time of starting biologics was 63.0. The average follow-up period was about 2.2-year. Patients were subdivided as follows;(1) TAC and biologics added, (2) TAC+MTX and Biologics added, (3) Biologics and TAC added. In each group, number of patients, average age, duration of the disease, number of the biologics, change of disease activity and survival late were compared. [Results] TAC+MTX and Biologics added group had a highest average age and disease duration. (1) TAC and biologics added group met 7 patients and had a good response and 5 patients continued over one-year. (2) TAC+MTX and Biologics added group met 7 patients had a moderate response and 5 patients continued over one-year. (3) Biologics and TAC added group met 5 patients had a good response and 4 patients continued over one-year. [Conclusion] To add on tacrolimus when the secondary failure of biologics agent was maybe one of the strategies of the RA treatment.

P3-061

The efficiency and safety of tacrolimus to elderly RA Patient

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Conflict of interest: None

[Objective] Methotrexate (in the following, MTX) should be included in an early stage treatment strategy of RA in EULAR recommendation 2016. In patients with a contraindication to MTX (or early intolerance), LEF or SASP should be considered as part of the first treatment strategy. To evaluate efficancy and safety of tacrolimus (in the following, TAC) in active elderly RA patient. [Methods] 35elderly RA patients was enrolled. The average age were 77.2years old. The tacrolimus prescription amount was an average of 1.2 mg, and average blood level was 3.5ng/ml. TAC monotherapy was 6patients, and combination therapy was 29patients. Predonisolone was used by 20patients (51%), and the average prescription amount was 5.8mg. MTX was used by 13patients (37%), and the average prescription amount was the 6.8mg/week. Response to therapy is evaluated by EULAR response criteria. [Result] 12 months later, 18patient (51%) were improvement beyond moderate response. Adverse event were occurred in 7 patient, digestive organ symptom was occurred in 2 patient, pneumonia, urticaria, dizziness, blood level rise was occurred in each 1 patient. [Conclusions] Tacrolimus indicated good clinical results in eldery RA patient, and there was no severe adverse event.

P3-062

Treatment for rheumatic diseases by tacrolimus in our hospital

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Conflict of interest: None

Background: Methotrexate (MTX) and biologicals are sometimes insufficient effective for rheumatoid arthritis (RA) and are inappropriate due to complication such as renal dysfunction. We often treat them by tacrolimus (TAC), so we checked actual situation of TAC in our hospital. Method: We found rheumatic disease patients treated with TAC at October 31th 2016. Then, we investigated reasons for administration of TAC, a change of the disease activity, influence on renal function. Result: 28 cases were treated with TAC included 23 RA cases and five lupus nephritis (LN) cases. LN cases were younger, and had more TAC and corticosteroid dosage compared to RA-TAC group. RA-TAC were older than other RA cases. Six months after TAC administration, disease activity of RA decreased. RA-TAC group were further divided into two groups; A) TAC were added on due to insufficient effect of MTX, B) MTX were inappropriate. Group A was older and had more TAC dosage compared to Group B, but there were no significant difference in disease activity before TAC administration. When compared with MTX without TAC cases, there was no significant difference in the rate of decrease in renal function. Conclusion: TAC is relatively safe and effective for cases with insufficient MTX effect or MTX inappropriate.

P3-063

Evaluation of the Efficacy of Add-on Combination Therapy with Tacrolimus Tablets in Patients with an Inadequate Response to Methotrexate Tablets in Our Hospital - Safety and Efficacy of Generic Drugs –

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Conflict of interest: None

OBJECTIVE: We evaluated the efficacy of addon combination therapy with tacrolimus (TCA) in rheumatoid arthritis (RA) patients who had an inadequate response to methotrexate (MTX) administered alone or in combination or in whom the effects of MTX were exhibited but were subsequently reduced. **METHODS:** This evaluation was conducted in 22 patients with an inadequate response to or second failure of MTX (one male and 21 females; average age, 66.7 years old) of those who started administration of this drug alone or in combination in our hospital. TCA was additionally administered to the 22 patients at a dose of 1 mg per day (administered to only one patient at a dose of 0.5 mg per day). Changes in DAS28, SDAI, and serum MMP-3 and remission rate were evaluated 6 months after the start of this add-on combination therapy with TCA. **RESULTS:** Of the 22 patients to whom TCA was additionally administered, only one discontinued the therapy due to adverse events; 21 patients continued it at 6 months. Of the 21 patients, 19 achieved low disease activity or remission; 2 showed no effective improvement. **CONCLUSION:** TCA was considered useful for addon combination therapy in RA patients with an inadequate response to MTX administered alone or in combination or with second failure of MTX.

P3-064

A case of cerebral hemorrhage considered with vascular disorders due to tacrolimus

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Conflict of interest: None

A case of a 48-year-old woman. She was diagnosed with rheumatoid arthritis at 40-year-old and had received a treatment at another hospital, obtaining low disease activity (LDA) by abataceptABT. In April, X-1 year, she visited our hospital with high disease activity. Although we restarted a treatment with ABT, it was not effective enough. TacrolimusTAC was started in June, ABT was switched to tocilizumabTCZ in July, and then they led to LDA. In March X year, having headache and malaise, the head CT revealed the right occipital lobe subcortical hemorrhage, she admitted to the department of neurosurgery. TAC and TCZ were discontinued. Angiography showed multiple arterial caliber irregularity on the third hospital day. A surgery underwent on the 11th hospital day, the caliber irregular was not seen with re-exam of angio. The pathological findings of vasculitis was not observed in the specimen. In May, TCZ was resumed for the flare of arthritis. She has LDA again, recurrence of cerebrovascular disorder has been not occurred. «Clinical significance»TAC sometimes has vascular endothelial injury known as a side effect, but cerebral hemorrhage is rare. Here we report a case of cerebral hemorrhage suggested to be induced by TAC, it was considered with an instructive case.

P3-065

Clinical and Radiographic Efficacy and Safety of Tofacitinib for Rheumatoid Arthritis

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Conflict of interest: None

[Object] To evaluate the clinical and radiographic efficacy and Safety of Tofacitinib (Tofa) for RA patients. [Methods] The medical records of 52 patients (48 females) who were administered Tofa and followed up for more than 52 weeks were retrospectively evaluated. [Results] The mean age was 63.2 and disease duration was 17.9 years. MTX was used in 46.3% and the average dose was 7.75 mg/week. LOCF analysis revealed that DAS28-ESR decreased significantly from 5.24 to 3.77 in 12 weeks and to 3.62 in 52 weeks respectively ($P<0.01$). Remission and LDA rate in DAS28-ESR were 11.5% and 34.5% at week 52. HAQ-DI score decreased from 1.73 to 1.45 at week 52. The percentage of patients with no radiographic progression ($\Delta mTSS<0.5$) was 54.2%, while that of rapid radiographic progression ($\Delta TSS >5$) was 4.2%. The mean estimated yearly progression was 7.86 at baseline but was significantly reduced to 1.27 ($P<0.01$) after 52 weeks of Tofa treatment. Severe adverse events were seen in 5 cases: sepsis due to UTI, malignant lymphoma, herpes zoster meningitis, diverticulitis and cellulitis. [Conclusions] Tofa was effective both clinically and radiographically in patients with severe established RA. However severe infections must be kept in mind.

P3-066

Inhibitory Effect of Small and Middle to Large Joint Destruction by Tofacitinib in 14 Advanced Rheumatoid Arthritis Patients with Inadequate Response to Biological Disease-Modifying Antirheumatic Drugs

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Conflict of interest: None

Objectives: To evaluate inhibitory effect of both small (8 cases) and middle to large (ML) (6 cases) joint destruction by Tofacitinib (TOF) in 14 advanced rheumatoid arthritis (RA) patients with inadequate response to biological disease-modifying antirheumatic drugs (bDMARDs). **Methods:** Clinical efficacy was assessed by disease activity score of 28 joints including CRP (DAS28-CRP). Radiographic outcome was assessed by the modified total Sharp score (mTSS) in small joints, and by Larsen score in ML joints. MRI and ultrasound approach were also shown. **Results:** Mean age (years), 60.6; disease duration (months), 149.4. DAS28-CRP significantly decreased from 4.4 to 3.5, 3.1, 3.2 after 1, 3, 6 months, respectively. Rapid radiographic progression (RRP) in small joints at baseline were all recognized in eight cases. After taking TOF, two cases were progressive but six cases did not show another destruction. Shoulder joint was improved with remodeling. Knee and hip joints had no progression of bone destruction. Pain relief was observed in ML joint early after TOF administration. **Conclusions:** This study showed that TOF had inhibitory effects against the progression of radiographic joint damages in advanced RA patients with inadequate response to bDMARDs.

P3-067

Treatment with Tofacitinib for RA at our hospital

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Conflict of interest: None

[Purpose] Approved in Japan in March 2013 was Tofacitinib (TOF) is a molecular targeted therapy of small molecules, unlike biologics (Bio), is an agent that can be used as an oral medicine. This time, we report examined the efficacy and safety of TOF for RA patients. [Methods] 12RA patients that are treatment with TOF for more than 24 weeks in our hospital and, I was examined that, effectiveness (DAS28-ESR), survival rate, and side effects [Results] As patient background, age is from 54-year-old to 87-year-old. they were switching patients from in 6 cases anti-TNFα formulation (GLM3•ETN3). MTX had been combined in the 7 cases (4mg-10mg). In DAS28-ESR the course of more than 24 weeks after, 2 cases of good response, 7 cases moderate response, 3 cases of no response. All treatments also continues currently. [Conclusion] In our hospital, the effect of TOF were good results. Major side effects have been able to continuously administered in all cases without any. The future, by overlapping cases, by the long-term administration, it is considered necessary to require further consideration.

P3-068

The efficacy and safety of tofacitinib in patients with rheumatoid arthritis in our clinic

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Conflict of interest: None

To investigate the efficacy and safety of tofacitinib in patients with rheumatoid arthritis in our clinic. We evaluated 17 patients with RA in whom methotrexate, bDMARs caused an inadequate or toxic response. Methods. All subjects were fulfilled with the 2010 ACR/EULAR classification for RA and evaluated by DAS 28 (ESR), SDAI, HAQ, and MMP-3. Results. 1. Of the 17 patients treated with tofacitinib, 9 patients (52%) achieved DAS28 remission and 12 patiets (70%) showed more than low disease activity.2. The adverse events reported were Pneumocystis pneumona (one patient), Herpes zoster (3patients). 3. The 4 of 5 patients who treated with more than different 3 bDMARDs showed no response by DAS28 evaluation. 4. The patiets who achieved the lower value of CRP or MMP-3 after administration of tofacitinib showed the good respone or remission. Conclusion. Our findings indicate that tofacitinib is efficatious in the treatment of RA, especially in patients previously treated less than 2 bDMARs.

P3-069

Effect of Tofacitinib on Bone Homeostasis in Rheumatoid Arthritis

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Conflict of interest: None

Objective: To clarify the effect of tofacitinib on osteoclast regulating factor such as receptor activator of NF-kappa B ligand (sRANKL) and osteoprotegerin (OPG), dickkopf (DKK)-1, NTx, and osteocalcin (OC) in patient with rheumatoid arthritis. **Methods:** 14 patients with active RA who inadequate response to DMARDs were started on treatment with tofacitinib 5mg twice daily. Next, circulating levels of sRANKL, OPG, DKK-1, NTx, and OC were examined at baseline and week 2 to 48. **Results:** Average of sRANKL levels decreased immediately from 0.15 pmol/L at the baseline to 0.09 at week 2 (p<0.01), to 0.05 at week 48 (p<0.01). Consequently, average of sRANKL/OPG ratio decreased significantly from 4.81% at the baseline to 2.62 at week 2 (p=0.0177), to 2.36 at week 48 (p<0.01). On the other hand, statistically significant changes in DKK-1 levels were not observed during 48 weeks. Average of NTx levels tend to decrease after week 12. Interestingly, average of OC levels increased from 6.89 ng/mL at the baseline to 8.79 at week 12 (p=0.0283), to 19.45 at week 48 (p<0.01). **Conclusions:** Here, we show tofacitinib has improved inflammatory bone metabolism immediately through the regulation of sRANKL levels and sRANKL/OPG balance in patients with RA.

P3-070

Understanding the Importance of a Patient's Role in the Management of RA in Japan: Results from a Physician- and Patient-Based Survey

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Conflict of interest: Yes

Objectives: To identify and understand healthcare provider (HCP) and patient (pt) perspectives on RA management in Japan. **Methods:** HCP and pt surveys developed by the RA NarRAtive initiative were fielded online across 16 countries (Aug–Oct 2015 and Sept 2014–Jan 2016). Responses are from rheumatologist-treated pts and HCPs who were rheumatologists in all countries (including orthopedists in Japan). **Results:** 138 pts from Japan responded (global n=1805); female: 66%(global 64%), mean age: 54.7 yrs (global 51.7 yrs), median time from diagnosis: 7 yrs (global 7 yrs). 139 HCPs from Japan responded (global n=1736); most were satisfied with communications (HCP: 81% vs 90% global; pt: 73% vs 84% global). 52% of pts felt that discussing symptoms/experiences would be most effective in managing RA (global 36%) vs open discussions about RA for 49% of HCPs (global 34%). More HCPs than pts indicated remission as a treatment goal (HCP: 70% vs 69% global; pt: 56% vs 40% global). Side effects were the main medication issue (HCP: 68% vs 76% global; pt: 27% vs 40% global). 13% of HCPs (global: 34%) reported that pts requested a medication change due to adherence issues. **Conclusion:** Treatment goal differences were seen in Japan. Pt and HCP communication could improve adherence and management.

P3-071

Current status of treatment for elderly rheumatoid arthritis patients in our hospital

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Conflict of interest: None

Objective: The number of elderly RA patients has been increasing with aging society and advancement of antirheumatic drugs. We report current status of treatment for elderly RA patients in our hospital. **Methods:** We examined total 482 RA patients (111 male and 371 female). Analytical parameters included age, onset age, onset joint, antirheumatic drugs and their side effects. **Results:** 77% of male and 71% of female were 60 years old or older. A majority of male patients had disease onset in their 50s or later. In contrast female patients showed bimodal distribution with their early 40s and around 60. The patients with disease onset in their later age tended to develop it in their large joint more frequently. Among antirheumatic drugs, MTX was used most commonly. However, the use rate was decreased with increasing age. Discontinuation rate of MTX due to side effects was higher in elderly patients compared to younger patients, and severe side effects were more frequently observed. Use rate of PSL was increased with increasing age, and use rate of biologics decreased with increasing age. **Conclusion:** MTX and biologics require more cautious use for severe side effects in elderly patients. PSL tended to be used more frequently as replacement for MTX with increasing patients' age.

P3-072

Clinical features of rheumatoid arthritis patients who did not use MTX within a year after diagnosis

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Conflict of interest: None

OBJECTIVE: We investigated the clinical features of RA patients who did not use MTX within a year after diagnosis METHOD: A retrospective study was conducted of patients with RA in our division diagnosed during from April 2011 to July 2015 RESULT. Out of 289 patients, 125 patients didn't receive MTX (group A), and 163 patients received MTX (group B). The reasons for avoiding MTX were mainly interstitial pneumonia (IP) (35 cases), liver dysfunction (16 cases), and chronic kidney disease (CKD) (15 cases). The most frequently used DMARDs in group A were salazosulfapyridine (SASP) (87 cases, 69.6%) and bucillamine (BUC) (73 cases, 58.4%). The number of patients using prednisolone (PSL) in group A was larger than in group B (42 cases vs 35 cases, p=0.024), while biologics were less frequently used in group A (9cases vs 44cases, p<0.0001). The disease activity of RA in a year in group A was

higher in any scoring system such as DAS28 (3.27±1.10 vs 2.77±1.04, p=0.0003), SDAI (8.24±7.43 vs 5.97±6.01, p=0.02). CONCLUSION: The main reasons of avoiding MTX were IP, liver dysfunction, CKD. The most frequently used DMARDs in group A were SASP and BUC. The activity of the patients in MTX non-users in a year was higher than MTX users.

P3-073

Injectable gold for rheumatoid arthritis combination therapy

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Conflict of interest: None

[Object] It is well known that the anchor drug for rheumatoid arthritis (RA) is methotrexate (MTX). The patients with uncontrollable disease activity were derived to treat with biologics. However, some patients did not accept biologics because of expensiveness, fair of infection and malignancy. I selected gold injection, which was rarely used drug, as a next drug for combination therapy. [Methods] During usual clinical practice, injectable gold (Sodium Aurothiomalate, gold) was selected the next drug as combination therapy. Eight patients were included. Average age was 61 years old. Average duration of disease was 11 years. Average MTX dose was 10mg per week. As gold therapy, first adminstration was a 10mg of gold intramuscularly. No side effect was complained, patients were administered 25mg of gold intramuscularly at each visit (one dose per one to two months). [Results] Cessation of gold injection was in two cases (one; dermatitis, one; not effective). Other 6 cases, average follow-up period was 9.3 months. Averaged data at final follow-up were DAS-CRP (base-line, p value): 1.70 (2.9, p=0.0223), CRP: 0.38 (0.88, p=0.0244). [Conclusions] Gold is recommended weakly in JCR guideline for RA. However, in some patients, it is effective and useful as combination therapy.

P3-074

A case of yellow nail syndrome difficult to distinguish from rheumatic pleuritis

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Conflict of interest: None

【Back ground】Yellow nail syndrome (YNS) is characterized by a triad of yellow nails, lymphatic edema and pulmonary manifestation. YNS can be induced by drugs such as Bucillamine (BUC). When a pleural effusion is detected while treating with BUC, it becomes problem to distinguish between YNS and rheumatoid pleuritis.【Case】A 75-year-old man complaining of joint pain was diagnosed with rheumatoid arthritis, and started treatment with PSL 5mg/day and BUC 200mg/day. Three years later, he developed bilateral pleural effusions. We suspected rheumatoid pleuritis because the results of culture and cytodiagnosis of pleural fluid were negative. After that, yellow nails had appeared. BUC was discontinued because YNS was suspected, but that was not effective. Although a pleural biopsy was performed, the result of pathological examination was nonspecific inflammation. Because pleural effusions were not under control despite thoracic drainages, PSL dose was increased to 30mg/day. Since then, pleural effusions have improved and PSL dose has been tapered to 9mg/day.【Clinical significance】In this case, it was thought that the pleural effusion had been caused by YNS and had improved by increase of PSL dose. Since pleural biopsy for YNS is rare, we report this case with some literature review.

P3-075

The case of RA developed as a consequence of immune reconstitution inflammatory syndrome (IRIS)

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Conflict of interest: None

(Case) A 48-year-old man was diagnosed with HIV infection on June 2012. He had been on antiretroviral therapy (ART) for 2 years but stopped going to the hospital. He presented to our hospital again on July 2016 with general malaise. HIV-RNA viral load in plasma was of $8.9*10^4$ cp/mL, CD4+cell count was 27/μl. One month after ART therapy was restarted, he showed polyarthritis. Serologic assessment for RF was positive compared with 4 years ago but anti-CCP was negative. Serum levels of ESR and CRP were elevated (67mm/h, 0.58mg/dL, respectively). A definite diagnosis of RA was confirmed. Disease activity of RA was so active that treatment was started with low dose prednisolone and Salazosulfapyridine. One month later, his joint activity was still persistent, then Iguratimod was added, after that his RA symptoms gradually improved. (Discussion) In this case, RA was developed as a consequence of IRIS. Recent studies have revealed that the IRIS could lead to autoimmune disease, such as RA, but there have been no definitive treatment policy yet. We report this case with the follow-up observation and consideration.

P3-076

Risk factors for the development of pneumocystis pneumonia in RA patients in *NinJa*

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Conflict of interest: None

Objective: To identify risk factors for pneumocystis pneumonia (PCP) in patients with RA. Method: We conducted a case-control study, sampling from cumulative total of 86,397 subjects in a Japanese nationwide multicenter RA database, *NinJa*. We identified 62 cases developing pneumocystis pneumonia and matched them to controls on hospitals and year of PCP onset in the rate of 1 to 6. Results: Age older than 65 and treatment with methotrexate, steroids, tacrolimus and TNF inhibitor were identified as risk factors using conditional logistic regression analysis. We developed a scoring system based on the risk factors identified in the current study. In the ROC analysis, this score showed a good prediction for the incidence of PCP with the AUC of 0.84. Sulfasalazine was considered to have possible preventable effect against PCP on the basis of the observation that none of our cases took sulfasalazine before the onset of PCP. Conclusions: Our study indicated that the incidence of PCP can be estimated with the score comprising risk factors identified. A prospective cohort study is needed to validate our results.

P3-077

Three case reports of rifampicin induced acute adrenal insufficiency in the treatment of prosthetic joint infection in rheumatoid arthritis patients

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Conflict of interest: None

The combined use of Rifampicin (RFP) for prosthetic joint infection (PJI) is recommended as first choice in the guidelines by IDSA, and in particular, the use of RFP for MRSA infection is increasing in recent years. We report three cases that developed acute adrenal insufficiency, after using RFP for PJI in rheumatoid arthritis (RA) patients. The patients are 31 y.o. man, 79 y.o. woman, and 72 y.o. woman, had been treated with 3mg, 4mg, 5mg prednisolone (PSL) respectively, for many years. After we started to treat with RFP for PJI, all patients had slight fever, sudden rise of CRP, general malaise, two patients had polyarthralgia, hyponatremia, hypoglycemia, and one patient had nausea, anorexia, headache. We did not confirm the relapse of local infection in all cases. So, we diagnosed acute adrenal insufficiency clinically. All symptoms improved by only stop using RFP in two cases, and in addition steroid cover with hydrocortisone in one case. We considered that all cases developed acute adrenal insufficiency, because RFP enhanced the metabolism of PSL, in addition the requirement of adrenocortical hormone was in-

creased by infection. We should consider increasing steroid drugs, when it was necessary to use RFP together, even if it was a case of low dose use of steroid.

P3-078

A rheumatoid arthritis (RA) patient who was produced symptoms similar to Drug Hypersensitivity Syndrome due to administer Salazosulfapyridine (SASP)

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Conflict of interest: None

Background: We report a case of the patients with RA who was observed drug hypersensitivity-like syndrome due to SASP. *Case:* The patient with RA is a 28 year-old woman. She has reached remission due to a combination therapy of etanercept (ETN) 50mg/week and methotrexate (MTX) 8mg/week for RA. Because she desired pregnancy, she received a monotherapy of certolizumab pegol (CZOP). However, her disease activity was increased after quitting of loading dose of CZOP, SASP 1000 mg/day was added. Seventeen days after adding SASP, high fever-up, dysfunction of liver enzyme and cervical lymphadenopathy was observed. Although she recieved prednisolone (PSL) 30mg/day, she had erythema and oral mucosal erosion. Drug-induced hypersensitivity syndrome (DIHS) was suspected and PSL was increased to 50mg/day after hospitalization. After improving of her symptoms, PSL was gradually tapered and she left hospital. Because leukocyte abnormalities and HHV-6 reactivation was not shown in this case, she was not fulfilled the diagnostic criteria of DIHS. *Conclusions*: Data of offending drugs causing DIHS is limited, this case was highly suspected the diagnostic of DIHS.

P3-079

Reactivation of hepatitis B virus in rheumatoid arthritis patients : three case reports

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Conflict of interest: None

[Object] Recently, reactivation of hepatitis B virus (HBV) and de novo hepatitis are important concerns in patients with rheumatoid arthritis (RA) treated with disease-modifying antirheumatic drugs (DMARDs), such as immunosuppressants and biological agents. But the clinical features of RA patients suffered from HBV reactivation are yet to be elucidated. We report 3 cases of HBV reactivation in the patients of RA in our hospital. [Methods] Before administration of DMARDs, we performed screening of HBV infection for all patients in our hospital. Patients who had the sign of prior infection of HBV regularly received test for HBV-DNA while receiving therapy by DMARDs. [Results] Three patients suffered from HBV reactivation in recent 5 years. In each patients (76m/77f/67f), disease duration were 16/5/36 years respectively. Each patient's comorbidities were diabetes mellitus/osteoporosis/Sjögren's syndrome and osteoporosis. Each DMARDs were infliximab+methotrexate/tocilizumab+tacrolimus+bucillamin/abatacept, respectively. Duration between start on prescribing DMARDs and the onset of HBV reactivation were 10.8/3.4/3.0 years, respectively. [Conclusions] HBV reactivation could be observed after ten years from start of infliximab. HBV reactivation can be seen while abatacept monotherapy.

P3-080

Analysis of risk factors related to new transamylase elevation during rheumatoid arthritis treatment

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Conflict of interest: None

The titer of transaminase, which was normal before the treatment of rheumatoid arthritis (RA), is often elevated and abnormal in using several DMARDs. We analysed retrospectively the risk factor using our multi center cohort.900 cases were available, which were undertreatment of RA in 2015 and had normal range of transaminase titer at the first time of the year. The number of abnormal group was 246, whose transaminase titer exceeded its normal range even once in 2015. The number of normal group was 654, whose transaminase titer kept its normal range in 2015. In univariate analysis, the risk of transaminase elevation was statisitically higher among the patients with corticosteroid (CS) and methotrexate (MTX), and lower among those with bucillamine. On the other hands, in multivariate logistic regression analysis, the risk of transaminase elevation was statisitically higher among the patients with corticosteroid, methotrexate and biological DMARDs. The use of CS may induce fatty liver and those of MTX drug-induced liver injury. We should take care of liver damage in using biologic DMARDs, although the etiology is not well known.

P3-081

Does the risk of hemorrhage due to decreased coagulation factor XIII activity actually increase in rheumatoid arthritis patients receiving tocilizumab therapy?

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Conflict of interest: None

Purpose: It has recently become known that decreased coagulation factor XIII activity (FXIIIA) develops in rheumatoid arthritis (RA) patients during tocilizumab administration. Patients with extreme decrease in FXIIIA present with severe hemorrhagic symptoms such as serious pelvic and intramuscular hemorrhage. However, there are some questions such as frequency and severity of hemorrhage during treatment. Methods: We investigated FXIIIA in 88 RA patients who received tocilizumab therapy at our hospital. The observation period was the one-year period from august 2014 to july 2016. Results: Hemorrhagic diathesis was observed in one patient. Decreased FXIIIA (70% or lower) was observed in 38 patients (43.2%). The results were as follows: 60% ≤ FXIIIA < 70% in 14 (15.9%), 50% ≤ FXIIIA < 60% in 11 (12.5%), 40% ≤ FXIIIA < 50% in three (12.5%), 30% ≤ FXIIIA < 40% in three (3.4%), 20% ≤ FXIIIA < 30% in four (4.5%), and 10% ≤ FXIIIA < 20%(3.4%); no patients had FXIIIA level less than 10%. 50 patients (56.8%) were within the normal range. Conclusion: Decreased FXIIIA was noted in 43% of RA patients during tocilizumab administration. No patients presented with serious hemorrhagic symptoms. Even if FXIIIA decreased by tocilizumab, discontinuation of tocilizumab therapy did not occur.

P3-082

The retention rates of abatacept in elderly RA patients who cannot be treated with methotrexate: comparison with etanercept and tocilizumab

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Conflict of interest: None

[Objectives] To analyze the retention rate of abatacept in elderly patients with rheumatoid arthritis (RA) who cannot be treated with methotrexate (MTX). [Method] Data was collected retrospectively from the

medical records of RA patients in our center. Abatacept (ABT), etanercept (ETN), or tocilizumab (TCZ) was administered to 68 elderly RA patients (over the age of 65) who could not be treated with MTX. We analyzed the retention rate of each group by Kaplan–Meier curves and log-rank test. [Results] In the abatacept group (26 cases: 77.8 ± 6.3 years), the cumulative retention rates for both 12 and 24 months was 0.699. In the etanercept group (26 cases: 75.8 ± 5.1 years), the cumulative retention rates for 12 and 24 months were 0.450 and 0.314, respectively. In the tocilizumab group (16 cases: 73.7 ± 5.6 years), the cumulative retention rates for 12 and 24 months were 0.433 and 0.325, respectively. There was a significant difference in the retention rates between ABT group and the other two groups [log-rank test, p = 0.018 (ABT vs. ETN), 0.047 (ABT vs. TCZ)]. [Conclusion] Our data suggested that for elderly RA patients who cannot be treated with methotrexate, abatacept can be used for a period longer than etanercept or tocilizumab.

P3-083

The review of glucocorticoid-induced osteonecrosis of femoral head developed in autoimmune patients

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Conflict of interest: None

Objectives: To clarify clinical problems of glucocorticoid (GC)-induced osteonecrosis of femoral head (ONF) through reviewing patients with autoimmune diseases treated with moderate to high dose glucocorticoids in our departments. Methods: 17 cases patients with autoimmune diseases treated with GCs who developed ONF in our department from April 2007 to October 2016 were retrospectively reviewed. Results: 8 out of 17 cases patients were prescribed GCs for systemic lupus erythematosus (SLE), 2 for adult onset Still's disease, 2 for Bechet disease, and 2 for mixed connected tissue disease. The age at onset was 36.3±9.6 (mean±SD), the maximum dose of GCs was 49.5±15.2mg (PSL), the dose of the GCs at onset of ONF was 7.9±4.5mg (PSL). Both-sided ONF on MRI imaging was identified in eleven patients, while three had only unilateral pain. Total Hip Arthroplasty (THA) was performed in 7 patients. only a patients were taking lansoprazole. Conclusion: The most common primary disease was SLE. Recently, lansoprazole is reported prevention of GC-induced ONF, and only a case took the drug in this study. Even when symptom was limited in one side, both-sided ONF could be identified, indicating that early diagnosis by MRI imaging may contribute to improve diagnostic accuracy for GC-induced ONF.

P3-084

Adherence and safety of self-administered biologics for patients with rheumatoid arthritis

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Conflict of interest: None

[Object] In our country, we can use 5 self-administered biologics for rheumatoid arthritis (RA) now. The objective of this study was to assess the safety and adherence RA patients treated with self-administered biologics. **[Methods]** The subject is the RA patients continuing self-administration by the end of March, 2016 from April, 2015. We interviewed based on a follow-up sheet and confirmed a real self-administration procedure. **[Results]** The problem of the procedure was found in approximately 20% in 85 patients. In three years, there was not the dropout case for self-circumstances, and the compliance was good. **[Conclusions]** The self-administration follow-up for the biologics can expect an effect to raise compliance and safety.

P3-085

Management of Rheumatoid Arthritis (RA) Complicated With Pulmonary *Mycobacterium avium* complex (MAC) Infection

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Conflict of interest: None

[Object] To elucidate a proper management of RA patients complicated with pulmonary MAC. [Methods] Among 1162 patients of RA who have visited our department between April 2014 and March 2015, 7 patients (5 female) were found to fulfill the 2008 diagnostic criteria of pulmonary nontuberculous mycobacterial disease. We reviewed the medical records of the 7 patients retrospectively. [Results] Mean age 65.3, disease duration 21.4 years, mean HAQ-DI 2.125,6 cases had moderate disease activity (CDAI>10), 6 had preexisting lung diseases other than MAC, 5 had steroid, 6 had csDMARDs and 6 had bDMARDs. After diagnosis of MAC, csDMARDs were continued in all patients but all bDMARDs were stopped. For MAC, 4 cases started anti-mycobacterial therapy and 3 without treatment. RA activity was flared up after cessation of bDMARDs in all 6 patients, and steroids were increased in 3 of them and another csDMARD was added in 4. Two cases resumed bDMARDs but their MAC got worse after 3 months later and then those was improved by anti-MAC therapy. As a result their MAC improved after 18 months. [Conclusions] In the management of RA with MAC, csDMARDs should be continued. Although bDMARDs should be stopped in general, re-try of bDMARDs might be possible with intensive anti-mycobacterial therapy for MAC.

P3-086

A case of cytomegalovirus cornea inflammation caused by Abatacept

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Conflict of interest: None

*(Clinical significance)*Biological agents including abatacept might frequently cause opportunistic infections due to host's diminished immune function. We report an extremely rare case with corneal disorder caused by cytomegalovirus infection which is often observed in opportunistic infections. (*Case report)* The case was for male at the age of 80 with rheumatoid arthritis (RA). He was orally taking MTX and prednisolone, then abatacept was introduced. The clinical manifestation of RA was improved from the early stage, but the patient complained a rapid visual loss after 2months of the administration. Corneal disorder (endotheliopathy with widespread edema) was found in the detailed examination and cytomegalovirus became positive due to hydatoid PCR. Corneal symptom was relieved with cessation of abatacept, ganciclovir, and steroid eyedrops, and then vision was also recovered 4 months after the onset. There are only a few reports for cytomegalovirus infection with abatacept administration, but there is no report for the infection causing corneal disorder as far as we could search for. Although opportunistic infections could possibly be caused from compromised condition by abatacept administration, a careful observation will still be required from now on.

P3-087

Assessment of pain by Adalimumab subcutaneous injection and usefulness of support by nurses in patients with rheumatoid arthritis

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Conflict of interest: None

Purpose: The aim is to evaluate pain by adalimumab (ADA) subcutaneous injection. We also assessed usefulness of support by nurses for improving pain by injection and anxiety. Methods: Patients with RA self-infected with ADA were enrolled. Pain by ADA injection was divided 4 parts. General, needle insertion, drug injection, needle removal. These pains were evaluated using VAS scale. Usefulness of support by nurses was also assessed. Results: 11 patients (M:F 4:7)were enrolled. Average age and duration were 62 and 7.6 years. Pain VAS (mean) were 27.3 (General), 20.3 (needle insertion), 26.6 (drug injection) and 7.5 (needle removal), respectively. General pain did not show statistically significant difference compared with needle insertion or drug injection. There were statistically significant differences between removal and general pain (p=0.009) or drug injection (p=0.023). Approximately half of patients answered support by nurses was useful for improvement of pain, reduction of anxiety and improved motivation for treatment. Conclusion: These data indicate that needle insertion and drug injection pain have great influences on general pain. Support by nurses may reduce anxiety and pain by injection, resulting in increase of motivation for treatment.

P3-088

Anaphylactoid reaction when switching the route from subcutaneous TCZ injection to intravenous TCZ infusion :Case report

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Conflict of interest: None

A 34-year-old man with a 11 year history of poly-arthritis like Rheumatoid Arthritis (RA). He developed marked myalgia in both legs from 2 years ago. We diagnosed him as having Granulomatosis with polyangitis (GPA). Combination therapy of oral corticosteroids (prednisolone 1mg/kg/day) and intravenous cyclophosphamide (IVCY) pulse was provided. He had once achieved remission. When steroid dose was lowered, his arthritis flared. We started to treat him with biweekly injection of 162mg of tocilizumab (TCZ) subcutaneously. He could not achieved good response. Therefore we switched a type of TCZ treatment from subcutaneous injection to intravenous infusion. After starting intravenous TCZ infusion, anaphylactoid reaction was occured 30 minutes later. Some patients with TCZ-related severe reactions, antibodies against TCZ were detectable. Our patient had IgG antibody against TCZ. When switching the route from subcutaneous TCZ injection to intravenous TCZ infusion, it is necessary to pay attention to anaphylaxis or anaphylactoid reactions.

P3-089

2 case of MTX-associated lymphoproliferative disorders in the oral area

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Conflict of interest: None

Methotrexate (MTX) is the key drug for rheumatoid arthritis (RA). On the other hand, the occurrence of MTX-associated lymphoproliferative disorders (MTX-LPD) in the oral area is reported one after another. We reported two cases of the MTX-LPD of the maxillary gingiva associated with RA. First case; a 66-year-old woman, her RA disease duratation is about 5 years, she had been receiving MTX continuously. She was referred to our hospital because of severe pain on right maxillary gingiva and upset of molar tooth. Second case; a 78-year-old woman, her RA disease duratation is about 10years, she had been receiving MTX about 5 years. She was referred to our hospital because of severe pain associated with an ulcer on left maxillary gingiva. And Both case were it in the past of Bisphosphonate-Related Osteonecrosis of the Jaws. And we eoforced biopsy, these were showed lympho proliferation to doubt MTX-LPD. We therefore requested discontinuation of MTX, and both cases lesions were decreased and sympsons Sequestrectomy was operated only in second cases. Now, both case showed no evidence of recurrence. We reviewd reports documenting about some cases of oral MTX-LPD in Japan.

P3-090

A case of relapsing and metastatic state of renal cell carcinoma with RA patient who had been treated with a multi-targeted receptor tyrosine kinase inhibitor, sunitinib

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Conflict of interest: None

Sunitinib, a receptor tyrosine kinase inhibitor become commercially available as an agent for malignant tumors, renal cell carcinoma (RCC) and GIST. This agent is known as a multi-target drug which inhibits VEGF/VEGRF signaling, PDGF/PDGFR, c-Kit, Flt-3. On the other hand, inhibitors of cytoplasmic tyrosine kinases regarding inflammatory signals of rheumatoid arthritis (RA), for example, JAK inhibitor, revealed effective as one of therapeutic strategy. We recently experienced a case of relapsing and metastatic state of RCC with RA patient who had been treated with a multi-targeted receptor tyrosine kinase inhibitor, sunitinib. Not only reducing the size of RCCs, his symptoms and clinical examination of RA had dramatically improved by administration of sunitinib. We overview the possible therapeutic mechanisms of sunitinib in RA treatment.

P3-091

A case of rheumatoid arthritis complicated with deteriorated interstitial pneumonia after the administration of abatacept

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Conflict of interest: None

A 71-year-old man was diagnosed rheumatoid arthritis (RA) in 2014. On the computed tomography (CT) scans, ground-glass opacities were observed, but his interstitial pneumonia was not progressed compared with CT scans of 5 years ago. He was given Salazosulfapyridine (SASP) and tacrolimus (TAC). After 6 month, SASP and TAC was not effective, therefore these drugs were discontinued and we started administration of abatacept (ABT). After 4 month, his interstitial pneumonia were deteriorated. ABT was discontinued, he was given oral PSL (20mg) and admitted to hospital. After admittion, administration of ciclosporin was added. His interstitial pneumonia were improved gradually and oxygen therapy were not needed. 2 month after admittion, he was discharged. We report a rare case of RA complicated with interstitial pneumonia that deteriorated after the administration of ABT.

P3-092

A case of successful continuation use of abatacept to treat rheumatoid arthritis with psoriasis form lesions associated with abatacept

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Conflict of interest: None

A 70-year-old woman presented with a 10-years history of rheumatoid arthritis (RA). She had been treated with methotrexate (8mg/week), her RA disease activity remained high. She was administered tacrolimus (TAC)with good response. However, she had discontinuation of MTX because she developed digestive symptoms and respiratory symptoms. After discontinuation of MTX, disease activity of RA was worsened, she treated abatacept (ABT) therapy. Disease activity score 28 was improved from 4.2 to 2.49 after 4 months. After 4 months ABT therapy, she noticed a few eruption without pruritus on her legs, arms, abdomen and face. Histological findings from a skin biopsy showed the diagnosis of psoriasis. Therefore, ABT was discontinued and the skin lesions improved substantially under topical treatment with steroids. After the termination of abatacept her RA disease activity was worsened. She was administered ABT again, her skin lesions were deteriorated. She was able to continue

ABT with topical treatment for psoriasis.

P3-093

A case of relapsing organizing pneumoniae during Infliximab therapy in rheumatoid arthritis

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Conflict of interest: None

A 60-year-old woman who is non-smoker was referred to our hospital because of deterioration RA. She was high disease activity (HDA), we prescribed methotrexate (MTX). She remained HDA, we prescribed infliximab (IFX). But she still remained HDA. Soon later she has been appeared productive cough had not amelioration after antibiotic therapy, she underwent bronchoscopy. Bronchoalveolar lavage fluid showed increase in lymphocytes (63%), and decrease CD4/8 ratio to 0.28, we diagnosed organizing pneumoniae (OP) from transbronchial lung biopsy. Her respiratory condition was not so bad and OP has improved spontaneously without prednisolone therapy. She has been treated with MTX and IFX, but her disease activity has remained HDA. In the meantime, she had suffered from OP that has been spontaneous remission several times. Fourth time of relapsing OP, her respiratory condition was bad, so we prescribed prednisolone and OP has improved immediately. We suspected OP is related to IFX, so switched IFX to tocilizumab. Six months later, She ameliorated to low disease activity and there is no relapsing OP until now. <Conclusion>Recently, it has been reported that OP develops when patients with RA treated with biologic disease-modifying antirheumatic drugs. We add review of the literatures.

P3-094

A case of anti aquaporin 4 autoantibody positive optic neuritis occurring during anti TNF-α therapy

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Conflict of interest: None

A 35-year-old woman, who had had RA for twenty years, had beeen treated with ETN 25 mg/week and PSL 5mg/day. Three weeks before, she gave birth to a baby by caesarean section. Two weeks before, she had been conscious of visual impairment and narrowing of visual field. She saw ophthalmologist and was indicated decreased light reflex and relative afferent pupillary defect. MRI showed T2W1 high signal intensity of optic nerve neurilemma, a diagnosis of left retrobulbar optic neuritis was made. Anti aquaporin 4 autoantibody was detected. Steroid puls therapy was started and plasma pheresis was given seven times. After that she was treated with PSL 30mg /day. ETN was discontinued, and switched to TCZ. Her vision did not recovered, but stable remission had been maintained without recurrence of optic neuritis and PSL could be tapered quickly. There have been a number of reports of demyelinating events in patients receiving anti TNF-α therapy. We considered the possible association between drug and optic neuritis in this case. Sometimes it is difficult to keep remission by corticosteroid and immunosuppressants. Recently, the efficacy of the anti-IL-6 receptor antibody therapy in a patient with neuromyelitis optica has been reported. In our case, TCZ was effective in optic neuritis.

P3-095

Six cases study about How to deal withTocilizumab (TCZ) introduction from Etanercept (ETN) failure of RA treatment

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Conflict of interest: None

[Object] From 66 ETN RA cases, 6 Cases changed to TCZ be studied. [Method] Survival rate for 12 months be revealed. Each case, check for intraarticular steroid injection and systemic steroid addition after TCZ introduction. Check CRP for 6 months [Results] Survival rate 12 months is 50%. CRP negative is achieved. Noncontinual 2 Cases are MTX free from ETN administration, they gave up ETN cause of skin rash of injection site, and also have skin rash and infusion reaction at the second time of TCZ administration. We give up TCZ and any BIO-DMARDs, now treat with combined csDMARDs and joint injection. Non-continual one Case was MTX free, achieved CRP0.01 below, still MMP-3 high, arthritis symptoms, move to GLM100mg. Continued 3 cases, steroid injection are administrated at TCZ. Nursing home injection is good for drug adherence, makes elder lady with a bit dementia remission. [Conclusion] For TCZ administration after ETN, CRP negative must be achieved, and check arthritis. Arthritis happening sometime requires to steroid injections. Nursing home injection is good for adherence. Pay attention to infusion reaction at 2nd TCZ administration for patient with injection site reaction and give-up ETN. csDMARDs or Tofacitinib administration may be consider alternatives.

P3-096

DNA integrity index represents an unique pharmacological effect of TCZ

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Conflict of interest: None

Objective: Circulating cell-free DNA (ccfDNA) is detected in peripheral blood of patients with rheumatoid arthritis (RA) because of damage of cells or physiological cell division. We have previously reported that amounts of ccfDNA indicated the therapeutic effects of biological DMARDs. In this study, we examined the effect of tocilizumab (TCZ) on primary cultured human synovial cell by using DNA integrity index representing a relative ratio of ccfDNA that was not derived from cell death. **Methods:** Culture-supernatants were collected after stimulation with interleukin (IL)6/soluble IL6 receptor (sIL6R) or TNFα, and successively treated with TCZ (100μg/mL) or etanercept (ETN: 10μg/mL). Then, ccfDNA in supernatants was examined by qPCR to evaluated DNA integrity index. Viabilities of synovial cells were also examined by WST-8 assay. **Results:** DNA integrity index was significantly reduced by TCZ, but not by ETN. No significant differences were detected in cellular viabilities between non-treated and biological DMARDs-treated groups. **Conclusions:** TCZ did not affect synovial cell proliferation, but were considered to inhibit physiological cell division that is distinct from cell death. An unique pharmacological effect of TCZ was proposed.

P3-097

Identification of baseline gene expression signatures predicting therapeutic effects of TNF inhibitors in rheumatoid arthritis patients

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Conflict of interest: Yes

[Object] Aim of this study is to identify gene expression signatures predicting therapeutic effects of TNF inhibitors. [Methods] Rheumatoid arthritis (RA) patients who responded inadequately to MTX and to be commenced with either infliximab (IFX), etanercept (ETN), or adalimumab (ADA) as their first biologic, were enrolled. Blood gene expression

data were obtained prior to administration of TNF inhibitors. We employed Gene Set Enrichment Analysis (GSEA) to identify functional gene sets differentially expressed in remission and non-remission groups according to CDAI at 6 months of therapy. We have developed "signature score" to grade each individual and performed ROC curve analysis. [Results] There were 140, 29, and 50 cases of IFX, ETN, and ADA, respectively (total 219). At 6 months of therapy, the CDAI remission rate was 31.5%. GSEA showed that genes associated with inflammasome (INF) and type I interferon (IFN) pathways were significantly upregulated in non-remission group. In ROC analyses using signature scores, individual AUCs of INF and IFN pathways were 0.62. When both were combined, AUC was 0.65. [Conclusions] We have shown how gene expression signatures underlying therapeutic effects of TNF inhibitors. INF and IFN pathways may be contributing to the heterogeneity of RA.

P3-098

Serum peptides as putative modulators of the joint inflammation of psoriatic arthritis

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Conflict of interest: None

[Objective] We tried to identify novel serum peptides associated with the pathophysiology of psoriatic arthritis (PsA). [Methods] Serum peptides from 24 patients with psoriasis vulgaris (PV), 10 patients with PsA, 14 patients with atopic dermatitis (AD), and 23 healthy control subjects (HC) were purified by weak cation exchange and analyzed by mass spectrometry. [Results] A total of 93 peptide peaks was detected. Ion intensity of 18 and 6 peptides was changed at least 1.2-fold and -1.2 (1/1.2)-fold, respectively in the PV+PsA group compared to the HC group ($p<0.05$). Similarly, ion intensity of 11 and 9 peptides was changed at least 1.2-fold and -1.2-fold, respectively in the PV+PsA group compared to the AD group ($p<0.05$). Parent proteins of these peptides included a coagulation factor and proteins involved in maintenance of skin. Interestingly, ion intensity of 7 and 16 peptides was changed at least 1.2-fold and -1.2-fold, respectively in the PsA group compared to the PV group ($p<0.05$), parent proteins of which included a coagulation factor and a protein related to cytoskeleton. [Conclusions] Serum peptide profiles of PsA were different from those of PV. The peptides showing different ion intensity between PsA and PV would be associated with the pathophysiology of arthritis in PsA.

P3-099

Efficacy and Safety of Golimumab 100mg for elderly RA patients ~ Sweet cohort ~

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Conflict of interest: None

Objectives: Assessment of efficacy and safety of Golimumab 100mg for elderly RA patients Methods: Twenty two of 70 years old or elderly RA patients treated with GLM who had clinical data at least through 24 weeks are target for this retrospective analysis among forty five RA patients treated with GLM at Kurashiki Sweet hospital. Efficacy was compared between the patients divided into a group of 100 mg treatment arm and a group of 50 mg treatment arm by means of persistence rate, change on disease activity, and rate of adverse events. Result: Sixteen of elderly RA patients (73%) over 70 years old among the twenty two pts were treated at 100 mg of GLM at least once. Five pts initially treated at 100 mg, three pts escalated dose at second treatment, and four pts escalated dose at third treatment. Fourteen pts (64%) were treated with MTX and the others (8 pts, 36%) are not combined with MTX. Persistence rate of GLM at 24 weeks is 100% for 50 mg and 81.3% for 100 mg. Rate of LDA / Remission at 24 weeks is 60% in 50 mg group and 33% in 100 mg group. Rate of adverse events is significantly lower in 100 mg group (19%). Summary: For elderly RA pts, rate of adverse events is lower in 100mg GLM compared to 50 mg GLM. It is optional to switch to 100 mg treatment on basis of disease activity.

P3-100

Histopathological analysis of podoplanin expression in various synovial tissues using anti-podoplanin monoclonal antibodies

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Conflict of interest: None

Introduction: Podoplanin (PDPN), a platelet aggregation-inducing factor, is expressed in several normal tissues and malignant tumors. In this study, we analysed various synovial tissues using anti-PDPN monoclonal antibodies (mAbs). Materials and methods: Synovial tissue samples obtained from forty patients (rheumatoid arthritis [RA; n=11], osteoarthritis [OA; n=9], aseptic foreign body granuloma of loose implants [Loose; n=11], periprosthetic joint infection [Infection; n=9]) undergoing knee or hip surgery were enrolled in this study. The degree of synovitis was evaluated using Krenn histopathological grading system. We used multiple anti- PDPN mAbs (NZ-1, LpMab-3, 7, 10, 12, 13, 17) for immunohistochemistry. Result: Inflammatory synovitis score in RA was significantly higher than others (7.4 in RA, 4.3 in OA, 5.2 in Loose, 5.6 in Infection, respectively [$P < 0.05$]). In immunohistochemistry, inflamed synovial lining cells were positive for PDPN of all pathologies, especially in RA. The most clearly stainable anti-PDPN mAb was LpMab-12. Conclusion: PDPN was expressed in synovial lining cells of various joint diseases, which is expected to be useful for evaluating synovitis. LpMab-12 may have potential to visualize the inflammatory reaction of the synovium effectively.

P3-101

Prognosis of anti CCP antibody negative rheumatoid arthritis with treatment of biological agent

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Conflict of interest: None

Objectives: To evaluate the prognosis of ACPA negative RA with the treatment of biological agent (Bio). Methods: 41 ACPA negative RA patients treated with Bio (IFX:15, ETN: 9, ADA: 4, GLM: 5, CZP: 1, TCZ: 6, ABT: 1) were evaluated. We analyzed about continuation rate, clinical evaluation, and differences of RF positive at 1 year after administration of Bio, and the possibility of Bio discontinuation. Results: The continuation rate at 1 year was 75.6%. Clinical evaluation was improved at 1 year (DAS28: 4.44±0.98→2.45±1.23, SDAI: 17.98±9.91→4.99±6.04 (mean± SD, LOCF)). Higher continuation rate at 1 year were observed with RF-ACPA- compared to RF+ACPA- RA (92.3% vs 60%). The change of clinical evaluation at 1 year was same above (DAS28: 4.41±1.05→2.13±1.08 vs 4.52±0.83→3.15±1.27, SDAI: 18.74±11.43→3.55±4.04 vs 16.67±6.67→7.48±7.94). In addition, after first Bio failure, all cases achieved clinical remission after switching to second Bio. About the Bio discontinuation, six cases (IFX: 3, ETN: 2, GLM: 1) were observed, and all cases were DN. Conclusions: The prognosis of ACPA negative RA treated with Bio was good, and it was suggested that the pathogenesis of ACPA negative RA was different from

ACPA positive RA.

P3-102

The treatment option of elderly-onset rheumatoid arthritis

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Conflict of interest: None

Background: Meticulous drug selection should be taken to treat elderly-onset rheumatoid arthritis (EORA), because elderly patients have high prevalence of comorbidities, such as lung disease, liver disease, diabetes, and malignancy. **Purpose:** We conducted this study to investigate the difference in treatment options between EORA and younger-onset rheumatoid arthritis (YORA). **Patients and Method:** Eighty patients of diagnosed RA were enrolled. The patients divided into 2 groups by age: patients aged ≥ 70 (EORA) and < 70 (YORA). We compared the administration rate of corticosteroid, methotrexate, and biologics between both groups. **Results:** Twenty-two patients were categorized as EORA. The frequency of major joints onset, erythrocyte sedimentation rate, and C-reactive protein levels were significantly higher in the EORA than in the YORA. The administration rate of corticosteroid was higher than in the EORA than in the YORA. However, methotrexate administration rate was lower than in the EORA than in the YORA. There was no significant difference of the biologics use rate between both groups. **Conclusion:** Because the EORA patients present with high frequency of major joints onset and severe serological inflammatory reaction, corticosteroid could be easily prescribed.

P3-103

The combined therapy of DMARDs with Japanese Kampo for rheumatoid arthritis

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Conflict of interest: None

【Object】Treatment of rheumatoid arthritis (RA) has dramatically advanced. However, it is often difficult to improve a general assessment of disease activity by patients (VASG). In addition to DMARDs, we use Japanese Kampo to improve various symptoms of RA patients. The purpose of this study is to investigate the effect of Japanese Kampo on RA on disease activity.【Method】The subjects were 41 RA patients visited at our hospital from 2014 to 2016, average age 67 years, mean disease duration 13 years. The number of tender joint joints, number of swollen joints, CRP, VASG, and Japanese Kampo and DMARDs were investigated at the beginning of Kampo therapy and follow up period was one year.【result】Significant improvement was admitted in tender joint number (2.4 → 1.7) and DAS-28 CRP (2.5→ 2.2). DAS 28-CRP remission increased from 19 to 25, and Boolean remission increased from 3 to 6. There were 25 cases that did not change DMARDs during the year, and their VASG (3.7→ 2.5) improved significantly. We used 40 Japanese Kampo for various symptom such as arthralgia, etc.【Conclusion】Combined therapy of DMARDs with Japanese Kampo for RA was an effective for achieving Boolean remission because it could improve disease activity by improving VASG.

P3-104

Efficacy of concomitant iguratimod with biological agents

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Conflict of interest: None

Objective: To determine the efficacy of iguratimod (IGU) as a treatment for rheumatoid arthritis (RA). **Methods:** A retrospective analysis was performed and 62 RA patients treated with IGU at our institute were assessed for age, Steinblocker Stage and Class, disease duration, methotrexate (MTX) use and dosage, prednisolone (PSL) use and dosage, and disease activity as the baseline characteristics. We got the questionnaire from these patients at 24 weeks. **Results:** Average values obtained with SD were as follows: age (years), 62.0 ± 12.0; Stage I, 19; II, 13; III, 10; IV, 20; Class 1, 26; 2, 27; 3, 9; 4, 0; disease duration (months), 151.2 ± 153.6; MTX use and dosage (mg/week); 76%, 9.9 ± 2.7; PSL use and dosage (mg/day); 58%, 4.6 ± 1.8; DAS28-ESR, 4.09 ± 0.89. Total retention rate over 24 weeks was 90.3% for all patients. Patients with biological agents showed better retention rates and efficacies than patients with MTX or IGU monotherapy. Most patients reported satisfaction with overall effectiveness of IGU. **Conclusion:** At our institute, most patients showed good efficacies and reported satisfaction with IGU. This finding is important in the IGU therapy management for RA.

P3-105

A case of showing repaired bone erosion by add-on iguratimod after joint destruction progress despite of methotrexate

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Conflict of interest: None

【Case】The patient was a 58 years old Japanese woman. She was under the medical treatment at several local hospitals after the RA onset in 2001 and visited our hospital in April, 2013. The disease activity at the initial visit is as follows;CRP0.11mg/dl, ESR 7mm/h, MMP3:24.6ng/dl, ACPA:338IU/ml, DAS-ESR:3.50 and SDAI:19.41. We continued MTX 8mg/w. After one year, we added iguratimod (IGU) because she showed the grade2 of PD signal by musculoskeletal ultrasound (MSKUS) and the progression of joint destruction at left 2nd MTP joint by simple X-ray. After IGU addition one year later, she achieved clinical remission (DAS-ESR:2.10 and SDAI:1.47) and X-ray showed healing of bone erosion of left 2nd MTP joint, an improvement effect of joint destruction and confirmed disappearance of PD signal in MSUKS. Another one year later, the progression of bone erosion did not show in X-ray and continued disappearance of PD signal in MSUKS at left 2nd MTP joint.【Discussion】We experienced the case that it was thought that we can expect prevent of joint destruction, an improvement effect by obtaining calming down of synovitis by IGU treatment, we add some discussion from other references and report it.

P3-106

Efficacy and safety of igratimod in the patients of rheumatoid arthritis in our Hospital

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Conflict of interest: None

[Object] To assess the efficacy and safety of iguratimod (IGU) for rheumatoid arthritis (RA) patients at our hospital. [Method] Sixty-one patients were enrolled in this study. We researched on the reasons to administer IGU, the reason to stop IGU (n=61) and evaluated rend of DAS28-CRP and CDAI, SDAI at 0 to 52 weeks (n=32). [Results] Forty-seven patients were added IGU to existing formula, four patients were switched, and ten were 1st choice. The reason to stop were no effect (n=2) and nineteen ware adverse events. Adverse events were peptic ulcer (n=1), digestive symptom (n=3), pharyngeal pain (n=1), liver dysfunction (n=1), renal dysfunction (n=5), skin symptom (n=3), elevations in creatine kinase (n=1), drug refusal (n=1). The DAS28-CRP, CDAI, SDAI all significantly decreased at week 52. [Conclusion] IGU had significent clinical effects on the RA patients within 52w.

P3-107

Treatment of high dose Methotrexate and Anti-tumor necrosis factor α in Rhumatoid Arthritis

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Conflict of interest: None

Introduction: The objective of this study was to demonstrate clinical outcome of Methotrexate (MTX group) at dose over 10mg/week and Anti-tumor necrosis factor α(TNFα group) at dose under 8mg/week in Rhumatoid Arthritis. **Materials and Methods:** Twenty five patients who had been treated with MTX and 53 patients who had been treated with TNFα were the subject of the study. We estimated patients demographics, DAS-28CRP, MMPIII and the adverse event at last follow up. **Results:** The significant difference was shown that compared with patients demographics (age, DAS28) between 2 groups. No significant difference was shown that clinical outcomes. MTX group of the adverse events were 4 hepatic dysfunctions, one interstitial pneumonia and one pneumocystis carinii pneumonia. TNFα group of the cancellation treatment were 3patients. **Discussion and Conclusion:** These results suggest that treatment of high dose MTXcan be sufficiently effective with comparison of Anti-tumor necrosis factor treatment for RA.

P3-108

Efficacy of disease activity in rheumatoid arthritis patients overlapped systemic sclerosis treated with tocilizumab

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Conflict of interest: None

A 74-year-old Japanese woman was affected by generalized RA in 2003. In 2015, she had poor control of arthritis and increase of KL-6 without progression of lung fibrosis on chest CT. She was introduced for RA treatment in our hospital. She received treatment with prednisolone (PSL), MTX and SASP. However, DAS28-ESR and CDAI showed a high value of 5.35 and 31.8. Sclerema from the fingers to the upper arms, dorsum of feet and face were also observed. Serological examination found that ANA measurement at 1280×(centromere), anti centromere antibody at 178.8 U/ml were increased. We diagnosed the RA patient with overlap syndrome involving SSc with interstitial lung disease. We decided to treat the patient with tocilizumab (TCZ). Administration ofPSL, MTX and SASP was continued. Her skin symptoms resolved and the swelling and tenderness of the joint began to improve 1 month after initiating TCZ treatment (162 mg every 2 weeks). The m-Rodnan TSS reduced from 23 to 5 within 9 months, and joint tenderness and swelling of most joints. DAS28 and CDAI decreased to 1.98 and 7.8 in 9 months. Tocilizumab therapy allowed tapering of the glucocorticoid without exacerbation of the patient's condition. TCZ may be effective against RA and SSc for which conventional treatment is inadequate.

P3-109

Tofacitinib was efficacious after the failure with tocilizumab in patients with rheumatoid arthritis − FIT-RA registry −

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Conflict of interest: None

[Objectives] To investigate the efficacy of tofacitinib (TOF) in patients with rheumatoid arthritis (RA) who showed inadequate response to tocilizumab (TCZ). [Methods] We investigated clinical outcomes by TOF treatment of patients with RA who terminated TCZ for inefficacy. Patients demographics and disease activity parameters were collected at base line, 3, 6 and 12 months after TOF treatment started. [Results] A total of 8 patients detected. They all have used more than 2 biologics including TCZ. Two patients were in high disease activity states defined by DAS28CRP, 6 moderate disease activity states, no patients in low disease activity states and remission at baseline. Six patients used prednisolone and 3 methotrexate at baseline. One patients terminated TOF for breast cancer at 10 months. Seven patients continued TOF at 12 months. With regard to treatment effects of EULAR response by DAS28CRP, 4 patients achieved good response, 3 moderate response and 1 no response at 6 months, and 4 good response, 4 moderate response at 12 months or the TOF termination, respectively. All concomitant prednisolone dosages at 3 months, 6 months, and 12 months were less than those at baseline. [Conclusions] TOF was efficacious in patients with RA and inadequate response to TCZ.

P3-110

A study on the effect of tofacitinib (TOF) in DMARDs refractory patients with rheumatoid arthritis

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Conflict of interest: None

【OBJECTIVE】We examined the effect of TOF in DMARDs refractory RA.【METHODS】38 patients who received TOF were examined. The effect of TOF was evaluated by DAS28-ESR (improvement at 24 weeks after initiation, remission rate, EULAR response) and joint echo.【RESULTS】Bio-naive was 26 cases, Bio-switch was 12 cases (2 drugs 7, 3 drugs 2, 4 drugs or more 3). Previous DMARDs were MTX in 31 patients (82%) 9.7mg/week on average, and tacrolimus (TAC) in 23 patients (74%) 1.6 mg/day on average. Initial TOF doses, 28 cases (74%) started at 5 mg/day, mainly naive cases. In 14 cases, the effect was insufficient and dose was increased to 10mg and it was effective. Ten cases (26%) started at 10mg/day, mainly switch cases. In 12 cases with TOF discontinuation, discontinuities was often observed within 3 months, 26 cases continued, dropouts were small after 6 months and the 3-year continuation rate was 64%. In the continuation cases, DAS28-ESR at 24 weeks after initiation is 1.94 lower than baseline, LDA/remission rate is 73%, EULAR response good/moderate was 88%, and maintained until the last observation.【CONCLUSION】In Bio-naïve cases, even TOF 5mg was effective, and considering high drug prices, starting with 5mg and increasing to 10 mg was considered to be useful in naive patients.

P3-111

Rapid efficacy of tofacitinib: results from a retrospective analysis based on the outcome reported by patients

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Conflict of interest: None

Objective: To determine the efficacy of tofacitinib (TOF) as a treatment for rheumatoid arthritis (RA). **Methods:** A retrospective analysis was performed and 12 RA patients treated with TOF at our institute were assessed for age, height, body weight, Steinblocker Stage and Class, disease duration, number of biologic agents before TOF, methotrexate (MTX) use and dosage, and disease activity as the baseline characteristics. Disease activity was evaluated at 24 weeks. **Results:** Average values obtained with SD were as follows: age (years), 58.3 ± 8.2; height (cm), 156.4 ± 9.6; body weight (kg), 62.4 ± 16.4; Stage I, 2; II, 3; III, 2; IV, 5; Class 1, 3; 2, 8; 3, 1; 4, 0; disease duration (months), 121.3 ± 63.3; number of biologic agents before TOF, 0 (2 patients); 1 (7); 2 (1); 4 (1); and 5 (1); MTX use and dosage (mg/week); 83.3%, 10.0 ± 3.1; DAS28-ESR, 4.9 ± 0.8. Total retention rate over 24 weeks was 100% for all patients; younger patients showed better remission rates than elderly ones (P = 0.030). Most patients reported satisfaction with the treatment, especially regarding its fast efficacy and overall effectiveness. **Conclusion:** At our institute, most patients reported satisfaction with the rapid efficacy of TOF. This finding is important in the TOF therapy management for RA.

P3-112

Characterization of Changes in Lymphocyte (LYM) Subsets in Baricitinib (Bari)-Treated Patients (pts) with Rheumatoid Arthritis (RA) in a Phase 3 Study (RA-BEAM)

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Conflict of interest: Yes

Object: To examine changes in absolute lymphocytic count (ALC) and LYM subsets in pts with active RA treated with Bari. **Methods:** 1305 pts (249 Japanese [JP]) were randomized to placebo, Bari, or adalimumab (ADA), and received study drug. ALC, T cells/subsets, B cells/subsets, and natural killer (NK) cells were quantified by flow cytometry at baseline (BL) and Week (wk) 4, 12, and 24. **Results:** ALC and T cells/subsets increased with Bari and ADA at wk 4, returning to near BL at wk 12 and 24 in Bari but remaining elevated in ADA. B cells/subsets increased at wk 4 in Bari and ADA, and remained elevated through wk 24. NK cells were increased at wk 4 in Bari and were below BL but within the normal range at wk 12 and 24. NK cells were increased at wk 12 and 24 in ADA. There was no notable difference between JP and overall. **Conclusions:** Changes in ALC and subpopulations with Bari in RA-BEAM were largely within normal ranges and are consistent with previous data (Emery P, et al. *Arthritis Rheumatol.* 2015;67 [suppl 10]). Sustained increases in B cells were observed in Bari and ADA. Sustained increases in ALC and T cells were only seen in ADA.

P3-113

Improvement of gut microbiota in rheumatoid arthritis patients may alter the disease activity

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Conflict of interest: None

Introduction The research has been going to identify the etiological role of the alteration of gut microbiota on the RA progression. The purpose of this study is to identify the effect of butyric acid producing bacilius tablet (B-tab) on the RA management. Materials and Methods 38 patients who were prescribed B-tab were enrolled in this study. M:F=8:30, the average age is 61.4 years. The disease activity and adverse event were recording at 3 and 6 months following the B-tab prescription. Results All patients except one were treated with anti-rheumatic drug. The baseline DAS28 (CRP4) was 4.1 and significantly improved as 3.1 at 3 month later and 2.6 at 6 months later. Similarly, the baseline mHAQ of 0.6 was significantly improved to 0.4 and 0.26 at 3 months and 6 months, respectively. The group (18 patients) who were supported with mental consultation and recommended fermented food consumption was showed the better improvement of disease activity compared with others. Discussion As a possible drug for the improvement of gut microbiota, and as a message for the RA patients to tell them how important to keep the “good” gut microbiota on the RA management, B-tab is safe and patient-oriented drug on RA treatment.

P3-114

Overview of patients with severe autoimmune-diseases treated with plasma exchange due to insufficient response to medication in our department

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Conflict of interest: None

Objective:To clarify clinical characteristics and problems regarding plasma exchange (PE) in our department for severe autoimmune-diseases due to insufficient response to medication. Methods:We retrospectively reviewed 7 hospitalized patients treated with PE at our department during July 2009 and April 2016. Results:Clinical characteristics were;age 49±20 [18-76] years old, all females, and 4 patients with AOSD (57%),2 with SLE (28%) and 1 with SSc (14%). The reasons for induction of PE were;poorly controlled AOSD in 1 patient, HPS in 3, TTP in 2, and scleroderma renal crisis in 1. They had been treated with metication before initiating PE;high-dose corticosteroid therapy including mPSL pulse in 1 patient (85%), CsA in 4 (57%), MTX+ADA in 1 (14%) and ACEI+ARB in 1. Frequency of PE was 4.3±1.6 [3-7] times. All 7 patients showed clinical effectiveness (100%). However,6 patients discharged after amelioration, while 1 patient died due to an adverse event. She died from hemorrhagic cerebral infarction followed by brain edema. Conclusions:We performed PE for patients with severe autoimmune-diseases intractable to medication. All patients acquired clinical effectiveness and 85% of them survived, however unfortunately one patient died. Careful attention for circulatory disorder should be emphasized.

P3-115

Study of effectiveness of leukocytapheresis in rheumatoid arthritis

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Conflict of interest: None

[Objective] To estimate the effectiveness of leukocytapheresis (LCAP) for rheumatoid arthritis (RA), and determine factors associated with good response. [Methods] RA patients who underwent LCAP at our institute from April 2004 to September 2016 were included. Characteristics and DAS28CRP before and after LCAP were retrospectively analyzed. [Results] 26 patients were included to this study. Median age was 72 years, 24 cases (92%) were female, median disease duration was 13 years. Mean DAS28CRP before LCAP was 5.07. 6 cases (23%) had advanced cancer, 14 cases (54%) had interstitial lung disease, 9 cases (35%) had airway disease. DAS28CRP decreased 1.3 after LCAP (p=0.0001). 15 cases (58%) were moderate or good responders according to the EULAR criteria. There were no differences of baseline characteristics and laboratory data between responders and non-responders. Most adverse effects were mild hematological abnormalities. [Conclusion] Patients who underwent LCAP at out institute were of old age, had long disease duration, had comorbidities such as advanced cancer and pulmonary complications. More than half patients responded well after LCAP, but factor associated with good response were unclear. LCAP can be a choice of treatment for whom immunosuppressive therapy are not suitable.

P3-116

Consideration of the safety and the utility of Leukocytapheresis in rtheumatoid arthritis with chronic respiratory organ infection

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Conflict of interest: None

[Purpose] We have consider of the safety and the utility of Leukocytapheresis in rtheumatoid arthritis with chronic respiratory organ infection such as pulmonary nontuberculous mycosis. [Method] LCAP of total of 7 time cour which carried out a chronic respiratory organ infection of a pulmonary nontuberculous mycosis to 3 cases of rtheumatoid arthritis was considered. [Result]< case 1> a 77-year-old female. With mergers of the past of phthisis and a pulmonary nontuberculous mycosis. The 1st cour made DAS28CRP 6.38 to 4.59. The 2nd 4.97 to 3.47, The 3rd 5.42 to 4.30. The 4th 5.62 to 4.64. < case 2> a 77-year-old female. With mergers of a pulmonary non-tuberculous mycosis. The 1st cour made DAS28CRP 4.1 to 4.15, The 2nd 5.11 to 4.89. < case 3> a 71-year-old female. With mergers of the past of phthisis and chronic bronchitis, etc. 1 cour made DAS28CRP 4.50 to 3.19. No case got worse in their respiratory organ infection. [Conclusion] LCAP is a useful treatment in rtheumatoid arthritis case which would like to evade reinforcement of immunosup-

pressed.

P3-117

Efficacy of tramadol/acetaminophen combination tablets for rheumatic disease patients

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Conflict of interest: None

[Objective] We previously reported the clinical effect of tramadol hydrochloride/acetaminophen combination tablet (TRAM/APAP) in rheumatoid arthritis (RA) patients with chronic pain. In this presentation, we investigated the efficacy and safety of TRAM/APAP in rheumatic disease patients with uncontrolled pain. [Methods] Of 93patients receiving TRAM/APAP to rheumatic disease in our hospital, 12 patients without RA were evaluated. Polymyalgia rheumatica is five patients, SLE, fibromyalgia is two, ankylosing spondylitis, enteropathic arthritis, RS3PE syndorome is one. Four male patients and eight female patients were between 47 and 81 years of age (mean age 65.8). The clinical response was assessed by a 100-mm visual analog scale (VAS). [Results] The mean VAS score decreased from 73.7mm to 41.7mm. Two patients discontinued because of drowsiness and nausea. [Conclusion] TRAM/APAP was highly effective for pain relief in rheumatic disease patients. Use of TRAM/APAP is valuable treatment option for rheumatic disease patients with poor pain control.

P3-118

The efficacy of anticancer drugs, paclitaxel and bevacizumab, for rheumatoid arthritis; case report

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Conflict of interest: None

[Objective] This case report presents a female woman with rheumatoid arthritis (RA) complicated by ovary cancer. [Case Presentation] A 46-year-woman with RA which was well controlled with MTX and ETN experienced ovary cancer. ETN was discontinued and anticancer chemotherapy (CT) was initiated. At first, she was treated with combination chemotherapy of paclitaxel (PTX) and carboplatin. The joint symptoms of RA were kept in acceptable. But, after the termination of the CT, the condition of RA became worse. TCZ was administrated and the joint condition was somehow re-improvement. Next, she experienced recurrent ovary cancer when she was 52 years old. TCZ was discontinued and anti-VEGF antibody drug, bevacizumab (BV), was administrated. The condition of RA was managed better during the treatment with BV than that during the CT with PTX. [Conclusions] Both PTX and BV may be effective for the treatment of RA.

P3-119

Effect of Concomitant DMARDs on the Efficacy and Safety of Ixekizumab in Biological agent-naive Patients with Active Psoriatic Arthritis: A Randomized, Double-blind, Active- and Placebo-controlled Phase 3 Study (SPIRIT-P1, 24-weeks treatment)

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Conflict of interest: Yes

Objectives: To evaluate efficacy/safety of ixekizumab (IXE) alone or with (wt) DMARDs in biological agent-naive (bio-naive) patients (pts) wt psoriatic arthritis (PsA). **Methods:** Data from Double-Blind Treatment Period (Wk0-24); N=417 (12 Japanese); placebo (PBO; N=106), adalimumab 40mg (ADA; active reference, N=101) once every 2-weeks (Q2W), IXE 80mg Q2W (N=103) or Q4W (N=107) after 160mg initial dose. Data were stratified by DMARDs status (naive+past use, current use), and ACR response and mTSS were evaluated at Wk24. Safety included %pts wt adverse events (AEs), serious AEs (SAEs), discontinuations due to AEs. Fisher's test or analysis of covariance model was used to compare treatments. **Results:** 267/417 pts received DMARDs through 24weeks. Significantly more pts in IXE wt/without (wo) DMARDs achieved ACR20/50/70 responses vs PBO. Pts in IXEQ2W wt/wo DMARDs, IXEQ4W or ADA wt DMARDs showed significantly less progression in mTSS from baseline vs PBO. In pts wt DMARDs, significantly more pts in IXE or ADA reported ≥1AE vs PBO; %pts wt SAEs or discontinuations due to AE were comparable among treatments. **Conclusion:** Although more pts in IXE wt DMARDs reported ≥1AE compared wt PBO, IXE showed improved PsA signs/symptoms and structural inhibition in bio-naive PsA pts wt/wo DMARDs use.

P3-120

The expression changes of circulating microRNAs isolated from patients with systemic lupus erythematosus passing through plasma adsorption membrane

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Conflict of interest: None

PURPOSE: circulating microRNA (circulating miRNA) is taken up in cells at distant sites, involved in protein synthesis. We focused on the removal of circulating miRNA by apheresis and have shown that blood circulating miRNA can be separated and removed by plasma separation membrane. In this study, we examined how changed the expression of circulating miRNA that passed through the plasma adsorption membrane as the secondary membrane. METHODS: Three patients with systemic lupus erythematosus who received plasma adsorption therapy at our hospital were examined. Selsorb and Immusorba were used for plasma separation membranes. Samples were collected before entering plasma adsorption membranes, and immediately after passing through the membrane. After extracting circulating miRNA from each plasma, expression analysis was performed comprehensively using array chip (Human miRNA Oligo Chip 3D-Gene). RESULTS: In all three patients, marked reduction in expression of miR-1246, miR-4732-5p, miR-6088 after passage through the membrane was observed. CONCLUSION: It was inferred that circulating miRNA in separated plasma was adsorbed by plasma adsorption membrane. In order to explore the possibility of selectively removing disease-related circulating miRNAs, further investigation is required.

P3-121

Fat dysplasia on MRI as predictor of the progression of sacroiliitis ~from 2 cases of ankylosing spondylitis~

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Conflict of interest: None

<Objective> To assess the clinical significance of fat dysplasia (FD) in the progression of sacroiliitis (SI) in ankylosing spondylitis (AS). **<Methods>** Two cases of a 15-year-old man with AS (case 1) and a 24-year-old man with AS (case 2) were assessed by Magnetic Resonance Imaging (MRI) before and after treatments. **<Results>** Both cases had HLA-B27. MRI of the sacroiliac joint (SIJ) before treatment showed bone marrow edema (BME), erosion and sclerotic change without FD in case 1, and BME, erosion and sclerotic change with FD in case 2. After

treatment with NSAID and physical therapy combined with TNF inhibitor, both cases achieved remission. 1.5 years later, MRI in case 1 demonstrated neither FD nor BME, and radiographic progression was not observed. In case 2, 2 years later, MRI demonstrated no BME, however increased FD lesions and progression of erosion with Backfill. **<Discussion>** The reports from western countries suggest that FD could be predictive factor of the progression of SI and spondylitis in AS. It's important for us to observe both clinical courses of AS with and without FD. We need further studies to identify the predictive factors of the progression of SI and spondylitis in Japanese patients with AS.

P3-122

What is appropriate classification of spondyloarthritis case whose initial predominant manfiestation was axial, but thereafter residual symptom was only peripheral?

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Conflict of interest: None

The new ASAS classification criteria for axial and peripheral spondyloarthritis (SpA) raise questions, what degree of axial involvement allows a patient to be classified as having peripheral SpA, and what degree of peripheral involvement allows classifying the patient as having axial disease? The classification may therefore change from axial to peripheral and vice versa at different time point in a patient (Zeidler, ARD 2011). We experienced a patient who initially represented axial SpA, successively converted into peripheral SpA, and finally achieved sustained remission. A 56-year-old female patients who represented chronic back pain with recent-onset seronegative oligoarthritis and polyenthesitis. Pelvic radiograph showed grade 2 left sacroiliitis. MRI showed active inflammation on left sacroiliac joint. At this time point, she was classified into axial SpA. After treatment with NSAIDs and MTX, her low back pain disappeared. Thereafter, her predominant manifestations were dactylitis and oligoarthritis. At this time point, she could be classified into peripheral SpA. Administration of local steroid injection and MTX were effective, resulting in sustained sign and symptom free condition over 2 years. Should we classified this case into axial or peripheral SpA?

P3-123

Characteristics of Japanese patients with axial spondyloarthritis. A single –center cohort in North of Nagasaki Prefecture

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Conflict of interest: None

Objectives: To investigate the characteristics of Japanese patients with axial spondyloarthritis (SpA) in North of Nagasaki prefecture. Methods: Nineteen patients who had been clinically diagnosed as axial SpA in our Hospital from April 2009 to March 2016 were enrolled. We investigated the characteristics of patients, HLA-B alleles and the response to treat. Results: All nineteen patients were fulfilled the Assessment of Spondyloarthritis international Society (ASAS) criteria for classification of axial SpA and twelve were fulfilled the modified New York Criteria for Ankylosing Spondylitis (AS). They were diagnosed in the age of 40.5 years old and 1.9 years later from the onset of symptoms. Seven of nine AS patients have HLA-B27 allele, two of six have in Non-radiographic axil SpA on the other hand. Four AS patients have been treated with biologic agents and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score of most of these patient rapidly decreased. Furthermore, in some case, the STIR high signal in spine on magnetic resonance imaging (MRI) has disappeared at after one year. Conclusions: It is necessary to confirm whether non-radiographic SpA will progress to AS in the future or whether treatment can prevent spinal ankylosis.

P3-124

The efficacy of adarimumab in ankylosing spondylitis—2year follow up

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Conflict of interest: None

(Object) Sinece 2010, the use of TNF inhibitor for ankylosing spondylitis (AS) has started in Japan, and long-term efficacy has already been reported. However, there are few reports of efficacy on long-term use in Japan. In this study, we examined the clinical course of AS patients who completed adalimumab for 2 years at our hospital. (Method) Nine patients completed administered adalimumab for 2 years in our hospital. We analyzed patients profiles and followed the course of disease activity until 2 years. (Result) BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) improved from 5.01 at baseline to 3.09 at 104 weeks. BASDAI 50 improvement was 75% at 12 weeks, 37.5% at 52 weeks, and 37.5% at 104 weeks, respectively. In ASDAS (Ankylosing Spondylitis Disease Activity Score)-CRP, the percentage below medium disease activity, witch is regarded as the therapeutic target in the EULAR recommendation, was maintained 88.9% from 12 weeks until 104 weeks. (Conclusion) Adalimumab showed high efficacy in AS patients for 2 years.

P3-125

Treatment with ADA, MTX, and CyA made successfully for nr-axSpA (A Case report)

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Conflict of interest: None

Clinical meaning: To describe a male patient with nr-axSpA was treated successfully using biologics positively in his early stage, who was a case of suggestively to diagnose difficulty as a nr-axSpA or peripheral SpA. Case: A 52 year-old male who had a history of inflammatory back pain (IBP), since childhood due to quadriceps contracture as a complication by intramuscular injection for his recurrent epileptic fit, however; he can participate in the classes of physical examination at school. At age of 43, he could not walk due to arthritis on his knees. Thus, he had been taken zolpidem, pregabalin, tramadol, and acetaminophen. At 48, he was performed injection corticosteroid into Tenon capsule for his uveitis. At age of 51, he reffered our clinic on his legs with crutches complaining with recurrent uveitis, dactylitis on his fingers, arthritis on his legs and IBP. The laboratory data showed inflammation (CRP 10.94 mg/dL), positive HLA-B*27, without any symptoms nor radiological findings of RA. He was to treat with anti TNF alpha antibody directly as a patient with SpA with high score of BASDAI. Thereafter, rubefactions had been shown. He was diagnosed having psoliasis with the biopsy from his skin lesions. Then, he was improved adding with methotrexate and cyclosporine.

P3-126

Treatment for spondyloarthritis in our hospital

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Conflict of interest: None

[Object] To investigate the treatment for spondyloarthritis in our hospital. [Patients and Methods] 37 patients (men: 24 patients, women: 13

patients) who were diagnosed spondyloarthritis (psoriatic arthritis, ankylosing spondylitis, pustulotic arthro-osteitis) were included in this study. Examination items consist of disease duration, treatment duration, treatment, treatment response and survival late. About the assessment of the treatment response, we used DAS28 and EULAR response criteria for peripheral spondyloarthritis, and general visual analogue scale for axial spondyloarthritis. [Results] In 22 psoriatic arthritis patients, 15 patients was taken methotrexate (MTX) and 7 patients had more than moderate response and 3 patients met remission. 6 patient was taken biologic agent, and 4 patient revealed good response, 3 patient got remission. In 11 ankylosing spondylitis patients, 8 patients took biologic agent, and 7 patients improved. In four pustulotic arthro-osteitis patients, a patient was taken biologics and he revealed response. [Conclusions] In the treatment of spondyloarthritis, biologic agents were effective. MTX was effective for peripheral spondyloarthritis. DAS28 and EULAR response criteria were useful for detamining the activity of peripheral spondyloarthritis.

P3-127

The Dominance of IL17i therapy, Secukinumab, for Psoriatic Arthritis in Patients with Mild Psoriasis

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Conflict of interest: None

[Object] PsA is likely to lower ADL. We experienced the dominance of IL17i therapy for PsA. [Methods] Subject: six male patients has been a standard systemic therapy. The average age 46, and BMI 32. 2, the average Ps duration is 9. 3 years. PASI score per person will be less than 2. 2015.4~2016.10 (continuation during the follow-up period). In all cases, all the Secukinumab (SEC) 300 mg/ 12 w over the subcutaneous injection. History of bio-agents before treatment: Five first-time selection. In all cases, leading with MTX and. Effectiveness: general situation, especially joint symptoms and imaging: XP, scintigraphy, front, 6, 12, (18, 24 months). [Results](Effectiveness) (1) in all cases admitted early, PASI clear arrival and joint symptoms. (2) together, early recognized improvement in evaluation of image, then light, which is maintained. (Side effects) (1) 12 w is 1, prevented the right facial phlegmone. (2) per person with a 4 w suspended, then stop immediately after resuming at 8 w, 150 w 24-stop resume again at mg/BW. Both, according to the multiple oral, and esophageal ulcers. [Conclusions] Now once a PASI score low PsA values indicate SEC early arthritis symptom management and its continuity. IL17i recommended in peripheral arthritis expected much in the future than this.

P3-128

The investigation of the efficacy of biological agents for Spondyloarthritis

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Conflict of interest: None

[Objectives] Spondyloarthritis (SpA) is a group of chronic inflammatory rheumatic disease including AS and PsA. We investigated the therapeutic effects of the biological preparations (Bio) in patients with SpA. **[Methods]** Between 2007 and 2016, 10 patients with SpA were treated with Bio in our institute. Efficacy was evaluated using patients' pain VAS, DAS28-CRP, BASDAI, and inflammatory markers. **[Results]** Seven patients with PsA and 3 with AS were included in this study. ADA was used in 6 patients and IFX in 4. The average age at diagnosis was 38.2 years old (yo) and Bio was started at avg. 40.9 yo (21-64). The follow-up period was average 49 months (6-120). In PsA, average DAS28-CRP was decreased to 1.6 at 48 weeks (w) and 2.0 in the last follow-up from 3.4 at the induction time, and dermatitis was improved or diminished in all cases. In AS patients the average BASDAI at the induction time was as high as 5.1, but that improved to 1.3 (48w) and 1.1 at the last follow-up. **[Conclusion]** Recently, Bio became usable to AS and PsA in our country. Our study showed good therapeutic effects in the patients with SpA.

P3-129

Spondyloarthritis complicated with fibromyalgia, administered by adalimumab

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Conflict of interest: None

Backgroud: Compared to the rheumatoid arthritis, there is a higher frequency of insufficient cases. In the western countries, the number of the cases with SpA, complicated fibromyalgia (FM), has been reportedly increasing. This time, Adalimumab (ADA) administration cases complicated with FM, were investigated. **Objevtives**: We assessed 29 patients, administered the ADA in our department. **Methods:**We evaluated the visual analogue scale (VAS), widespread pain index (WPI), and calculated value, multiplied VAS to WPI (VW). Eight cases has been poor effective (PE). We compared these PE cases with effective cases (EC). **Results**: PE consists of 8 cases, 4 males and 4 females; 4 ankylosing spondylitis, one pustulotic arthro-osteitis, 3 undifferentiated SpA. Three patients have never been effective; others have considerably early secondary non-responsiveness to ADA. In comparison with EC and PE, VAS prior to the administration of EC is 7.02, and WPI 7.42, VW 575, while VAS of PE is 8.69 ($p = 3.6\%$), WPI is 14.62 ($p = 0.2\%$), and VW value 1309 ($p = 0.15\%$). These values of PE patients are significantly the higher than that of EC. In spite of the ADA administration, the effect is not sufficient for some of the patients. FM complications often should be also considered in treatment.

P3-130

Association of anti-cyclic citrullinated peptide antibody with clinical features in patients with psoriatic arthritis

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Conflict of interest: None

<Background> Although anti-cyclic citrullinated peptide antibodies (anti-CCP Ab) are reported to be found in 5-20% of patients with psoriatic arthritis (PsA), its clinical significance has not elucidated. <Objective> To clarify the association of anti-CCP Ab with clinical features in PsA. <Methods> The patients who fulfilled CASPAR criteria and visited our hospital from 2006, were enrolled. We compared 1) clinical findings, 2) autoantibodies, 3) treatments, and 4) response to treatments, between anti-CCP Ab -positive (CCP+) and -negative group (CCP-), retrospectively. <Results> 1) We examined 41 patients (30 males/11 females), 7 were CCP+ and 34 were CCP-. Age (55.0±15.1 years old) and frequency of lung involvements (71.4%) in CCP+ were significantly higher than those (40.0±16.0 and 0%) in CCP-($P<0.05$). 2) RF (749.4±860.7 U/ml) in CCP+ was significantly higher than that (3.6±4.4) in CCP-($P<0.01$). 3) Usage of PSL, MTX, and biologics were similar between groups. 4 were treated with TNF-inhibitors (TNFi) (IFX: 2 and ADA: 2) in CCP+, while 11 (IFX: 6, ADA: 4, and ETN: 1) in CCP-. 4) Although arthritis was significantly improved by TNFi within 6 months in 11 of CCP-, 4 of CCP+ had no responses. <Conclusion> Anti-CCP Ab might relate to lung involvements and resistance to TNFi in PsA.

P3-131

A case of enteropathic arthritis complicated with calcification of sigmoid colon

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Conflict of interest: None

A 39-year-old female was referred to our hospital with complaints of

constipation, left lower abdominal pain and mass, and melena. She had histories of finger stiffness and polyarthritis. Laboratory tests showed increased inflammatory response. Imaging tests revealed thickening and calcification of sigmoid colon. Because she presented alopecia, oral ulcer, photosensitivity, polyarthritis and anti-cardiolipin antibody positivity, she was initially suspected as having systemic lupus erythematosus (SLE). Afterward, enthesitis of Achilles tendon was emerged. Prednisolone (PSL) 30mg/day was started, however, her symptoms did not improve. PSL was tapered and stopped, and eventually, she received low anterior resection. The postoperative pathologic specimen revealed chronic granulomatous inflammation with fistulas formation. She was diagnosed as having Crohn's disease with arthritis and enthesitis. Adalimumab was started, resulting in the improvement of arthritis, enthesitis and digestive symptoms. Calcification of colon is commonly observed in neoplasms or chronic infections, and rarely in Crohn's disease. Despite being rare, we should consider Crohn's disease as a differential diagnosis when a patient has calcification of colon, since immunosuppressive therapy can be effective.

P3-132

Clinical features, including HLA typing, of 33 cases referred on suspicion of fibromyalgia (FM) but diagnosed with spondyloarthritis (SpA)

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Conflict of interest: None

Purpose: To investigate the clinical features of cases with a wide distribution of extreme pain resembling FM but finally diagnosed as SpA. Methods: We reviewed data of HLA typing, blood test findings, clinical features, joint ultrasound, MRI, etc., in 33 cases (25 females, 8 males; mean age: 58.2 years) who were referred with suspected FM and who were later diagnosed with SpA by ASAS classification criteria. Results: All cases were negative for rheumatoid factor, and 18 had hyperlipidemia. Seventeen cases were diagnosed with sacroiliitis on MRI and 18 cases with enthesitis on joint ultrasound. Of the 30 cases that underwent HLA-B antigen examination, none were B27 positive, 14 were B61 positive, 7 were B46 positive, 6 each were B7, B51, and B54 positive, 5 were B35 positive,4 were B62 positive, 3 each were B60, B48 positive, 2 each were B39 positive. The 12 cases classified as axial SpA were either B7 or B61 positive. However, all cases that were B35, B39, and B62 positive had psoriasis. In addition, of the 12 cases that required TNF inhibitor, 10 were either B7 or B61 positive. Conclusion: HLA typing in SpA has frequently indicated HLA-B27 in Europe and America; however, as our results show, there are regional differences in Japan. Further research is needed to elucidate this.

P3-133

DIP arthritis: independent entity?

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Conflict of interest: None

DIP joint arthritis (DIPitis)is one of characteristic of Psoriatic arthritis (PsA). But we sometime experienced the cases of DIPitis without PsA or psoriatic skin disease.【Case 1】A 61-year-old female had been to our clinic because of severe finger joint arthritis from 2010. Periodic several exacerbation occurred usually after episode of trauma, enteritis orother viral infection. Every-time remarkable inflammatory change was observed on Laboratory data. Clinical course showed progressive radiographic finding showing oligo-osteolytic change of DIPs or some PIPs.【Case 2】A 64-year-old female of CTD was referred to our clinic with DIP or PIP lesion like Heberden or Bouchard nodule. Routine check of labo data revealed positive ANA, dsDNA-Ab. Xp showed progression of distal joint arthritis.【Discussion】DIPitis (with some PIPitis) were often observed in the case of PsA. Sometimes patient has no psoriatic skin lesion. Such cases were called"PsA sine psoriasis". But if the patient has no characteristic of psoriasis like family history or nail lesion, or HLA-Cw6, it is difficult to call PsA. In such case, we couldn't help calling it,"only DIPitis without PsA".【Conclusion】We proposed that"DIPitis without PsA" is a independent entity among peripheral SpA.

P3-134

Is MTX effective to traumatic arthritis?

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Conflict of interest: None

【Case 1】A 56-year-old female fall a mug on her foot on September. From November she complain right foot arthralgia. Her right foot was swelling and CRP level was elevated. first prescribed antibiotics was in vain, steroid and colchicine, MTX was added to be effective. After MTX solo-therapy, MTX was discontinued. Her condition exacerbated again. She retreated with PSL and MTX which calm the inflammation well. MTX showed some effectiveness to her traumatic arthritis.【Case 2】A 69-year-old female was referred to our hospital. She crushed with car on March. She complain with right knee pain from May. She came to our clinic on July again. Her right knee was swollen and blood test showed positive inflammatory sign and high MMP-3 level. Treatment with MTX started. Her right knee arthritis healed. Discontinuation of MTX make no change【Discussion】There are few report about treatment of traumatic arthritis. In our case, MTX discontinuation induced exacerbation showed usefulness of MTX in Case 1. In Case 2, we could not conclude MTX effectiveness because of possible spontaneous recovery. But still MTX may contribute to calm the inflammation induced by trauma.【Conclusion】MTX was at least one therapeutic candidate for traumatic arthritis.

P3-135

A case of lumbar radiculopathy in ankylosing spondylitis

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Conflict of interest: None

Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease that mainly involves the spine and sacroiliac joints. Neurological complications of AS are uncommon. We report a case of lumbar radiculopathy in AS. A 60-year-old-man who presented with right drop foot was diagnosed 24 years previously with AS. His laboratory examination showed mild inflammatory values. He had not taken any medications since the onset. Four years ago, he experienced numbness and muscle weakness in his right leg. The symptoms gradually worsened, after which he presented to our department. Neurological examination showed that his right tibialis anterior, extensor hallucis longus and flexor hallucis longus were 1/5. His right deep tendon reflexes had disappeared. Laboratory results showed mild inflammatory values. Plain radiographs showed ankylosis of the entire spine and sacroiliac joints, and CT showed expansive erosion of the posterior T12 / L1 vertebral body. MRI revealed ventral cystic lesions scalloping the posterior T12 / L1 vertebral body, with hypointensity on T1WI and hyperintensity on T2WI, and shifting of the cauda equina to the anterior dura at the T12 / L1 level.

P3-136

Clinical study for 10 cases of SAPHO syndrome

Masao Tamura, Kiyoshi Matsui, Satoshi Kaku, Rei Tadokoro, Hidehiko Makino, Kota Azuma, Kazuyuki Tsuboi, Chie Ogita, Mei Tani, Tetsuya Furukawa, Yuichi Yokoyama, Takahiro Yoshikawa, Aki Nishioka, Mai Morimoto, Masahiro Sekiguchi, Naoto Azuma, Masayasu Kitano, Hajime Sano
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Conflict of interest: None

The SAPHO syndrome is not classified in spondarthritis, but spondarthritis may be detected, and, also, in late years treatment adaptation such as TNF - α inhibitor is found about the axon-related arthritis. Therefore we examined the results that measured clinical features, HLA of ten SAPHO syndrome, TNF alpha receptor, IL-17 of the serum which we ex-

perienced. We analyzed a clinical picture and laboratory findings, a therapeutic drug. The skin lesions showed chest rib chain hyperplasia symptom five cases, sacroiliitis one case, spondarthritis one case, peripheral arthritis in three cases about pustulosis palmaris et plantaris six cases, the osteoarticular lesion. Five patients had the CRP increase. As a result of having conducted an examination for HLA, HLAB27 was a precedent-negative, but detected HLA-B39, 61 several with the thing with the existing report. Merger one case of abortive. As for the treatment, five patients underwent tonsillectomy with one salazosulfapyridine with three methotrexate, prednisolone eight in NSAIDs. The TNF alpha receptor rose in five cases, and most were associated with increase of CRP. The significant increase was absent about IL-17. The possibility that the increase of the TNF alpha receptor helped the disease activity evaluation was thought about.

P3-137

Clinical evaluation of six cases of SAPHO syndrome with spinal involvement

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Conflict of interest: None

To ascess the clinical characteristics of SAPHO syndrome with spinal involvement, six patients (1 male and 5 females) were evaluated. Each patient was in their 30s, 50s and 70s, and the remaining three were in their 60s. Dermatological complications (3 pustulosis palmoplantaris, 2 acne and 1 without dermatological symptom) preceded in four cases and occurred together in one case. Spinal symptoms were as follows: 1 neck pain, 2 back pain, 2 low back pain and 1 numbness of the upper arm. They worsened after upper respiratory infection, severe acne and passive smoking. One patient had a past history of tonsilectomy and sternocalvicuar joint pain was recognized in two cases. Spinal involvement was found in one cervical, five thoracic and one lumbar spine. Only one vertebra in two cases and several vertebrae in four cases were involved. MR imaging showed fresh change in five cases and old change in one case and both in some cases. Fresh change had disappeared in one case. Pathologically osteitis was proved in one case. In the treatment, biotin in five of four and bisphosphanate in one of two cases were effective for the spinal symptom. In the case of spinal symptoms, SAPHO syndrome should be distinguished and biotin may be a alternatives for the spinal symptoms of the syndrome.

P3-138

A case of SAPHO syndrome complicated with large vessel vasculitis (LVV)

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Conflict of interest: None

【Case】A 46-year-old woman with pustulosis since 2002. The patient had a chief complaint of headache and neck pain in 2008. She was diagnosed as SAPHO syndrome because the compounds accumulated in cervical vertebrae by bone scintigraphy. It was impossible to get sufficient effect with NSAID, PSL, MTX, SASP, azathioprine, tacrolimus, and CPA. The patient had constant neck pain longer than 2 years. Thereafter, her SAPHO syndrome was accompanied with a complication of LVV by the results of CECT. The effect of IVCY and cyclosporine A with increased PSL was insufficient. Her neck pain got worse and CRP was elevated in 2015. We detected relapses based on the results of CECT and PET-CT diagnosis. The ensuing treatment with tocilizumab shows a trend toward improvement. 【Discussion】The complication of LVV with SAPHO syndrome is rare case. Recently the effects of anti-TNF therapy for refractory SAPHO syndrome were reported, whereas others presented it made the skin symptoms worse. This is a first evidence to show the therapeutic efficacy of tocilizumab against LVV complicated with SAPHO syndrome without side effects of skin manifestations. These results suggest that tocilizumab would be a useful treatment to remedy for LVV with SAPHO syndrome.

P3-139

A case of peripheral spondylarthritis acute onset as opportunity tonsil foci infection

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Conflict of interest: None

[Introduction] Spondylarthritis is a group that cause inflammation of spine and sacroiliac joint, peripheral joint. To be said SAPHO syndrome is subtype of spondylarthritis. It has been suggested that SAPHO syndrome is correlate with tonsil foci infection. [Case] 49-year-old female, chief complaints is arthralgia, medical history is Hashimoto's disease. She was at home with Sjogren's syndrome in our hospital, had anterior chest pain and polyarticular pain. Admission blood tests WBC:12700/μl, CRP:24.8mg/dl, ESR1H:122mm, ASO:1179IU/ml, ASK:10240. She has tenderness of both hand and finger joint, episode of repeat tonsillitis, pustular eruption. There were significant findings in imaging test. We doubted that she has peripheral spondylarthritis as opportunity tonsil foci infection. We administered NSAIDs, but it was a null effect. Next We used PSL and SASP, her symptoms ware better. [Conclusion] This case was that there ware high inflammation and tenderness of both hand and finger joint. Othe report don't say that, so I repot it added to the literature reports.

P3-140

Clinical features and predictive factors of bisphosphonate-related osteonecrosis of the jaws: an analysis of 12 cases in a single institution

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Conflict of interest: None

Objectives: To clarify the clinical features and predictive factors of bisphosphonate (BP)-related osteonecrosis of the jaws (BRONJ). **Methods:** We included 14 patients diagnosed with BRONJ between 2011 and 2016. Clinical information was obtained for each patient and the laboratory values of patients with BRONJ were compared with those of 250 patients who were treated with BP in October 2016 at our hospital. **Results:** The mean interval between the initiation of BP therapy and confirmation of the diagnosis was 41 months. Intravenous BP was used for metastatic bone cancer, while oral BP was administered to three patients with rheumatoid arthritis or multiple sclerosis, all of whom were treated with a maintenance dose of corticosteroids. The remaining three out of 5 patients treated with oral BP developed BRONJ after dental extraction. Serum hemoglobin and albumin values were significantly lower in BRONJ patients (10.4±1.7 g/dl and 3.7±0.4 g/dl, respectively) than in the control group (12.3±1.8 g/dl and 4.2±0.4 g/dl) (p<0.001, p<0.001, respectively). A pathological examination revealed actinomycetes in most cases. **Conclusion:** Patients with underlying debilitating diseases and with hypoalbuminemia or anemia need to be monitored carefully for the development of BRONJ.

P3-141

Incidence of beaking, a sign of atypical femoral fractures in patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] To investigate the incidence of beaking in the patients with rheumatoid arthritis (RA). [Methods] A total of 255 patients with RA [female, 77.3%; age, 53.9±15.3 years old; prednisolon (PSL) use, 75.3% and history of bisphosphonates (BPs) therapy, 74.1%] were enrolled. Focal lateral cortical thickening detected in femur X-ray was defined as beaking. Fisher's exact test and Mann-Whitney U-test were performed. [Results] Beaking was detected in three patients (1.3%). Patients with beaking were taking higher dose of PSL (7.0±2.7 vs. 3.9±3.6mg/day, p=0.013), and their rate of ALD use (p=0.048) and coexistence of autoimmune diseases (p=0.042) were higher. Duration of BPs therapy tended to longer in the patients with beaking (78.0±28.8 vs. 37.0±39.2 months, p=0.070). Each of their BPs therapy was ALD for 58 months, ALD for 65months, and denosumab for 19months followed to ALD for 65months. [Conclusion] It is reported that the incidence of beaking in the patients with autoimmune diseases treated with BPs and glucocorticoids is 8-10%. In the patients with RA, coexistence of the other autoimmune diseases, higher dose of PSL and ALD were associated with development of beaking.

P3-142

Hip fracture in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] Hip fracture cases with RA, since 2012 to 2015 in our hospital, were evaluated. [Methods] The total number of hip fracture treated in our hospital was 789, and mean age was 84±8 years old. The number and the details of RA patients with hip fracture were checked, and which were compared with the data of 10 years ago. [Results] The number of RA patients suffered from hip fracture was 11, which was 1.4% in all hip fracture. The mean age was 76±7 years old. The disease duration was 23±20 years. Three of RA patients were mutilated type, and they were 68 years old. Five patients were 70's, one patients had amyloidosis and hemodialysis, one patients had IP, one patients had Parkinsonism. There were 6 patients of femoral neck fracture and 5 patients of intertrochanteric fracture. There were 7 patients who were taking prednisolone and the mean dosage was 3.9mg. Anti-osteoporosis treatments were made in 7 patients, teriparatide was in 2, and bisphosphonate was in 4 patients. [Conclusions] The age when hip fracture occurred in RA patients was 4 years older than it evaluated in 10 years ago. The rate of femoral neck fracture, and the rate of patients who were taking prednisolone, were decreasing. The rate of patients who were taking anti-osteoporotic treatment was increasing.

P3-143

Insufficiency Fracture associated with rheumatoid arthritis

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Conflict of interest: None

[Object] Insufficiency Fracture (ISF) is a fracture produced by normal or physiological stress applied to bone with vulnerability. ISF occur rather frequently among patients with rheumatoid arthritis (RA) and often undiagnosed. The aim of the present study was to describe the underline characteristics in RA patients with ISF. [Methods] We retrospectively reviewed the medical records of 15 patients diagnosed with ISF during the course of RA. [Results] Fracture has occurred in various sites. 10 patients were corticosteroids current users, and bisphosphonates were prescribed to 7 patients of them. In regards to physical function, Steinbrocker classification of patients is as follows: class 1:1, class 2:7, class 3:3, class 4:4, respectively. Six of 12 patients who suffered fractures of spine, hip, and lower extremities had recovered the physical function to same level before ISF. [Conclusions] ISF associated with RA was characterized by deterioration of physical function. Half of patients who suffered fractures of lower part of the body had proceeded to further functional decline. It is difficult to prevent ISF only with medication, therefore, treatment strategy that focus on maintaining physical function and withdrawing corticosteroids should be adopted.

P3-144

We considered a strategy for treatment of osteoporosis with RA patients, with analysis of a risk factor for osteoporotic fracture

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Conflict of interest: None

【Object】Many RA patients with treatment of osteoporosis have severe osteoporosis. Osteoporotic fractures cause impairment of ADL. We consider that the early personalized treatment protects osteoporotic fractures. We examined the estimate factor for the opportunity of treatment. 【Methods】We chose 137 women with RA (mean age of 69 years, mean disease duration of 9 years, Remission 96, LDA 25, MDA 16 of DAS-28ESR, with MTX is 99, mean dose of 6mg/week, with PSL is 48, mean dose of 3mg/day, with cDMARDs is 56, with Biologics is 50). We statistical analyzed the estimate factor of BMD (lumbar spine and proximal femur) after treatment with age, FRAX, age of menopause, duration of menopause, BMI, data of TRACP5b and P1NP, history of medicine for osteoporosis, duration of disease, HAQ, VAS, dVAS. 【Results】Result of analysis with BMD was FRAX and BMI in patients of well controlled disease activity of RA and had medicine for osteoporosis. The fixed control point of YAM70% was FRAX≧15% and BMI<22. And HAQ was extracted for BMD of proximal femur. 【Conclusions】Some reports showed that FRAX≧15% increase the risk of osteoporotic fracture. We recommend to apply FRAX and BMI and to choose the strong treatment of osteoporosis (ex. PTH) avoiding osteoporotic fracture.

P3-145

Femoral neck insufficiency fracture after subtrochanteric femur fracture treated with intramedullary nail

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Conflict of interest: None

Case: An 80-year-old male who had been taking steroids for RA had a right-sided subtrochanteric femoral fracture repaired with an intramedullary nail. He was able to walk after the operation. However, at 7 postoperative months he complained of pain in his right hip. He had not suffered any traumas after the operation. Radiographs showed a right-sided femoral neck fracture and the cutout of a lag screw. We performed bipolar hemiarthroplasty. A histopathological examination indicated that the bone had regenerated after the initial fracture. Therefore, we diagnosed the patient with a femoral neck insufficiency fracture. **Conclusion:**It was considered that the femoral head and neck were severely osteoporotic and that the femoral head had fractured around the lag screw after a load had been placed upon it. Subsequently, cutout of a lag screw gradually progressed and loads depended on femoral neck as the result, the femoral neck fracture might occur. Recently, by use of biologics and DMARS, the rheumatic cures evolve, and the treatment outcome and ADL are improved, however corticosteroid is still used. For the use of corticosteroid, merger of DM and aging of the RA patients and so on, it is important of the treatment of osteoporosis and fracture with it of RA patients.

P3-146

Efficacy of denosumab in patients with rheumatic diseases

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Conflict of interest: None

[Object] Denosumab, an anti-RANKL monoclonal antibody, was reported to improve bone mineral density (BMD) and to reduce fracture risk, offering a favorable efficacy in postmenopausal osteoporosis. This observational study was performed to clarify the efficacy of denosumab in patients with rheumatic diseases. [Methods] Serum levels of bone turnover markers and lumber BMD in 100 patients with rheumatic diseases (52 RA, 14 SLE, 11 PMR, 5 PM/DM, 4 SjS, 3 MCTD, 3 SSc, 2 vasculitis syndrome and 6 other diseases) [age: 67.5±12.2 (mean±SD), 7 male, 85 postmenopausal female, mean daily dose of prednisolone: 4.7±6.1 mg] were examined at baseline, 6 month and 12 months after denosumab therapy. [Results] Serum levels of NTX and TRACP-5b were statistically significantly decreased after 12 months. Serum levels of PINP and BAP were also significantly decreased. BMD was significantly increased from baseline. On the other hand, in 7 patients, BMD was decreased. Bone turnover markers were not decreased in the BMD decreased patients. [Conclusions] Denosumab decreased bone turnover markers, including both osteoblastogenesis and osteoclastogenesis, and increased BMD in patients with rheumatic diseases. Especially, denosumab was effective in the patients with low bone turnover markers.

P3-147

A comparative study of denosumab and teriparatide in patients with rheumatoid arthritis with osteoporosis

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Conflict of interest: None

[Objective] To compare the effectiveness of using deosumab and teriparatide for rheumatoid arthritis (RA) patients with osteoporosis. [Method] 107 RA patients over 60 years old with osteoporosis were divided into 68 patients in the Denosumab group (DMAB) and 39 in the teriparatide group (TPTD). Bone metabolism markers and bone mineral density (BMD) by DEXA were measured at 0, 6, 12 and 18 months. We also compared the number of new fractures. [Results] Bone resorption markers and bone formation markers decreased in the DMAB and increased in the TPTD. BMD of the femoral neck significantly increased from baseline in the DMAB. TPTD temporarily declined and turned up after 18 months, but TPTD was no significant difference compared with baseline. The BMD of the lumbar increased significantly in both groups than baseline, but the TPTD increased significantly more than DMAB. BMD at the distal radius increased significantly in both groups than baseline, and there was no significant difference. The number of new fractures was no significant difference. [Conclusion] The BMD of the femoral neck turned temporarily lower in the TPTD group and then increased after 18 months. In the BMD of lumbar, the TPTD significantly increased more than DMAB. The number of new fractures was no significant difference.

P3-148

Retrospective study on the usefulness of denosumab for the management of glucocorticoid-induced osteoporosis in patients with collagen diseases

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Conflict of interest: None

Purpose: To investigate the usefulness of denosumab (DSM) for glucocorticoid-induced osteoporosis (GIOP) in patients with collagen diseases (CD). **Methods**: We retrospectively reviewed the medical records of 77 CD patients (RA 36, SLE 11, PM/DM 9, SSc 4, vasculitis 9, PMR 4, Bechet 2, MCTD 1, sarcoidosis 1) who had received steroid therapy and were prescribed DSM from Dec. 2013 to Oct. 2015. **Results**: Patients' profiles: male 14, female 64, median age was 69 years old (39-86), 58 patients had a history of fragile fracture (Fx), the median duration of steroid therapy was 90 months (0–500), the median prednisolone dose was 5 mg/day (0–60), and the mean lumber bone mineral density (BMD) value was 0.78±0.16 g/cm^2, its YAM value was 75.7±14.9%. Previous therapy for GIOP; teriparatide 25, bisphosphonate 25, SERM 9, Vit D alone 5, new introduction 17. Mean lumber BMD and its YAM value (N=55) were 0.79±0.17 → 0.82±0.17 g/cm^2(P=0.3) and 76±15.6 → 79±16.6%(P=0.2) respectively after one year DSM therapy. New vertebral Fx developed in 9, but non-vertebral Fx were not seen. There were several minor adverse events, but none of them led to cessation of DSM. **Conclusions**: In patients with CD receiving long-standing steroid therapy, DSM may be useful for the management of GIOP.

P3-149

The therapeutic efficacy of denosumab for bone mineral density in patients with rheumatoid arthritis is effective as same as in patients with primary osteoporosis

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Conflict of interest: Yes

[Object] The aim of this study was to compare the effect of denosumab between patients with rheumatoid arthritis (RA) and patients with primary osteoporosis. [Methods] Sixty-three patients with RA (RA group) and 47 patients with primary osteoporosis (OP group) treated by denosumab were consecutively included. Bone mineral density (BMD) in lumber spine and proximal femoral were measured and the change of BMD during 1 year were analyzed. [Results] The data of 52 patients with RA and 36 patients with OP was analyzed. The BMD was increased 5.4% and 6.1%(p=0.612) at the lumbar spine, 2.9% and 3.8%(p=0.459) at the proximal femur and 0.7% and 2.3 (P=0.166) at the femoral neck, in RA group and OP group, respectively. The BMD of 17 patients with RA who treated using biological DMARDs was increased 8.2% at the lumbar spine, 2.2% at the proximal femur and 1.5% at the femoral neck. [Conclusions] The results of this analysis suggest that the effect of denosumab for osteoporosis in patients with RA is effective as same as in patients with primary osteoporosis. The result that BMD at the lumbar spine increased higher especially in patients with RA treated biological DMARDs, combination of biological DMARDs with denosumab could be an effective treatment for severe osteoporosis in RA patients.

P3-150

The position of denosumab for treatment of osteoporosis in rheumatoid arthritis patient

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Conflict of interest: None

[Objective] Characteristics of denosumab (d-mab) for treatment of osteoporosis (OP) in rheumatoid arthritis (RA) patient were investigated. [Methods] 180 RA patients who were underwent OP treatment were enrolled. Patients were classified into dMAB group, and other group (OTH). Change of %YAM (YAM) in minimum value of lumbar spine (LS), femoral neck (FN), and greater trochanter (GT), and increase of these indices were investigated for their correlations with parameters statistically using Multiple Linear Regression Analysis (MLR) and Binary Logistic Regres-

sion Analysis (BLR). [Results] There demonstrated no significant difference between the two groups for YAM change. YAM demonstrated common significant factor in all loci that positively correlated with YAM increase in MLR. For dMAB, no other factors demonstrated significant correlation. For OTH, improvement of mHAQ in LS, drug use out of bisphosphonate in FN demonstrated positive correlation. In BRL, YAM demonstrated significant regression in all loci, and shortness of thrown term, and drug naïve were picked up for OTH, and low TRAC-5b in FN and ageing, biologic agent usage, and low mHAQ in GT for dMAB. [Conclusions] d-mab have been estimated longevity in effectiveness for YAM increase regardless of term length of drug use.

P3-151

Observation of patients receiving denosumab in our center

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Conflict of interest: None

[Objective] Denosumab is a human monoclonal antibody to RANKL for the treatment of osteoporosis. We studied therapeutic effect of denosumab in patients with rheumatoid arthritis (RA) or other collagen diseases (non-RA). [Patients] Patients who received denosumab more than twice were studied. [Results] 52 patients with RA and 19 with non-RA (age average 67.4, F/M=67/4) were studied. In the RA, both young adult mean value (YAM) of lumbar spine and transcervical bone increased during 12 months (80 to 88, 66.1 to 69.7). As for non-RA, both YAM of lumbar spine and transcervical bone increased during 12 months (72.4 to 82.6, 69.1 to 71). Half of patients with RA treated by biological antirheumatic drugs (bio). In the RA treated by bio, YAM of lumbar spine and transcervical bone increased during 12 months (80.2 to 85.8, 65.3 to 70.8). As for RA treated by non-bio, YAM of lumbar spine and transcervical bone increased during 12 months (79.8 to 88.9, 66.8 to 69.2). There were no difference between bio and non-bio. [Conclusion] Denosumab increased YAM of patients with both RA and non-RA. Denosumab showed equal therapeutic effect for both RA treated with bio and non-bio.

P3-152

Study of denosumab in 37 patients with rheumatoid arthritis for 2 years

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Conflict of interest: None

[Object] We investigated the effect of denosumab with RA in Japanese Red Cross Kyoto Daini Hospital. [Methods] 37 RA patients less than 80% of YAM were administered denosumab 60 mg every 6 months. The mean age was 70.1, male 9 female 28, the mean disease duration was 11 years. MTX was administered for 26 patients. Steroids were administered for 13 patients. Biologics were administered for 20 patients. There were 17 patients of pretreatment with bisphosphonates. DXA scans of the lumbar spine (LS) and total hip (TH) were performed every 6 months, TRCP-5b and BAP were measured. We divided two groups according to gender, age, disease duration, steroids, biologics, pretreatment and analyzed using the U test. [Results] The mean BMD of LS increased to 7.6% until 24 months. That of TH increased to 3.0% until 18 months but decreased to 1.6% at 24 months. No significant differences were found between each two groups. The mean TRCP-5b decreased to -41.2% after 6 months as peak, then increased to -25.2% after 24 months. The mean BAP decreased to -31.7% after 18 months as peak and increased to -27.1% after 24 months. [Conclusions] Previous reports of denosumab with RA have fewer follow up longer than 1 year. We think that the effect of denosumab tended to weaken with the passage of time.

P3-153

Short term results of daily teriparatide in patients with gulcocorticoid-induced osteoporosis except for rheumatoid arthritis patients

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Conflict of interest: Yes

[Objectives] Gulcocorticoid-induced osteoporosis (GIOP) is iatrogenic osteoporosis with high risk of fracture. Although daily teriparatide (dTPTD) was reported to be effective in GIOP in clinical trials, reports in daily clinical practice are lacking. The aim of this study is to investigate outcomes of dTPTD on GIOP except for RA. [Methods] 11 GIOP cases (all female) treated with dTPTD were used. Patients' characteristics, BMD of lumbar spine (LSBMD) and total hip (THBMD) and bone turnover markers (BTMs) [BAP, P1NP, NTX, TRACP-5b] were evaluated. [Results] Mean age 65.4 years, prednisolone (PSL) 7.0mg/d (2.0-20.0), past history of fracture 9 cases (81.8%). Reasons for usage of PSL were PMR in 4 cases, SLE in 2 cases, MCTD in one case and others in 4 cases. Following results were from 8 cases who continued dTPTD over 6 months. %increase of LSBMD at 6 months was 2.2%(-2.3-9.7%). %increase of THBMD at 6 months was -1.7%(-6.4-71.8%). There were no significant difference in both BMD increase. All of 4 BTMs were significantly increase from baseline to 6 months. [Conclusions] Although BMD was not significantly increased in short term, BTMs were significantly increase. Long term follow-up is necessary in the future.

P3-154

Comparison between weekly teriparatide and bisphosphonate in patients with rheumatoid arthritis and secondary osteoporosis

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Conflict of interest: None

[Objectives] The aim of this study was to compare between weekly teriparatide and bisphosphonate in patients with rheumatoid arthritis (RA) and secondary osteoporosis. [Methods] We studied 38 patients (male; 6, female; 32) with RA and secondary osteoporosis. Median age was 69 years old and median disease duration was 13 years. Twenty-six patients received weekly teriparatide (P group) and 12 patients received bisphosphonate (B group). BMD (lumber, femoral neck), intact P1NP, TRACP-5b, pentosidine, homocysteine and RA disease activity were evaluated baseline and 12 months after starting weekly teriparatide or bisphosphonate. Drug continuation rate was also evaluated. [Results] Serum pentosidine was higher in P group and BMD was higher in B group at baseline. Disease activity and serum intact P1NP was higher in P group at 12 months. BMD was higher in B group. There were no significant differences in serum pentosidine. Drug continuation rate was 81% in P group and 92% in B group at 12 months. [Conclusion] Weekly teriparatide might have advantage in bone quality rather than bisphosphonate in patients with RA.

P3-155

Efficacy of teriparatide for secondary osteoporosis in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] The purpose of this study was to examine the effectiveness of daily teriparatide in 12 months for secondary osteoporosis in rheumatoid arthritis (RA) patients. [Methods] The study was conducted for 15 RA patients (male3, female12) with secondary osteoporosis. The mean age was 66 years old and average disease duration was 17 years. Bone

density (lumber supine and femoral neck), UCOC, intactP1NP, TRACP-5b, serum pentosidine, serum homocysteine, CRP, ESR, MMP-3, DAS28-ESR, DAS28-CRP, SADI, CDAI, HAQ were evaluated at baseline, 6 months and 12 months. We also evaluated the drug continuation rate at 12 months. [Results] IntactP1NP was significantly higher at 6 months and 12 months than baseline. Bone density of lumbar spine was significantly higher at 12 months than baseline butthere was not significant change in bone density of femoral neck at any point. The drug continuation rate was 87% at 12 months. [Conclusion] Teriparatide was effective for secondary osteoporosis in RA patients.

P3-156

Conservative treatment with teriparatide for pseudoarthrosis after the distal humerus fracture

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Conflict of interest: None

We report our experience with a case of pseudoarthrosis after the distal humerus fracture treated with teriparatide. (Case) 87-year-old woman. She was injured by a fall. She consulted a nearby doctor and received conservative treatment by plaster cast fixation by the diagnosis of the distal humerus fracture. However, she was introduced by our hospital because bone union was not accepted even if three months passed after start of therapy. In XP or CT, the callus formation was not confirmed and we had a diagnosis of pseudoarthrosis. The bone density was 71% and 66% of the young adult mean (YAM) at the lumbar vertebral and proximal femoral levels. We started weekly injections of teriparatide. We confirmed callus formation on CT performed at 6 months after treatment. And we confirmed bone union in 12 months. The teriparatide dosage was finished in 12 months. The range of motion of elbow joint was good, and everyday life does not have the trouble. (Discussion) Teriparatide has potent anabolic effects on bone because of its ability to stimulate bone formation. A few reports suggest that teriparatide is effective for fracture or pseudoarthrosis healing. Based on our experience, we conclude that teriparatide treatment is effective for pseudoarthrosis after the distal humerus fracture.

P3-157

Use of the Teriparatide injection preparation in the osteoporotic cases of the RA patient

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Conflict of interest: None

[Purpose] As for the teriparatide injection preparation with a high osteoplasty promotion effect, it is the effective treatment means for the severe osteoporosis example. I examined it mainly on a use example osteoporosis in rheumatoid arthritis (RA) patients this time. [Methods] 23 RA patients diagnosed for severe osteoporosis (male 2, woman 21, average age 70.3 years old) were treated by the teriparatide preparation. I investigated the bone mineral density (BMD) at start, a patient background and the treatment continuation and, about the treatment execution example, examined curative effect by BMD (lumbar vertebrae %YAM, femoral neck %YAM) or a bone metabolic marker (TRACP-5b, BAP) which measured it every six months from dosage start time. [Results] The change (at the time of a start, the end) of the mean BMD was 69.7% to 79.3% of lumbar vertebrae, 59.1% to 61.2% of femoral neck with dosage continuation 11 cases (64.7%) for 24 months in 17 day after day preparation. The change was 63.7% to 67.7% of lumbar vertebrae, 60.7% to 62.3% of femoral neck with dosage continuation three cases (50%) for 72 weeks with six one a week preparation. [Conclusion] a significant rise of BMD was recognized in the treatment successful execution example for severe osteoporosis of the RA patients.

P3-158

Risk factors for reduced bone mineral density in patients with rheumatoid arthritis

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Conflict of interest: None

【Objectives】To evaluate risk factors for reduced bone mineral density in patients with rheumatoid arthritis.【Methods】We examined 131 RA patients who were measured bone mineral density. We examined a cross-sectional study on the relationship between each factor of age, gender, BMI, disease duration, Steinbrocker classification, RA disease activity in a group of YAM 70% or less (A) and YAM more than 70%(B).【Results】There were 67 cases in group A and 64 cases in group B. The age was 74.5 ± 72.2 in group A, 69.8 ± 54.5 in group B (P = 0.001), BMI was 20.0 ± 9.6 in group A, 22.6 ± 8.0 in group B (P <0.001), Stage was 2.67 ± 0.86 in group A, 2.33 ± 1.02 in group B (P = 0.04), Class was 2.30 ± 0.45 in group A, 1.88 ± 0.37 in group B (P <0.001), patient VAS was i 26.4 ± 455 n group A, 18.7 ± 353 in group B (P = 0.03), there were significant differences. There were no significant differences in gender, duration of disease, DAS 28-CRP, SDAI, tender joints, swollen joints, CRP, MMP-3, steroid dosage, use of biological products, MTX dosage.【Conclusion】In RA patients, elderly, low BMI, high stage, high class, high patient VAS are considered risk factor of reduced bone mineral density.

P3-159

Denosumab treatment in patients with rheumatoid arthritis

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Conflict of interest: None

Objectives: To evaluate the efficacy and safety of denosumab treatment to osteoporosis in patients with rheumatoid arthritis (RA). Methods: 34 RA patients (male: female 6:28, average 73.7years old)who received denosumab over 1 year. Assessments included bone mineral density (BMD) of the femoral neck and lumbar spine, levels of serum tartrate-resistant acid phosphatase 5b (TRACP-5b) and bone-specific alkaline phosphatase (BAP). Results: Mean changes in femoral neck and lumbar BMD at 1 year were +1.5%($p<0.01$) and +3.34%($p<0.01$), respectively. Levels of serum TRACP-5b and BAP were significantly lower at 1 year than start point. One new vertebral fracture, one hip fracture, one pelvic fracture, one radius fracture and two leg fractures occurred. Conclusions: In patients with RA, denosumab treatment provided favorable benefits.

P3-160

Examination using Trabecular Bone Score (TBS) in patients with rheumatoid arthritis (RA)

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Conflict of interest: None

[Background] 30% of chancellors bone intensity is prescribed by trabecular constitution, so the bone microstructural deterioration is a fracture risk factor of decrease of BMD. We evaluate TBS from image findings by DXA. RA is a risk of osteoporosis, but there are few reports that examined TBS of RA patients. [Objectives] We measure TBS and BMD of RA patients, and examine factors affecting them. [Subjects & Methods] We intended for 22 RA patients with postmenopausal without a fracture history (average age 65 y.o., periods 7.4 years, steroid usage patients were 12). We measured TBS and lumbar BMD using TBS iNsight. [Results] Average TBS (1.234) and BMD (0.800 g/cm2) showed a positive correlation (p=0.0210). Age (p=0.0593) and periods (p=0.0778) showed a negative correlation for TBS. BMI (p=0.0713) showed a positive correlation, and periods (p=0.0826) showed a negative for BMD. By the multivariable analysis, age (p=0.0101) and periods (p=0.0356) showed negative correlation for TBS, and periods (p=0.0372) showed negative for BMD. Inflammatory marker and autoantibody were unrelated for TBS and BMD. Steroid usage (p=0.0559) showed a negative correlation for BMD. [Conclusion] In RA patients, age and disease periods for TBS, and

steroid usage and disease periods for BMD suggests risk factor.

P3-161

A status report of medical treatment for rheumatic patients' osteoporosis

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Conflict of interest: None

Purpose: In rheumatic arthritis, proliferative synovium make bones fragile and glucocorticoid is used for treatment, so the medical treatment for osteoporosis is very important. The treatment rate for fracture patients' osteoporosis was reported 13~25%, however, treatment rate for rheumatic patient was not reported previously. In this study we report the treatment rate for rheumatic patients' osteoporosis. Material and Method: We checked 50rheumatic patients, average 66.6±10.8 years old. There were 12males 66.4±9.5years old, and 38females 66.7±11.3years old. Selected antiosteoporotic drugs were bisphosphonate, parathyroid hormone and denosumab. Treatment rate were investigated and compared in aspects of their age, sex and dose of glucocorticoid. Result: The total treatment rate for rheumatic patients was 44%. There were no significant differences in aspects of age and sex. Treatment rate increased significantly in response to dose of glucocorticoid. Discussion: Rheumatic patients' treatment rate was higher in compared to fracture patients'. In osteoporotic treatment, only glucocorticoid was concerned, patients' age and sex should be concerned more seriously.

P3-162

The bone mineral density of patients with rheumatoid arthritis -Comparison with 20 years ago-

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Conflict of interest: None

[Objectives] Since the introduction to biologics as the treatment for rheumatoid arthritis (RA) in the 2000s, we have been using biologics to improve the disease activity of RA patients. The purpose of this study was to investigate the change in bone mineral density (BMD) between RA patients treated recently and 20 years ago. [Methods] We examined RA patients treated and measured BMD between 1991 and 1997 (group A) and between 2015 and 2016 (group B) at Tottori university hospital. Lumbar BMD between the two groups were compared. [Results] There were 28 cases (3 men, 25 females) in group A, and 53 cases (all females) in group B. Their mean age was 65.3 years in group A and 71.4 years in group B. The lumbar BMD was 0.774±0.189 g/cm^2 in group A, 0.842±0.139 g/cm^2 in group B, and the difference 8.7% was observed between the two groups, and the lumbar BMD was significantly higher in group B (p=0.027). [Discussion] In this study, the lumbar BMD increased in recent RA patients compared with those 20 years ago, though including the age 80's in recently group. We consider the major of the reason is the improvement of disease activities of RA patients along with the development of biologics. [Conclusions] The lumbar BMD increased in recent RA patients compared with 20 years RA patients.

P3-163

The treatment for osteoprosis with rheumatoid arthritis

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Conflict of interest: None

It is necessary to be careful to treat for osteoporosis with rheumatoid arthritis because of occurring pathological fracture based on synovitis. We reported treatment for osteoporosis with RA. We investigated 18 RA patients, all women. RA treatment was constituted MTX 15, biological products 4 (etanercept 2 Abatacept 2) prednisolone 4. Osteoporosis treatment was constituted Bisphosphonate (BP) 15, Denosumab (DMB) 5 Bone Mineral Density (BMI) and Young Adult Mean (YAM) in lumbar spine (L-spine) were changed each -0.001,-0.11% at BP. BMI and YAM in femoral neck were changed each -0.029,-1.9% at BP. BMI and YAM in L-spine were changed each +0.04,+2.5% at DMB. BMI and YAM in femoral neck were changed each +0.01,+1.8% at DMB. DMB was effective in the treatment of osteoporosis than BP. It is necessary to change DMB from BP in case of invalidity for osteoporosis treatment by BP.

P3-164

Less-invasive vertebroplasty reduces hospitalization of patients with acute symptomatic osteoporotic vertebral fractures

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Conflict of interest: None

[Material and method] From 1 April 2013 to 31 March 2016, 112 patients (33 males and 79 females) of acute symptomatic osteoporotic spinal fractures were admitted to our hospital. We investigated the effect of Less-invasive vertebroplasty to hospitalization term of these patients. 3 patients of changing hospital, 6 patients with large operation and 12 patients with heavy complications of general health were excluded. The rests (91 patients) were divided into 2groups, such as CONSERVATIVE therapy group (58patients) which was treated conservatively and VERTEBROPLASTY group (33patients) which was treated by vertebroplasty. [Our vertebroplasty] Under general anesthesia, we reduce the fractured vertebra with reduction device transpediculaly and pack hydroxyapatite granules to the fractured vertebral body through a minimum skin incision. This procudure is a less-invasive vertebroplasty. [Result] Average hospitalization period of CONSERVATIVE therapy group was 43.3 days. And that of VERTEBROPLASTY group was 38.6 days. [Conclusion] Less-invasive vertebroplasty is effective to reduce hospitalization.

P3-165

Survey of patients' understanding of possible side effects for osteoporosis treatment

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Conflict of interest: None

[Objective] It is reported that osteonecrosis of the jaw and atypical femoral fractures are related to the long term use of anti-resorptive agents. Although medical workers informed the patients the possible side effects before treatment, it is unclear if the patients fully understood the risks. [Patients and methods] 115 patients (4 male and 111 female, average 65.8 years old) receiving osteoporosis treatment were surveyed. The questionnaire asked whether they felt osteoporotic treatment was important and whether they recognized the name of the drug and its possible side effects. [Results] 79% of patients felt that osteoporotic treatment was important. 59.4% recognized the name of the bisphosphonates which they took. 32.7% recognized the name of the denosmub. Only 23% knew to stop their anti-resorptive agents at the time of dental treatment because of the risk of the jaw osteonecrosis. 0% knew the risk of the atypical femoral fracture. [Conclusion] Patients didn't fully understand the side effects of their anti-resorptive agents which they took. Patient education by nurses and pharmacists including oral care, medical and dental coordination is essential to resolve these problems to continue the safer osteoporotic treatment.

P3-166

Association between the treatment of osteoporosis and the renal function or parathyroid gland function

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Conflict of interest: None

We investigated the parathyroid gland function of the patient who received osteoporotic treatment and examined it. We intended for the osteoporosis patient of 169cases (15 men, 154 women, average age 75.8 years old). We excluded the previously treated case as CKD. We measured the Ca of these cases, P, BAP, TRACP5b, intact PTH, eGFR, lumbar vertebrae bone mineral density, proximal femoral bone mineral density and weighed it. We used SPSS software ver.21 (IBM JAPAN Corporation) for statistics processing. We recognized intact PTH exceeded the standard value in 16 cases (9.5%). With age, eGFR decreased, and intact PTH tended to increase. As Ca decreased, intact PTH tended to rise. It is said that the chronic kidney disease (CKD) and secondary hyperparathyroidism has an influence on the bone metabolism. On the other hand, aging in itself becomes the factor of the renal dysfunction in the elderly people receiving osteoporotic treatment. In the case of the osteoporosis, there is a case producing a renal dysfunction and hyperparathyroidism without the past illness of CKD, and we need the attention for treatment.

P3-167

Actual condition of medication for glucocorticoid-induced osteoporosis

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Conflict of interest: None

Object Osteoporosis is known to be one of a side effect of glucocorticoid (GC). Fragility fracture is also important factor which determines the QOL and life prognosis. GC-induced osteoporosis (GIO) is the most important issue of using GC for long time. To grasp actual condition of medication for GIO, we investigated cases with GC in our department. Method We designed retrospective observational study that patient with novel GC therapy at Iizuka Hospital from 1 January 2011 to 31 December 2015 and their drugs forward to GIO. Result We identified 261 patients with GC above 10mg/day and continued for 3 months. Female patients were 173. The number of patients with Rheumatoid Arthritis was 148. 105 cases followed by bisphosphonates (BP) in 246 cases, any drug were prescribed for GIO. Stratify to 3 groups with age, <50, 50 to 65 and >65, each involved 31, 44 and 186 patients. In these groups, prescription with BP were 12, 22 and 71 patients used BP, respectively. Conclusion This observational study suggested that almost all patients with GC were combined with anti-GIO therapy and the rate of using BP was effected by fertility on younger group, in contrast, by renal function on elder group.

P3-168

A treatment strategy for the patients with osteoporotic insufficiency fractures

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Conflict of interest: None

(Objective) In current study, we aimed to research the demographics of the patients who suffered osteoporotic insufficiency fracture (OIF) and to discuss the way to improve the adherences for treatment of osteoporosis (OP). **(Patients and methods)** In our hospital from September 2015 to September 2016, 108 patients had treated OIF by hospitalization. These 108 patients were included in current study. In these patients, we evaluated the risks for OIF before the index injuries by FRAX, and whether the appropriate treatment for OP to them had been done. **(Results)** Whereas of 108 patients, 48 patients had the histories of the OIF, only 19 patients had been treated for OP. Of 108 patients, 26 had been judged to have the risks of OIF under 15% by FRAX. On the other hand, it was revealed that 88 patients had family doctors, and 39 patients had been examined their bone mineral density (BMD). **(Conclusion)** In current study, all patients who had suffered OIF should be treated for OP. However of them only few patients had been treated appropriately. On the other hand, as many patients had family doctors and almost half of them had been examined BMD, it was considered that closer cooperation of us and general practitioners would make the intervention rate of treatment better.

P3-169

The bone mineral density of patients with systemic lupus erythematosus depends on body mass index regardless of the use of bisphosphonates

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Conflict of interest: None

Objective: Identify associations between clinical parameters and the bone mineral density (BMD) of systemic lupus erythematosus (SLE) patients in Japanese population. We also evaluated associations between clinical parameters and lateral lumbar BMD. **Method:** A total of 169 SLE patients were retrospectively assessed to identify associations between age, disease duration, body mass index (BMI) and disease activity on BMD. We evaluated the impact of age, disease duration, BMI, serologic SLE markers and high dose glucocorticoid use on anterior-posterior (AP) and lateral lumbar spine, total hip and femoral neck BMD using univariate and multivariate linear regression analyses of both bisphosphonate and non-bisphosphonate treatment groups. **Results:** Multivariate linear regression analyses showed that BMI was significantly related to femoral neck and total hip BMD, regardless of bisphosphonate treatment**. Conclusion:** Hip BMD in patients with SLE depends on BMI, regardless of bisphosphonate use. SLE serologic markers and glucocorticoid use were not negatively associated with general bone loss. SLE patients with low BMI have a high risk of general bone loss, and should be assessed and treated to prevent osteopenia and osteoporosis.

P3-170

Serum 25-hydroxyvitamin D status in patient with psoriatic arthritis

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Conflict of interest: None

The mean serum 25-hydroxylated D status of psoriatic arthritis (PsA) patients was 17.2 ± 6.5 ng / ml. Vitamin D deficiency was 25 cases (69.4%), vitamin D insufficiency was 10 cases (27.8%), and 97.2% of PsA patients were not satisfied with Vitamin D combined. Most patients with psoriatic arthritis were in vitamin D unfilled state.

P3-171

Serum 25-hydroxyvitamin D status in patient with Pustulotic Arthro-Osteisis

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Conflict of interest: None

The mean serum 25-hydroxylated D status of Pustulotic Arthro-Osteisis (PAO) patients was 19.3±8.2 ng / ml. Vitamin D deficiency was 5cases (50%), vitamin D insufficiency was 3 cases (30%), and 80% of PAO patients were not satisfied with Vitamin D combined. Most patients with PAO were in vitamin D unfilled state.

P3-172

Prevention of cartilage degeneration using TNIIIA2

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Conflict of interest: None

Introduction: We have demonstrated that tenascin-C (TNC) could prevent cartilage degeneration in mouse osteoarthritis model. TNIIIA2 is

a peptide of TNC. We hypothesized that TNIIIA2 could prevent cartilage degeneration. Method: Male 8-week-old BALB/c strain mice were used. The anterior cruciate ligament and medial collateral ligament were transected. 10μg/ml of TNIIIA2 was injected into the knee joint (group II). The control group had an injection of phosphate buffered saline (group I). OA model mice were sacrificed at 2 weeks (group I: n=12, group II: n=4) and 4 weeks (group I: n=12, group II: n=8) postoperatively. Result: At 2 weeks, no development of OA was found in both groups. At 4 weeks, we found OA development only in Group I. The articular cartilage was stained with Saf-O in group II. However, proteoglycan loss was observed in group I. Mankin scores were significantly higher in group I than in group II at 4 weeks (group I: 3.00, group II: 1.06, $p<0.01$). Type II collagen expression was maintained in group II, but it was decreased in group I at 4 weeks. Conclusion: Intra-articular injection of TNIIIA2 could prevent articular cartilage degeneration for 4 weeks in murine models of OA. TNIIIA2 could be an important candidate for preventing articular cartilage degeneration.

P3-173

Adenosine A3 receptor agonist inhibits human osteoclastogenesis

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Conflict of interest: None

【**Background and Objective**】A3 adenosine receptor (A3AR) is known to be overexpressed in synovial fluid cells and PBMCs from RA patients. It has been reported that A3AR agonist has an anti-inflammatory effect in arthritis model mice and that attenuates clinical manifestations in patients with RA and psoriasis (Rath-Wolfson L et al. 2006) (Fishman P et al. 2016) (David M et al. 2016). Our objective is to investigate the effect of A3AR agonist on human osteoclastogenesis. 【**Methods**】 1) Human monocytes (Mo) were cultured with M-CSF for 3 days. Next, Mo were cultured with M-CSF and sRANKL. We simultaneously added A3AR agonist, IB-MECA (1.0~30μM). After 10 days, Oc formation was evaluated by IHC using anti-CD51/61 Ab. 2) Mo were cultured with M-CSF and sRANKL for 14 days. Next, adherent mature Oc were separated from the culture plate. Mature osteoclasts were then cultured on Osteoassay™ plates with M-CSF, sRANKL and IB-MECA. After 3 days, we evaluated the areas of pit formation. 【**Results**】 1) IB-MECA significantly inhibited human Oc-genesis. 2) IB-MECA also significantly decreased the area of pit formation by mature Oc. 【**Conclusion**】A3AR agonist inhibits Oc-genesis and Oc activation. A3AR agonist has the inhibitory effect for human osteoclastic bone resorption.

P3-174

The role of B cells in osteoporosis

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Conflict of interest: None

RANKL from B cells is important for bone loss caused by estrogen deficiency and for bone resorption in rheumatoid patients. Estrogen causes the increase of the number of B cells in bone marrow, but this mechanism and the role of B cells are still unknown. There are some reports which say B cells can differentiate into osteoclasts in vitro. We made CD19Cre;tdTomato mice. And we showed that B cells do not differentiate into osteoclasts in vivo and in vitro no matter estrogen exist or not. B cells have a role not as progenitors of osteoclasts but as supporters for osteoclasts. And we made CD19Cre;ERalpha mice to investigate whether estrogen controls B cells number directly or not. This knockout mice did show bone loss and increase of B cells number in bone marrow like control mice. Estrogen does not control B cells number directly. B cells can become a good target for bone loss caused by estrogen deficiency and by rheumatoid inflammation.

P3-175

uPA-derived peptide suppresses inflammatory osteoclastogenesis and the resultant bone loss

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Conflict of interest: None

Objectives: Chronic inflammatory diseases such as rheumatoid arthritis and periodontitis frequently cause bone destruction. Inflammation-induced bone loss results from the increase of bone-resorbing osteoclasts. Recently, we demonstrated that urokinase type plasminogen activator (uPA) and its receptor (uPAR) regulate inflammatory osteoclastogenesis and the resultant bone loss. We herein investigated the effects of uPA-derived peptide (Å6) in inflammatory osteoclastogenesis and bone destruction. **Methods**: We investigated that the effect of Å6 on inflammatory OC formation and bone loss induced by lipopolysaccharide (LPS) *in vivo and in vitro*. **Results**: We found that Å6 attenuated inflammatory osteoclastogenesis and bone loss induced by LPS. We also showed that Å6 attenuated the LPS-induced osteoclast formation by inactivation of NF-kB in RAW264.7 mouse monocyte/macrophage lineage cells. **Conclusion**: These founding suggest that Å6 suppressed lipopolysaccaride-induced inflammatory osteoclastogenesis and the resultant bone loss, and provide a basis for clinical strategies to improve the bone loss caused by inflammatory diseases.

P3-176

Myositis-specific and Myositis-associateed autoantibodies in patient with IIMs

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Conflict of interest: None

MESACUP™anti-ARS test (MESA) is used for a diagnosis of IIMs in Japan. On the other hand, EUROLINE myositis Profile 3 (EURO) can analyze plural MSA and MAA at the time, which is used in Western countries. However, we haven't explored difference between MESA and EURO. (Objects) We clarify difference between EURO and MESA, extracts the problem of respective examination. (Method) 58 Patients diagnosed IIMs in our facility were enrolled. The MAA and MSA were analyzed using MESA and EURO. In case of MESA (+), MSA were identified by specific ELISA. When those results were different, immunoprecipitation was executed. (Results) MSA and MAA were detected in 43/58 (74%) (PL7:12, Jo1:7, EJ:3, PL12:1, OJ:0, Ro52:27, PM-Scl75:7, Ku:6, PM-Scl100:1) by EURO. On the other hand, MSA were detected in 20/58 (34%) (PL7:9, Jo1:7, EJ:4) by MESA. MESA (-) and EURO (-) patients had MDA5 or RNP or etc. Two of EURO (-) patients was positive in MESA (Jo1 and EJ). Three of MESA (-) patients was positive in EURO, which had plural MSA and MAA. Two of patients that detected plural MSA or MAA had RPIP. (Conclusion) EURO is a convenient and reliable method useful for detection of MSA and MAA. It was suggested the patients whom plural antibodies were detected by EURO have unique clinical course in others.

P3-177

Remission rate among myositis-specific autoantibodies with polymyositis/dermatomyositis

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Conflict of interest: None

[Object] The aim of this study is to clarify the remission rate after treatment among myositis-specific autoantibodies (MSAs) in PM/DM. **[Methods]** A total of 90 patients with PM/DM were enrolled in this

study. We retrospectively compiled the clinical data, which included complications, contents of treatment, and disease activity. **[Results]** The prevalence of MSAs were as follows: anti-ARS in 35 (39%), anti-MDA-5 in 14 (16%), anti-TIF-1γ in 8 (9%), anti-SRP in 4 (4%), anti-MJ in 3 (3%) and anti-SAE in 2 (2%) patients. Negative for MSAs were 24 (27%) patients. Complication of ILD was found in 90% of patients with anti-ARS or anti-MDA5, and in 50% of those with all-negative MSAs. Malignancy was found in 60% of patients with anti-TIF-1γ. The mortality rate of all was 6%, but significantly higher in anti-MDA-5 (21%). The remission rate was 50% in patients with anti-ARS, anti-MDA5, anti-TIF-1γ, or anti-SRP. As compared to patients with these four MSAs, the remission rate was 75% as higher in those without any of these four MSAs. Multivariate analysis revealed that a presence of DM and an absence of any these four MSAs were associated with achievement of remission. **[Conclusions]** In PM/DM, absences of anti-ARS, anti-MDA5, anti-TIF-1γ, and anti-SRP are associated with better outcome.

P3-178

A case of lymphocytic hypophysitis mimicking dermatomyositis

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Conflict of interest: None

Lymphocytic hypophysitis (LHP) is an uncommon disorder characterized by autoimmune inflammation of the pituitary gland with various degrees of pituitary dysfunction. We present here a case of LHP mimicking dermatomyositis. 【Case report】A 58-year-old man was referred to our clinic because of fever, weight loss, proximal muscle weakness and skin rash. Laboratory tests showed that creatine kinase was increased at 393 mg/dl. Magnetic resonance imaging (MRI) of the femoral region demonstrated high signal intensity in the muscle tissue on fat-suppressed T2-weithted images. Electromyogram showed myopathic changes. He had low serum levels of free T4, but normal TSH. The pituitary hormone levels and their stimulation tests indicated that he had a panhypopituitarism. Brain MRI showed an enlarged pituitary body with cystic lesion, and the suprasellar lesion was enhanced after gadolinium administration. These findings suggested LHP. High dose corticosteroids relieved the signs and symptoms of inflammatory conditions, such as skin rash and myositis. The follow-up MRI at 2 weeks revealed the pituitary mass regression. 【Clinical significance】We experimented a case of LHP mimicking dermatomyositis. The routine thyroid function tests gave a useful diagnostic clue for LHP.

P3-179

The case of dermatomyositis overlapped with sarcoido myopathy

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Conflict of interest: None

[Case] 48 years old, female. [Chief Complaint] myalgia, muscle weakness [Present illness] She was admitted to our hospital because of myalgia of both arms, leg edema and facial exanthema on August 2016. [Progress] An electromyography study disclosed slight views, however, a Computed tomography revealed interstitial pneumonia and a magnetic resonance imaging showed inflammation of muscle. The anti-aminoacyl tRNA synthetase (ARS) antibody was positive. She was diagnosed with dermatomyositis. She had swelling of the right rectus abdominis and abdominal ultrasonography showed hyperplasia of the right rectus abdominis. We performed biopsy from the right rectus abdominis and histological diagnosis was sarcoid myopathy. She was diagnosed with dermatomyositis overlapped with sarcoidosis. She was started oral administration of 1mg/kg/day of PSL and 4mg/day of tacrolimus. After the tapering of PSL, She is recovering from her illness well. [Discussion] Dermatomyositis overlapped with sarcoidosis is unusual. It is necessary to consider sarcoid myopathy, when the dermatomyositis patients have non-specific muscle symptoms.

P3-181

Two cases of different myopathy with positive anti-SS-A antibody and CK elevation

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Conflict of interest: None

[Case1] A 61-year-old female. She had fatigue and weakness. CK was 6692 IU/L and anti-SS-A antibody was 1200 U/mL. She had no dry symptom. SRP antibody was positive, so we diagnosed myopathy with anti-SRP antibody, and we started IVIG, which responded well. [Case2] A 55-year-old female. She had both lower extremity weakness and dry symptoms. CK was 258 IU/L and anti-SS-A antibody was over 500 U/ml. Muscle biopsy showed nemarine corpuscles. From this, we diagnosed Sporadic late-onset nemaline myopachy (SLONM). We accomplished IVIG, but muscle weakness and pain remained present. [Discussion] We realized the importance of muscle biopsy.

P3-182

A case of inflammatory necrotizing myopathy complicated with rectal ulcer caused by cytomegalovirus reactivation, rescued by intravenous immunoglobulin

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Conflict of interest: None

We describe a case of severe inflammatory necrotizing myopathy complicated with rectal ulcer caused by reactivated cytomegalovirus colitis. A 70-year old female presented with progressive limb weakness, with general fatigue and body weight loss. Serum creatine phosphokinase was 10785 IU/L. Muscle biopsy showed the features of inflammatory necrotizing myopathy. This case failed to respond to corticosteroids, and showed rectal ulcer bleeding caused by cytomegalovirus reactivation. She was treated with intravenous immunoglobulin (IVIG), which was selected with high titer lots for cytomegalovirus. This IVIG showed rapid and significant improvement, and then she treated the addition of methotrexate (MTX). She discharged hospital with 10mg of MTX and 15mg of prednisolone. While the prognosis of inflammatory necrotizing myopathy is poor when it is complicated by rhabdomyolysis, the early administration of IVIG has the potential to be the cornerstone of its management. Especially in this case, complicated with reactivated cytomegalovirus colitis, the selection of high titer anti-cytomegalovirus IVIG brought a good results.

P3-183

A case of anti-MDA5 antibody positive amyopathic dermatomyositis complicated with psoriatic arthritis

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Conflict of interest: None

Case report: A 30-year-old man had rash for one year, arthralgia for one month, and respiratory distress for one week prior to admission, respectively. Fine crackles were heard on his chest, and peripheral fibrosis in the back part of lower lungs were observed by chest CT. Restrictive impairment by the respiratory function test and elevated LDH and KL-6 were found, therefore, complication of interstitial pneumonia (IP) was indicated. Except for psoriasis-like rash on his head, the rash on the nail fold and the extensor of elbows and knees, which indicate dermatomyositis (DM), were found. Symptoms of myositis were not observed, and serum CK and muscle MRI were normal, thus amyopathic dermatomyositis (ADM) was suspected. However, the histology of skin biopsy on the head showed plaque psoriasis. In addition to the findings of arthritis, it was difficult to exclude either psoriatic arthritis or ADM. The treatment with prednisolone (1mg/kg) and cyclosporine were started, and these symptoms were improved. Later, elevation of MDA5 antibody, which is the marker of ADM, was reported. Conclusion: This was a rare complication case of psoriatic arthritis and ADM. Glucocorticoid and cyclosporine

treatment was successful.

P3-184

Two cases of dermatomyositis with thrombotic microangiopathy (TMA) during oral administration of calcineurin inhibitor

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Conflict of interest: None

[Case 1] A 60-year-old female developed dermatomyositis positive for anti-EJ antibody. Treatment started with prednisolone (PSL) and cyclosporine A (CsA). After CsA was changed to tacrolimus (TAC), drug eruption appeared and TAC was discontinued. When CsA was reintroduced, thrombocytopenia and crushed erythrocytes were observed, and TMA was suspected. After CsA was discontinued, they were improved. [Case 2] A 55-year old female developed dermatomyositis positive for anti-PL-7 antibody. Treatment started with PSL and CsA. After CsA was changed to TAC, thrombocytopenia and crushed erythrocytes appeared and TMA was suspected. Change from TAC to CsA, thrombocytopenia and crushed erythrocytes were relieved but they appeared again with increasing CsA. When CsA was discontinued, they improved. [Conclusion] Although TMA due to dermatomyositis has poor prognosis, TMA due to calcineurin inhibitor may be improved only by discontinuation of drugs, it is important to first consider withdrawal.

P3-185

Anti-aminoacyl-tRNA synthetases (ARS) antibody seems to be associated with the severity of muscular manifestation and alveolar-endothelial damages

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Conflict of interest: None

Objectives: The purpose of this study was to clarify the association between the disease activity of interstitial lung disease (ILD) and blood coagulation disorders in patients with polymyositis (PM) and dermatomyositis (DM). **Methods:** This was a retrospective observational study. Twenty-nine patients diagnosed as having PM/DM were recruited in the present study. PM/DM patients with ILD were divided into 2 groups, anti-ARS antibody positive and negative. To investigate biomarkers reflecting alveolar-endothelial damage in PM/DM patients with ILD (n=24), we analyzed the correlation between KL-6 and D-dimer, creatinine kinase (CPK), CRP levels. Obvious thrombotic cases affecting the blood coagulation test were excluded. **Results:** The levels of CPK and CRP is significantly higher in anti-ARS antibody positive PM/DM patients than in negative patients. The levels of KL-6 and D-dimer in anti-ARS antibody positive patients tended to be higher than those in negative patients. There is a positive correlation in the levels of between serum KL-6 and plasma D-dimer, significantly ($R= 0.28$, $p= 0.04$). **Conclusion:** In PM/DM patients with ILD, the hyper-coagulant state may be involved in the pathogenesis of ILD with PM/DM.

P3-186

Retrospective review of dermatomyositis patients with pneumomediastinum

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Conflict of interest: None

[Objective]: Pneumomediastinum (PM) is a rare but serious complication of dermatomyositis (DM) and is known to be a poor prognostic factor. We aimed to determine the characteristics of DM patients with PM. [Methods]: We conducted a retrospective review of DM patients who were admitted to our hospital between January 2012 and November 2016. [Results]: Among 21 patients who fulfilled the diagnostic criteria, 15 had interstitial pneumonia (IP) and four had PM. Of the four patients with PM, three had DM and one had CADM. Further, one patient tested positive for anti-MDA5 antibodies and two for anti-ARS antibodies. The CADM patient was not evaluated for anti-MDA5 antibodies, but he later succumbed to rapidly progressive IP despite intensive treatment. All four patients with PM presented with mechanic's hand, two of which exhibited sclerodactyly and enlargement of the esophagus. All patients responded to initial therapy, and the CRP level reduced. However, it increased again before PM occurred. Two patients had PM in the course of improvement in IP. Administrations of tacrolimus and IVCY were initiated at PM diagnosis. PM improved after several administrations of IVCY. [Conclusion]: Anti-ARS antibody-positive DM can result in PM, which may occur without worsening of IP.

P3-187

Risk factors and treatments of recurrent myositis in our department

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Conflict of interest: None

Objectives: Patients with polymyositis (PM) and dermatomyositis (DM) often experience repetitive exacerbation of myositis. Myositis with more than one relapse was classified as recurrent myositis, and its risk factors and treatment for re-induction were studied. **Methods:** Data on 107 patients with PM or DM hospitalized between 1991 and 2016 were examined. We only included patients who had been followed up for more than 1 year. **Results:** Recurrent myositis was documented for 14 cases (13.1%). The mean observation period was 11.3 and 7.5 years, and mean age at onset was 54.7 and 46.2 years in the recurrent and non- recurrent group, respectively ($P=0.26$ and $P=0.19$). The recurrent myositis rate was 15.8% in the interstitial pneumonia (IP)-merged group, 10.0% in the not-merged group ($P=0.41$), 16.3% in the PM group, and 10.9% in the DM group ($P=0.56$). There was no significant difference in relapse between men (11.8%) and women (13.7%) ($P>0.99$). 3 of 14 patients had successful re-remission induction and maintenance therapy. In 2 of 3 cases, 2 immunosuppressive agents were added. The remaining 11 patients were treatment-resistant. **Conclusion:** Recurrent myositis is often treatment-resistant, and remission cannot be induced with 1 immunosuppressive agent, but could be achieved with 2 agents.

P3-188

Successful control of rapid progressive interstitial pneumonia with amyopatic dermatomyositis (DM-IP) by Polymyxin B immobilized column direct hemoperfusion (PMX-DHP)

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Conflict of interest: None

[Objective] Even with new immunosuppression medications such as tacrolimus, DM-IP remains one of refractory diseases. The Polymyxin B immobilized column is known to remove various kinds of inflammatory cytokine including endotoxin by direct hemoperfusion, called PMX-DHP. Effectiveness of PMX-DHP to DM-IP is less studied. We report four DM-IP cases to which PMX-DHP was preformed. [Cases] The range of ages was 54-71 years old. In each case, 6 hours of PMX-DHP was performed twice. Two cases have been surviving. The other cases recovered once, although we lost them eventually due to pharyngeal cancer or re-exacerbation. The specific autoantibody was positive with anti-MDA in only one case. As for combination medication, the former two cases were given cyclosporin A, prednisolone (PSL) in cyclophosphamide IV infusion (IVCY), while the latter two cases were given Methylprednisolone

(mPSL) pulse, IVCY and PSL. AaDO2 improved in all cases from 74.9, 29.95, 34.85, 88.0 and 96.5 Torr before PMX-DHP to 626.0, 39.7, 49.25, and 102.6 Torr after PMX-DHP, respectively. P/F ratio also improved from 49.6, 328.0, 293.0, and 244, to 244, 368.5, 350, and 260, respectively. [Summary] PMX-DHP could contribute to prevent acute exacerbation of DM-IP.

P3-189

Dermatomyositis with "necrotizing" fasciitis: A Case report

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Conflict of interest: None

[Case report] A 39-year-old female who was diagnosed with dermatomyositis (DM) when she was 25-year-old have been stable with prednisolone (5mg/day) and methotrexate (2.5mg/week) for the last 10 years. One year before admission to our hospital, she realized slight difficulty in swallowing. 6 months ago, she became unable to keep up with her mother. One month ago, she also felt it difficult to stand up and to open her mouth. After admission, we conducted some examinations. The results of magnetic resonance imaging (MRI) and electromyograph (EMG) at the lower extremities mostly corresponded with DM. As a result of tissue biopsy, there was not only lymphocyte infiltration around small vessels but also neutrophil infiltration with necrosis on adipose tissue as like necrotizing fasciitis. Thus, we diagnosed this case with "necrotizing" fasciitis related to DM. We started to treat with oral prednisolone 1mg/kg. On 7 days after using it, muscle weakness improved. Surprisingly, on 14 days, the abnormal images of MRI almost all improved. We could decrease doses of prednisolone quickly. [Conclusion] We often find DM with fasciitis, but we present a rare case with "necrotizing" fasciitis. In addition, we indicate that it may be able to taper prednisolone more shortly than usually.

P3-190

Histologial study of skin in cases of dermatomyositis associated with interstitial pneumonia

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Conflict of interest: None

We studied histologically skin biopsy specimens of 26 cases of dermatomyositis associated with interstitial pneumonia. Hyperkerasosis, parakeratosis, acanthosis, epidermal cell necrosis, liquefaction degeneration, inflammatory cells infiltration and karyorrhexis in dermis were evaluated. Dominantly observed findings were hyperkeratosis, lymphocytic infiltration and liquefaction degeneration through all cases. We found neutrophilic infiltration (p=0.013584), parakeratosis, liquefaction degeneration and karryorrhexis in 11 cases with worse prognosis dominantly. We suggest those elements could be prognostic markers of interstitial pneumonia in dermatomyositis.

P3-191

An endometrial cancer-associated polymyositis case that presented with intense distal involvement and marked elevation of inflammatory markers

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Conflict of interest: None

[Case presentation] A 70-year-old woman was diagnosed with endometrial cancer with distal metastasis after an operation. Three months after the last chemotherapy which proved to have no efficacy, she suddenly developed fever, general fatigue and myalgia, and was found to have elevated CPK and C-reactive protein levels. PET/CT suggested not only cancer metastasis in lymph nodes but also scattered inflammation of systemic muscles, which was verified by muscle biopsy from right gastrocnemius muscle. Diagnosed with polymyositis, she received high dose corticosteroid treatment, which showed prompt and marked efficacy. [Clinical significance and discussion] This case has two characteristic features: severe involvement of distal muscles usually spared in polymyositis, and marked elevation of inflammatory markers usually slightly elevated at most. The significance of distal involvement in inflammatory muscle disease will be discussed; in addition, whether there is any association between elevated inflammatory markers and certain clinical features will be investigated.

P3-192

Hidden generalized edema in inflammatory myopathy; Generalized edema is a characteristic clinical feature of myositis

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Conflict of interest: None

Purpose Dermatomyositis (DM) /polymyoitis (PM) is a systemic disease with varieties of clinical symptoms and signs. We and others have reported cases of DM/PM with generalized edema. We found that there were many myositis patients who lost their body weight (BW) after starting of high dose glucocorticoid (GC) therapy. Therefore, we hypothesized that hidden generalized edema is a characteristic sign of myositis. The aim of this study was to evaluate the hypothesis. **Methods** The subjects were 79 of DM/PM and 77 of SLE patients who admitted our department, received immunosuppressive therapy including GC and did not have cardiogenic edema or hypoalbuminemia. To detect (hidden) generalized edema by inflammation, change in BW in 2 weeks after starting immunosuppressive therapy was analyzed. **Results** BW of DM/PM and SLE were 56.2±13.8 and 55.3±10.7 kg, respectively. Decrease in BW in 2 weeks after starting therapy were 2.9±3.0 kg of DM/PM and 1.2±2.8 kg of SLE, which was larger in DM/PM compared to SLE. The number of patients who lost the BW more than 2kg in 2 weeks were 48 in DM/PM (60.8%) and 23 in SLE (29.9%). **Conclusion** DM/PM lost BW after starting GC therapy, which suggests the existence of hidden generalized edema that might be a characteristic clinical feature in myositis.

P3-193

The relation of the nailfold capillary abnormalities and the pathologies in PM/DM-IP patients

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Conflict of interest: None

Objectives. We performed nailfold capillaroscopy (NFC) on patients with PM/DM-IP and analyzed the relation with the microvascular changes and the pathologies. Methods. Thirty-five PM/DM-IP patients (PM 3, DM 32 including 21 CADM) were evaluated by NFC. A semiquantitative rating scale to score NFC parameters was adopted. Results. The median age was 57-years and 12 patients were female. Both of the patients complicated with acute/subacute IP (A/SIP) and chronic IP (CIP) were 7. The anti-ARS antibody-positive cases (anti-ARS+) were 9 and the anti-MDA5 antibody-positive cases (anti-MDA+) were 3. The score of giant capillaries was higher in the A/SIP cases than the CIP cases and in the death cases from IP than the survival cases. The score for disorganization of the microvascular array was higher in the CADM cases than the control, in the A/SIP cases than the control, in the anti-MDA5+ than negative cases. The score of hemorrhages was lower in the anti-ARS+ than negative cases. Conclusions. The NFC abnormalities, such as giant capillaries and capillary disorganization were observed markedly in the anti-MDA+,

the A/SIP cases and the death cases from IP. These results suggested the NFC parameters have the possibilities for the index of progression and forecasting prognosis of PM/DM-IP.

P3-194

Pathological analysis of serum cytokines/chemokine levels in patients with interstitial pneumonia complicated with dermatomyositis or polymyositis

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Conflict of interest: None

Objectives. We evaluated the initial serum cytokine/chemokine levels of patients with interstitial pneumonia (IP) combined with PM/DM and examined their relationships with specific pathologies. Methods. Thirty-five PM/DM-IP patients (PM: 3; DM: 32, including 21 with CADM) were included. Results. The subjects' median age was 65 years, and 23 patients were female. Twenty-seven patients were complicated with acute/subacute IP (A/SIP), and 8 had chronic IP (CIP). Fifteen and 11 patients were positive for anti-ARS and anti-MDA5 antibodies, respectively. The A/SIP patients exhibited significantly higher serum IL-8 levels than the CIP patients. The anti-MDA5-positive patients displayed significantly higher serumCCL2, CXCL10, CXCL11, and IL-8 levels than negative cases. Serum KL-6 levels were correlated with serum IL-18 and CXCL10 levels; serum ferritin levels were correlated with serum IL-18, IL-2, TNF, CXCL11, and IL-6 levels; the $AaDO_2$ was correlated with serum IL-18, IL-8, and IL-6 levels; the %DLco was correlated serum IL-10 and IL-18 levels; and chest computed tomography scores were correlated with serum MCSF and IL-6 levels. Conclusions. High Th1-, monocyte/macrophage-, and neutrophil-associated cytokine/chemokine levels were correlated with disease activity markers of PM/DM-IP.

P3-195

Cluster analysis using antibody profiles of line immunoassay in patients with polymyositis/dermatomyositis

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Conflict of interest: None

Background: Although several autoantibodies were identified in diagnosis of polymyositis/dermatomyositis (PM/DM), clinical significance of these autoantibodies were not elucidated. **Method:** Patients with PM, DM, including clinically amyopathic dermatomyositis (CADM), who were evaluated autoantibody profiles using line immunoassay in our hospital, were enrolled. Cluster analysis was performed using antibody profiles and clinical symptoms. Relapse rate was compared among determined clusters. **Result:** Of 63 enrolled patients, 19 patients were classified as PM, 32 patients as DM, and 12 patients as CADM. Hierarchical cluster analysis determined following four clusters: cluster 1, Ro-52 positive and higher levels of KL-6 (≥400 U/mL); cluster 2, Ro-52 positive and lower levels of KL-6 (<400 U/mL); cluster 3, PL-7 positive; cluster 4, Ro-52 negative. The patient in cluster 4 had interstitial lung disease (ILD) less frequently compared to other clusters (p=0.004). One-year relapse rate was significantly higher in patients in cluster 1 than those in cluster 2 (log-rank test, p=0.011) and cluster 4 (p=0.013). **Conclusion:** Previous reports showed that Ro-52 positivity and ILD were associate with poor prognosis in patients with PM/DM. Our clustering also may be useful for prediction of prognosis.

P3-196

Association between serum soluble CD163 and rapidly-progressive interstitial lung disease in patients with polymyositis and dermatomyositis: A retrospective study

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Conflict of interest: None

[**Object**] We aimed to retrospectively study the association between serum soluble CD163 (sCD163), a macrophage activation marker, and rapidly-progressive interstitial lung disease (RP-ILD) in patients with polymyositis (PM) and dermatomyositis (DM). [**Methods**] We measured the levels of sCD163 by ELISA in sera of patients with PM/DM (n=167) and healthy controls (n=68), and compared them. We also analyzed the association between the levels of sCD163 and clinical information in PM/DM patients. We also compared the sCD163 levels in pre- and post-treatment sera of available patients (n=46). [**Results**] Serum levels of sCD163 in PM/DM patients were significantly higher than those in healthy controls (p<0.01). The sCD163 levels were correlated with the levels of ferritin (r=0.21), but not with CK or CRP in PM/DM patient sera. The sCD163 levels in patients with ILD were significantly higher than in those without ILD (p=0.02). However, there was not significant difference between the sCD163 levels in those with RP-ILD and chronic ILD (p=0.45). sCD163 levels significantly declined after treatment in PM/DM patients (p<0.01). [**Conclusion**] This study suggested that serum sCD163 increased in PM/DM patients, especially those with ILD. However, the association between sCD163 and RP-ILD was not shown.

P3-197

Fluctuations of plasma microRNA productions by treatments in polymyositis/dermatomyositis patients

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Conflict of interest: None

[Objective] This study was performed to investigate the expression of microRNA (miRNA) in the plasma from polymyositis (PM) and dermatomyositis (DM) patients, which fluctuated by treatment. [Methods] Total RNA was isolated from the plasma of 10 patients with pre- and post-treatment condition. The Expression of miRNAs in 8 patients sample was determined using miRNA array analysis. The expression validated using RT-qPCR method. Human Skeletal Muscle Myoblasts (HSMMs) were treated with TNF-α, and we determined the miRNA expression. The miRNA mimic transfected into HSMMs. The fluctuation of the gene expression was evaluated using DNA microarray analysis. [Results] There were 8 significantly fluctuated miRNAs. We found 12 in DM and 3 in PM differentially expressed miRNAs. Among them, hsa-miR-4442 was down regulated after treatment. TNF-α stimulation significantly increased the expression of hsa-miR-4442 in HSMMs. The hsa-miR-4442 mimic transfection regulated several genes involved in the signals that were concerned with muscle cell development. [Conclusion] We showed the plasma miRNA expression profiles in the PM/DM patients. The present data suggest that the fluctuation of miRNA expression by treatment is disease specific and may have the effects to muscle cell functions.

P3-198

A case of polyarteritis nodosa diagnosed with perirenal hematoma due to rupture of renal artery aneurysm

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Conflict of interest: None

A 49-year-old woman presented with three mounths of anorexia. She suddenly developed left flank pain on 14 February 2015 and was admitted to other hospital. Abdominal computed tomography (CT) showed left perirenal hematoma. Angiography findings pointed out multiple bilateral renal artery aneurysms and rupture of left renal artery aneurysm. Embolization of the left artery was performed. Laboratory finding indicated increased level of C-reactive protein. And then she transferred to our hospital. Magnetic resonance (MR) angiography showed multiple aneurysms of bilateral renal and cerebral artery. She had fever, body weight loss and hypertension. Together with the clinical, laboratory and MR angiography findings, she was diagnosed with polyarteritis nodosa (PAN). She was treated with oral prednisolone 40mg per day. After treatment, she was complicated with retroperitoneal abscess. An drainage of abscess was performed. Thereafter her symptoms were gradually relieved and unruptured renal artery aneurysms reduced in follow-up MR angiography. A rupture of renal artery aneurysm is life-threatening entity characterized by acute onset of nontraumatic perirenal hematomas. Therefore, we must consider vasculitis syndrome included PAN in the diagnosis of a rupture of renal artery aneurysm.

P3-199

Case report: successful treatment of elderly onset large vessels vasculitis with a predonisolone (PSL) and mycophenolate mofetil (MMF) for remission-induction therapy

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Conflict of interest: None

A 75 years old woman with asymptomatic hepatitis B carrier was admitted because of fever of unknown origin, elevation of C-reactive protein and anemia. To exclude malignancy and non-infectious inflammatory disease FDG-PET/CT (PET) was performed and FDG was uptaked in wall of ascending aorta and bilateral subclavian artery. By the MRI scan it was also suggested that it was the large vessel vasculitis. HLA B52 positive. Aortic valve regurgitation and rapidly progressive glomerulonephritis were accompanied. There was no tenderness on the temporal artery. We diagnosed her as elderly onset large vessels vasculitis and started with 45mg/day predonisolone. Intravenous cyclophosphamide (IVCY) therapy was considered but could not tried due to anemia, renal dysfunction, and poor performance status. We choiced the combination of PSL and MMF for remission-induction therapy as substitute with IVCY. MMF dose was 1000 mg/day. During 3 months course, Activities of large vessel vasculitis was improved dramatically and complications did not accepted.

P3-200

A case of Takayasu arteritis complicated with ulcerative colitis presenting with atrial and venous thrombosis

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Conflict of interest: None

A 26-year-old female was admitted to our hospital with left sided hemiparesis. Two years ago, she suffered from fever, polyarthritis and erythema nodosum, and was diagnosed with ulcerative colitis (UC) based on colonoscopy findings in another hospital. Her symptom was improved by the treatment with 10mg of daily oral prednisolone (PSL) and 5-ASA, but her C-reactive protein level did not decrease. Four months ago, she suddenly stopped to visit the hospital. On admission, her severity of UC was moderate to severe. MRI of the brain revealed an acute infarction in the right middle cerebral artery (MCA) area. MRA showed an occlusion of the right internal and external carotid artery and the origin of the right MCA. Computed tomography showed thickened walls of thoracic aorta and its primary branches. In addition, left renal vein occlusion and pulmonary embolism were observed. A diagnosis of Takayasu arteritis (TA) was made based on these findings, and we administered 60mg of daily oral PSL. Despite the addition of Methotrexate, Cyclosporine and Infliximab (5mg/kg), TA remained active. After starting Tocilizumab (8mg/kg), clinical manifestations improved, and the PSL dosage could be tapered. Co-existence of arterial and venous thrombosis in the case of TA with UC is relatively rare.

P3-201

A case of palmoplantar pustulosis osteoarthritis with large vessel vasculitis during treatment of Golimumab

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Conflict of interest: None

Case: A 67-year-old woman had been treated with prednisolone (PSL) by the diagnosis of polymyalgia rheumatica in X-5 year. Methotraxate was added because of relapse. In X-2 year the arthritis of the right knee and the right elbow were seen and in January, X-1 year we prescribed Golimumab on the diagnosis of rheumatoid arthritis. In May, X year pustules of both palms and plantares were seen and she was diagnosed pustulosis palmaris et plantaris by dermatologist. At the same time she had a fever of 38.6℃ and CRP levels elevated. In July 27, X year she was admitted to our hospital. Pelvic Xp shows an osteosclerosis of sacroiliac joint. Bone scintigraphy shows accumulation at sternoclavicular joint, right shoulder and right knee. We had a diagnosis of palmoplantar pustulosis osteoarthritis with pustulosis palmaris et plantaris and imaging study. Contrast-enhanced MRI shows contrasting effect to subclavian artery, left total carotid, brachiocephalic artery from the aortic arch and was complicated with the large vessel vasculitis. In August 9, X year we started treatment with PSL 40mg (1mg/kg) and fever, arthralgia was improved immediately. Conclusion: We experienced one case that palmoplantar pustulosis osteoarthritis with large vessel vasculitis developed during golimumab treatment.

P3-202

A case of the Takayasu arteritis that urinary tract infection was the opportunity of the diagnosis

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Conflict of interest: None

【Case】The patient was 20-year-old woman. She received the urology department because of fever and backpain. WBC and CRP level were 8800/μl and 5.95 mg/dl. Her urinary WBC was positive. She was diagnosed urinary tract infection and given cefcapene pivoxil hydrochloride, but WBC and CRP level were 8800/μl and 10.30 mg/dl. Change to levofloxacin by local doctor was not effective, she was admitted to our hospital. Staphylococcus epidermidis resistant to levofloxacin was detected by urine culture. Her urinary WBC became negative by Ceftriaxone intravenous feeding. But CRP level was not decreased. We recognised an artery wall thickening from the aortic arch part to descending aorta, the abdominal aorta by an examination for CT and MRI. Laterality of the blood pressure became than 10mmHg. We diagnosed Takayasu arteritis, and gave 30 mg of prednisoloneand and 100 mg of aspirin. Her symptom was improved and CRP became negative. 【Clinical significance】Takayasu arteritis is one of fever of unknown origin of the young woman. The diagnosis is often difficult because a specific symptom is not seen early. When we met with the infectious disease that we could not control by an antibiotic treatment, it is necessary for us to think about the possibility of the vasculitis.

P3-203

Analysis of clinical features of Takayasu arteritis in our hospital

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Conflict of interest: None

【Purpose】We examined clinical features and treatment outcomes of Takayasu arteritis (TKA). 【Method】We analyzed retrospectively from the medical record for 17 patients with TKA who visited our hospital between January 1, 2006 and October 30, 2016. 【Result】The average age at onset was 48.6years, 3males, 14females. The disease type was type I: 7, IIa: 1, IIb: 1, III: 1, IV: 0, V 7. Vascular stenosis was confirmed in 7cases, and aneurysm formation in 3 cases. Distribution of the lesion was left subclavian artery12, the common carotid artery10 cases. All patients started treatment with glucocorticoid alone, the average dose was PSL 34.1 mg/day, and steroid pulse therapy and immunosuppressant were not used. The average CRP was 11.2 mg/dl, and all were CRP negative a month later. Immunosuppressants were used in 3 and Biologics (TCZ) in 1 case. In 9 cases in the last 5 years,1 male,8 females, the average age was 58.1 years, the average CRP was 13.8 mg / dl, and the average dose was PSL43.3 mg/day. 【Conclusion】TKA is characterized by juvenile onset, but especially in the last 5 years, cases of middle-aged and elderly women, with high value CRP, and requiring higher-dose glucocorticoid were more frequent. It is also suggested that TKA of middle-aged and older age may be increasing.

P3-204

The case of patients with Takayasu's disease developed after Caesarean Section and cured without any treatments

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Conflict of interest: None

[Introduction] We encountered the patient with Takayasu's diseases (TAK) developed after Caesarean Section and cured without any treatments. We report this case because few cases of TAK were observed without any treatments. **[Case]** The 30-years-old woman gave birth at caesarean section in the previous hospital. After that, she had a fever and bilateral cervical pain. Despite the use of antibiotics, her fever remained high. Laboratory data showed WBC 14500/μL and CRP 19.1mg/dL. Carotid artery ultrasound (US) examination and other imaging studies showed findings suspected of TAK. After 8 days from onset, she discharged because she wanted treatment in our hospital near from her parent's home. After 9 days from onset, her temperature became normal. The next day, she entered our hospital. Laboratory data showed WBC 6200/μL and CRP 3.29 mg/dL. The US examination showed the intima media thickness (IMT) progression. Despite no treatments, she had no symptoms for 2 days. We judged that there is no necessity to treat immediately and she discharged. After follow-up began, CRP and IMT became insignificant within 6 months. **[Conclusion]** When we encounter an asymptomatic patient with IMT progression and without arteriosclerosis, there is a possibility of a spontaneous relief of TAK.

P3-205

A case of Takayasu arteritis with relapse in left common carotid aneurysm after the onset of right common carotid aneurysm and tocilizumab therapy was effective

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Conflict of interest: None

Case. One year ago, A 23-year-old man was diagnosed with Takayasu arteritis with a right common carotid aneurysm and treatment started with prednisolone (PSL) 60 mg / day. After that, fever fever, CRP decreased promptly, but he fainted and the common carotid artery was occluded. When angiography was performed, the carotid bifurcation was high, and the collateral circulation of the upper thyroid artery confirmed the blood flow distal to the right common carotid artery occlusion. Since his medical condition was stable. After reduced PSL 25 mg / day, contrast CT examination showed a new left common carotid artery aneurysm. Starting with tocilizumab (TCZ) 8 mg / day after hospitalization, CRP was rapidly negativeized, and TCZ therapy was performed three times at 2 week intervals. After that he received TCZ therapy every 4 weeks, it was possible to gradually reduce PSL. Ten months after TCZ therapy, enhanced CT showed improvement in wall thickening of left common carotid artery. He is still undergoing TCZ therapy and has taken PSL 5 mg. In this case, TCZ therapy was able to introduce and maintain clinical and image remission after relapse, and TCZ was considered to be an effective treatment for Takayasu arteritis treatment which is difficult to reduce steroid.

P3-206

Pulmonary hypertension during giant cell arteritis treatment

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Conflict of interest: None

A 78-year-old woman presenting with fever and shoulder and hip pain was diagnosed with polymyalgia rheumatica. She was given 15 mg prednisolone, but this was ineffective. As she developed headache and jaw claudication during the treatment and carotid ultrasonography showed vertebral arterial wall thickening, we confirmed giant cell arteritis (GCA) as a complication. We initiated 500 mg methylprednisolone pulse treatment for 3 days, followed by 40 mg prednisolone. Her prednisolone dose was then reduced every 2 weeks, but relapse occurred when the dose reached 10 mg/day. During the relapse, she presented with dyspnea on exertion, and echocardiogram showed a marked increase in estimated pulmonary artery systolic pressure (60 mmHg). We suspected pulmonary hypertension associated with GCA and immediately added methotrexate to her glucocorticoid therapy; her systolic pressure rapidly decreased to 25 mmHg. GCA typically presents in superficial temporal arterial, vertebral arterial, and ophthalmic arterial lesions. Lesions of the aorta and its major proximal branches sometimes exist as large-vessel GCA. However, GCA with pulmonary hypertension is considered rare. The present case is of particular interest as it demonstrates an atypical presentation of GCA with pulmonary hypertension.

P3-207

A Case of Ludwig's Angina with Polymyalgia Rheumatica: It is Difficult to Distinguish from Giant Cell Arthritis

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Conflict of interest: None

85-years-old women with Polymyalgia Rheumatica (PMR) presented to our hospital with a headache. She received corticosteroid therapy, and 5 days before this presentation, she reduction of dosage 10 mg/day. She had relapsed on a reduction to same dose steroid regimens. She complained of ache from right temporal region to shoulder joint, and she worried about vision haze. CRP elevated to 2.56 mg/dL. Her intraocular pressure was normal and had no vision disorder. There were no remarkable CT and MRI image examination findings. No infections agents were detected in the patient's blood on admission. PMR relapse or complications of Giant Cell Arthritis (GCA) were suspected. PSL 45mg/day was administered. In spite of the treatment, her status worsened and *Streptococcus Constellatus* was detected in second blood culture. On the next day of the positive blood culture, her right mandible was become extremely swollen. Her status was getting improvement with an antibiotics therapy and surgical management. [Conclusion] Ludwig's Angina is a skin bacterial infection that extends into floor of the oral cavity. Severe airway obstruction was sometimes occurred with rapidly developed. Our case is an instructive example of severe infection with PMR.

P3-208

A case of giant cell arteritis with cervical radiculopathy

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Conflict of interest: None

【Case】A previously healthy 72-year-old man with one month history of bilateral shoulder pain gradually presented difficulty in raising his both arms. He visited a local doctor where elevated serum CRP (12.62 mg/dl) was noted, and was refered to our hospital. As there were no signs of tenosynovitis and bursitis in his shoulders by ultrasonographic examination, PMR was unlikely. Elderly-onset rheumatoid arthritis was also ruled out, because both RF and ACPA were negative and there were no signs of synovitis. Precise neurologic examination revealed that there were bilateral C5 and C6 radicular involvement and left diaphragmatic weakness (C4 involvement). No sensory impairment was noted. Since cervical MRI showed no mechanical causality, cervical radiculitis of unknown origin was suggested. PET/CT revealed increased FDG lineal uptake along the vessel walls including temporal arterys, vertebral arterys and subclavian arterys. Biopsy of the right superficial temporal artery was compatible with giant cell arteritis. 30mg (0.6mg/kg) of prednisolone was started, resulting favorable outcome. He was well and able to raise his arms and left the hospital.【Discussion】Giant cell arteritis must be considered in elderly patients presenting with C5 radiculopathy and elevated inflammatory markers.

P3-209

A case of Giant cell arteritis was diagnosed with the onset of cerebellum infarction

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Conflict of interest: None

A 69 year-old woman admitted to our hospital because of dizziness and general fatigue. She did not have a fever and a headache. Her laboratory date showed anemia (Hb 9.2gdl) and high CRP level (6.83mg/dl). She was diagnosed as cerebellum infarction by head MRI. Enhanced computed tomography (CT) showed diffuse wall thickening of aortic arch and cervical branches, and ultrasonography (US) showed wall thickening of not only common carotid artery and subclavian artery but also superficial temporal artery. We diagnosed Giant cell arteritis on the basis of the typical CT and US findings. Oral prednisolone (50 mg/day) after m-PSL pulse therapy with antiplatelet agents was administrated. We started to use MTX together when we reduced the dose of PSL. Then her dizziness and general fatigue was improved, her CRP level returned to normal, and ultrasonography showed improvement of arterial wall thickening.

P3-210

A case of giant cell arteritis (GCA) without significant findings in CE-CT and FDG-PET/CT diagnosed by temporal artery biopsy

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Conflict of interest: None

An 81-year-old man was hospitalized because of general fatigue and weakness of the thigh 10 days before visiting. He had no headache, vision abnormality, joint pain, or jaw claudication. Physical examination of temporal arterites revealed normal findings. WBC 8000/μl, ESR 65mm/h, CRP 8.06mg/dl, ANA <40, MPO-ANCA<0.5IU, and PR3-ANCA<0.5IU. There wes no abnormal findings in bilateral temporal arteries, aorta, and its major branches by both CE-CT and FDG-PET/CT. Although there was no findings supporting GCA, we still suspected GCA because of mild dailation of right superficial temporal artery (right 2.7mm, left 1.6mm). So we underwent biopsy of the right superficial temporal artery. Histopathological examination revealed inflammatory cell infiltration of the artery with multinucleated giant cells. With the diagnosis of GCA, 0.8mg/kg/day of prednisolone was initiated, resulting favorable response. It is considered that FDG-PET/CT examination is an useful daiagnostic tool for GCA. It's sensitivity and specificity are reported 56-100% and 77-99%, respectively. However, CE-CT and FDG-PET/CT examination showed no findings suggesting of GCA in this case. Moreover, clinical signs of GCA was obscure. Nevertheless, biopsy of the superficial temporal artery was useful for the diagnosis of GCA.

P3-211

Analysis of initial symptoms and diagnosis latency of relapsing polychondritis

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Conflict of interest: None

Object: Apart from auricular chondritis, relapsing polychondritis (RP) presents various manifestations as its initial symptoms. The object is to investigate the differences of latency of diagnosis between patients with different initial symptoms of RP. Methods: From the medical records of all RP cases retrospectively extracted in our hospital, initial symptoms and time from their onset to diagnostic histopathological results were collected. The difference in diagnosis latency was statistically analyzed from the viewpoint of initial symptoms. Results: Among 12 cases extracted, major initial symptoms were auricular chondritis (42%), arthritis (33%) and fever (33%). Median diagnosis latency is 135 days (range 13-1200 days). The diagnosis latency among cases with each initial symptom (median of with vs without each symptom) is 30 days vs 210 days in auricular chondritis, 405 days vs 135 days in arthritis, 90 days vs 195 days in fever. As for the diagnosis latency, Wilcoxon's rank sum test revealed no statistical significance between cases with vs without each symptom as well as between cases with different initial symptoms. Conclusion: It is suggested that longer days are required in diagnosing RP in patients without auricular chondritis, with fever or with arthritis.

P3-212

Misdiagnosis of Relapsing Polychondritis as Serongative Rheumatoid Arthritis

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Conflict of interest: None

【Introduction】The relasping polychondritis (RP) diagnosis is difficult until overt chondritis manifests. We report RP case who presented with polyarthritis, occipital neuralgia, nonproductive cough and conjunctivitis. 【Case】61 years old housewife presented with neck and shoulder girdle pain and polymyalgia rheumatica was diagnosed. Then PSL 20 mg was started and during PSL tapering, arthralgia worsened and DMARDs were added. Anti-CCP antibody and rheumatoid factor were negative. 1 year later, she was referred to our hospital and peripheral polyarthritis were noted. Seronegative rheumatoid arthritis was diagnosed. She developed occipital neuralgia, nonproductive cough and conjunctivitis. Her arthritis symptoms fluctuated and improved during next year and all DMARDs and PSL stopped. 6 months later, she developed auricular chondritis complicated with aseptic meningitis and oculomotor nerve palsy. RP was diagnosed and mPSL pulse therapy promptly improved all her symptoms. 【Clinical significance】RP should be considered, even before chondritis is not evident, when seronegative inflammatory polyarthritis patients have fluctuating articular symptoms and be complicated with headache, chronic cough and conjunctivitis. RP can be a cause of occipital neuralgia.

P3-213

Case Report; A case of Cogan's syndrome associated with aneurysm of the coronary artery

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Conflict of interest: None

A 20-year-old woman was referred to us for fever of unknown origin. 10 days previously, she had right-sided neck pain, and, on the following day, she started to have fever. She visited the otolaryngologist, who found right cervical lymphadenopathy. The patient was admitted to the hospital for acute hepatitis. She had also noticed side-to-side hearing abnormality. The audiometric evaluation showed the threshold of 125 and 250 Hz elevated at 40 dB. Past medical history included Meniere-like attack with vertigo and hearing abnormality 18 months previously. On physical examination, her eyes were red. Laboratory data on admission showed white blood cell counts 18200/μL, CRP 18 mg/dL, T-bilirubin 3.6 mg/dL, AST 65 IU/L, ALT 231 IU/L, and ALP 656 IU/L. CT of the abdomen showed hepatomegaly and splenomegaly. Ophthalmologic examination revealed bilateral scleritis. The diagnosis of atypical Cogan's syndrome was made because of Meniere-like attack and scleritis, according to the previous criteria (Haynes 1980). Coronary CT angiography was performed, which revealed aneurysm of the left main coronary trunk. Therapy with prednisolone (1mg/kg/day) alleviated her symptoms. To our knowledge, this case is the first case with Cogan's syndrome associated with aneurysm of the coronary artery.

P3-214

Tocilizmab markedly improved the two patients with vasculitis. Case report

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Conflict of interest: None

Case 1 Cogan`s syndrome A 33-year-old, female Case 2 Aortitis symdrome with ulceritive colitis A 26-year-old male Tocilizmab remarkably improved two cases who suffered from vasculitis. Conclusion: Tocilizmmab may be a good option of the treatment to the patient with vsculitis.

P3-215

Unsuccessful late treatment in a case of atypical Cogan's syndrome

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Conflict of interest: None

Cogan's syndrome is an autoimmune disorder characterized by nonsyphilitic interstitial keratitis and progressive audiovestibular impairment. Haynes et al. modified diagnostic criteria for patients with other ocular or vestibular symptoms and suggested this to be atypical Cogan's syndrome. A 41-year-old man with sensorineural hearing loss and conjunctivitis was diagnosed with atypical Cogan's syndrome. He was referred to us with high CRP and bilateral hypoacusis. Serological test results for syphilis, antinuclear antibodies, and antineutrophil cytoplasmic autoantibodies were negative. Positron emission tomography/computed tomography (PET/CT) revealed diffuse aortitis. Remission induced by treatment with high doses of prednisolone was followed by three and a half years after onset. Although his inflammatory response and aortitis were successfully improved by prednisolone, his hearing condition was resistant to therapy. Late steroid therapy for Cogan's syndrome could not prevent progression of the hypoacusis.

P3-216

Successful treatment of IgA vasculitis complicated with bowel perforation by steroid, cyclosporine and replacement of factor 13

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Conflict of interest: None

[Case] An 18-year-old man developed fever, tenderness of elbow joint and purpura on his extremities. Physical examination showed abdominal pain, arthralgia, purpura on both arm and low extremities. Laboratory tests on admission gave the following results: C-reactive protein 11.2 mg/dL; serum IgA 165 mg/dL; factor 13 26%; PR3-ANCA, and MPO-ANCA were negative. Urine test showed that massive proteinuria and hematuria. Blood and urine culture were both negative. CT scan revealed edematous small intestine and free-air suggestive of a perforated intestine wall. Histopathological examination of the kidney showed cellular crescent glomerulonephritis with mesangial IgA deposit. Therefore, he was diagnosed as IgA vasculitis. His symptoms including arthralgia, purpura, abdominal pain and proteinuria were improved by high dose glucocorticoid, cyclosporine and replacement of factor 13. Glucocorticoid was able to tapered without relapse of IgA vasculitis. [Discussion] There is limited data with immunosuppressant on IgA vasculitis. In addition to steroid, cyclosporine and replacement of factor 13 may be beneficial in patients with IgA vasculitis complicated with bowel perforation and crescent glomerulonephritis.

P3-217

Successful outcome of Crecentic glomerulonephritis due to Immunogloblin A Vasculitis developed after using antibiotic: a case report

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Conflict of interest: None

Immunoglobulin A vasculitis (Henoch-Schönlein purpura) is a small vessel vasculitis with deposition IgA immune complexes, clinically renal involvement is more common on adult onset IgA vasculitis than childhood, and it has been reported association of bad prognosis. We report the case of a 70-year-old male diagnosed IgA vasculitis 2 months after antibiotic therapy (Sulbactam / Ampicillin, Levofloxacin) for pneumonia, who presented with purpura and renal hypertension. Renal biopsy revealed histopathological findings showing crescent formation, mesangial proliferation and IgA deposition in the glomerular mesangial, and skin biopsy revealed that in cutaneous vascular walls, which led to diagnosis of IgA vasculitis. He was treated with high-dose steroids and cyclophosphamide pulse, then he improved and achieved remission after half a year. A drug lymphocyte stimulation test was positive for both anti biotics, it is possible that antibiotics associated with the development of IgA vasculitis.

P3-218

Adult onset IgA vasculitis concomitant with gastrointestinal lesions: 4 cases reports

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Conflict of interest: None

【Background】Adult onset IgA vasculitis (IgAV) is a rare autoimmune disorder. The incidence of cases with gastrointestinal lesion was about 50%, and few studies reported. We report about the clinical features and course of treatments with some literature review.【Case 1】36-year-old woman presented nausea and purpura, and then developed hemorrhagic

shock and anuria. Although mPSL pulse and IVCY were effective for the gastrointestinal lesions, refractory nephrotic syndrome was persisted. 【Case 2】19-year-old man presented fever, abdominal pain, and purpura. Treatment with 60 mg PSL was started. Because of relapsing, mPSL pulse was applied, followed by the combination with azathioprine. 【Case 3】54-year-old man presented polyarthralgia, fever, and purpura. Treatment with 15 mg PSL was effective. Because of relapsing, mPSL pulse was applied, followed by increase the dose of PSL to 40mg. 【Case 4】39-year-old man presented purpura. Treatment with 30 mg PSL was started. However, he developed abdominal pain with hematochezia. Endoscopic examination showed multiple ulcers in the gut. His symptoms were significantly improved by mPSL pulse therapy. 【Conclusion】It is suggested that adult onset IgAV with gastrointestinal lesions need high dose steroid and immunomodulatory agents.

P3-219

A case of refractory type II mixed cryoglobulinemia vasculitis (MCV) associated Sjögren syndrome (SS) induced remission by rituximab

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Conflict of interest: None

A 57-year-old woman with a 15-year history of SS developed palpable purpura, arthralgia, hematuria, proteinuria in 2011, and was diagnosed of MPGN associated with type II MCV in kidney biopsy. Due to refractory to immunosuppressant and repeated infection, it was very difficult to treat. In April 2016, against exacerbation of MCV, remission was induced by Rituximab, cryofiltration and increasing PSL. In September 2016, when PSL was tapering with using MMF for maintenance, glomerulonephritis relapsed at PSL 9 mg, it was judged exacerbation of MCV, Rituximab, cryofiltration and increasing PSL promptly made improvements. Currently PSL is tapering but it has passed without exacerbation of MCV. Combination of MCV in SS has significant relevance to extragonadal symptoms and B-cell lymphoma complications and decreased survival rate, so appropriate treatment is important, Most of the reports are successful with steroids, steroid pulses, and CY. There are also many reports that Rituximab + IFNα + ribavirin is successful for HCV association, which accounts for more than 90% of the underlying disease of type II MCV. Reporting of rituximab for MCV assosiated SS is rare and we have experienced refractory cases requiring rituximab, so we will report it including literature considerations.

P3-220

Occupational therapy for vasculitic neuropathy

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Conflict of interest: None

Vasculitic neuropathy is associated with motor and sensory injuries and hinders activities of daily living (ADLs). However, a few studies have examined the rehabilitation for vasculitis, especially for ADLs using upper limbs. In this study, we examined the effect of occupational therapy (OT) for ADL improvement in 6 patients with vasculitic neuropathy. The patients were received OT during the hospitalization for the initial treatment of the vasculitis. Their hospitalizations were 81 days, and the OT was started from the 17th hospital day, in average. The OT included sensory re-education, application of short opponent orthosis, and compensational ADL exercises using self-help devices. It was found that the participants' performances on self-care activities using the Functional Independence Measure (FIM) were improved on discharge. Our results indicate that OT is useful for ADL improvement in patients with vasculitic neuropathy.

P3-221

A case of myelodysplastic syndrome initially presented with cutaneous leukocytoclastic vasculitis complicated with disseminated Mycobacterium kansasii infection

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Conflict of interest: None

We present a fifty-one year-old man with a history of chronic anemia for years. He was admitted to a hospital because of persistent fever followed by erythema in the trunk and extremities. Skin biopsy of the knee showed leukocytoclastic vasculitis. CT of the thorax showed scattered small nodules, but not interstitial pneumonia. He had no signs of renal involvement. Both MPO- and PR3- ANCA were negative. He was treated with 40mg prednisolone which resulted in rapid resolution of fever and rash. However, 2 months later, he was referred to our hospital and hospitalized because of recurrent fever and severe pancytopenia followed by gradual tapering of prednisolone. At 9 days of admission, he developed respiratory failure and diffuse ground-glass opacity on CT of the lungs. Mycobacterium Kansasii was detected in bone marrow and blood culture. Diagnosis of myelodisplastic syndrome (MDS) was also made based on bone marrow findings. He was initially treated with isoniazid, rifampicin, and ethambutol. Addition of levofloxacin and streptomycin resulted in gradual improvement of fever, respiratory failure, and pancytopenia. Because vasculitis could be the initial presentation of MDS, thorough hematologic examination should be considered in a patient with undifferentiated vasculitis.

P3-222

Association of serum C3 levels with renal pathological classification in children with silent lupus nephritis

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Conflict of interest: None

[Object] To search the association of serum complement levels with renal pathology in children with silent lupus nephritis. [Methods] We determined serum C3 levels and International Society of Nephrology/Renal Pathology Society classification in children with juvenile systemic lupus erythematosus who were classified as having silent lupus nephritis based on normal urinary findings at renal biopsy. [Results] Decreased serum C3 levels were associated with renal pathological classification in children with silent lupus nephritis. [Conclusions] Serum C3 levels were associated with renal pathological classification in children with silent lupus nephritis. We believe that serum C3 levels could provide a useful biomarker for predicting latent severe nephritis in children with systemic lupus erythematosus.

P3-223

Myocardial infarction in a young patient (20 years of age) with childhood-onset SLE

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Conflict of interest: None

Acute myocardial infarction is a rare and severe manifestations in patients with systemic lupus erythematosus. Coronary atherosclerosis should be managed through preventive measures including drug therapy from childhood.

P3-224

Characteristics of anti-DFS70 antibodies positive juvenile idiopathic arthritis (JIA) with uveitis

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Conflict of interest: None

Objectives: Anti-DFS70 ab is ANA reported to be more common in children with uveitis (Healty:3%, idiopathic uveitis:14%, JIA without uveitis:2%, JIA with uveitis:11%). The purpose of our investigation is to examine the difference in anti-DFS70 ab positive group (+G) and a negative group (-G) in the JIA patient with uveitis. *Method:* 10 patients of JIA with uveitis were enrolled. We measured their blood anti-DFS70 ab, and compare clinical characteristics in +G and -G. *Results:* Anti-DFS70 ab +G were 5patients, and –G were 5patients. The mean age at the time of JIA onset, uveitis diagnosis, and measurement anti-DFS70 ab was +G: 1.8 years/ -G: 3.2 years, +G:5.0 years/ -G:4.6 years, and +G:13.2years/ -G:8.4 years, respectively. All cases were persistent oligo arthritis, and took a methotrexate. Biologic was used in +G: 2 patients/ -G: 3 patients. The percentage of the period when steroid eye drops was +G:78.8%/-gG:68.7%. Ocular complications were found in +G:1 patient/ -G:2 patients, and operations were needed in +G:1 patient/ -G:1 patients. There was no statistical significant differences in any parameters between 2 groups. *Conclusion:* In this study, there was no difference for clinical characteristics in JIA with uveitis between anti-DFS70 ab positive group and a negative group.

P3-225

Rheumatoid factor and/or anti-citrullinated protein antibody positive oligoarticular juvenile idiopathic arthritis

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Conflict of interest: None

Among 73 cases of oligoJIA, four RF (+)ANA (-)cases had aggressive arthritis affecting both wrists progressing to carpal bone ankylosis within one year. Case 1. A 10 year-old girl has complained for 2 months of right wrist pain and swelling. She was started on naproxen and aspirin and later on weekly methotrexate with good results. Case 2. A 4 year-old girl has complained for 2 months of right wrist pain and swelling. She had already suffered from bilateral ankylosis moderately improved by salazosulfapyridine. Case 3. A 7 year-old girl complained for 4 months of right wrist pain and swelling, 64.2 U/ml of ACPA. She was started on weekly methotrexate with good results with positive RF 3 years later. Case 4. 12 year-old girl complained for 6 months of wrists pain and swelling with carpal bone ankyloses, 43.3 U/ml of ACPA. She was started on weekly methotrexate and followed by infliximab without pain six months later and positive RF 3 years later. These four cases of RF positive oligoJIA were compatible to neither extended oligoJIA nor RF positive polyarticular JIA. The two cases positive in ACPA at presentation became RF positive several years later. A new clinical entity of aggressive type of oligoJIA complicated with bilateral carpal bone ankyloses might be considered.

P3-226

The therapeutic effect and long-term continuation rate of etanercept in juvenile idiopathic arthritis

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Conflict of interest: None

【Objective】To evaluate the efficacy and long-term continuation rate of etanercept, and to find out the factors predicting the therapeutic efficacy in JIA.【Method】We divided the cases entered in clinical trials of ETN in JIA into the four groups by the use situation as of August, 2016 that evaluated patient's characteristics from the beginning of introduction of ETN to 12 weeks and various parameters of arthritis retrospectively.【Results】The subject cases were 23 cases (82.6% of female) started ETN a median 12.4 years ago, the most common ILAR subtype was polyarthritis (87%). 11 stopped due to inefficacy, 3 for other reasons. Seven child stopped for remission. There was no significant difference in various parameters from the time of introduction of ETN to 12 weeks between the 4 groups.【Conclusions】Finally, 30% of JIA patients treated with ETN could be stopped for remission. In this investigation, long-term effects could not be predicted for arthritis parameters at 12 weeks from the start of treatment.

P3-227

Chronic Recurrent Multifocal Osteomyelitis: four pediatric cases

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Conflict of interest: None

Chronic Recurrent Multifocal Osteomyelitis (CRMO) is a rare autoinflammatory disease characterized by multiple, chronic and recurrent aseptic osteomyelitis. CRMO mainly affects children and adolescents and the lesion can be seen at any part of the body. It often accompanies other inflammatory diseases such as palmoplantar pustulosis and inflammatory bowel disease. Synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome is an adult disease considered to be closely related to CRMO. Early diagnosis and long-term follow-up for CRMO is necessary because the prolonged inflammation can result in bone deformity and leg length discrepancy. First line therapy is oral nonsteroidal anti-inflammatory drugs (NSAIDs) but some cases need bisphosphonates or anti-TNF-α agents. From 2011 to 2016, four children were diagnosed of CRMO at our hospital. Here we report the detailed clinical pictures of these patients and the effect of NSAID and bisphosphonate therapies in these cases.

P3-228

Chronic recurrent multifocal osteomyelitis as fever unknown origin

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Conflict of interest: None

Chronic recurrent multifocal osteomyelitis (CRMO) is auto-inflammatory syndrome that is non-infectious and malignant disorder of skeletal system mainly occurred in children and adolescent, but also reporting in adult. We report a case of CRMO in 43 years-old, female presenting with fever, erythema, and swelling and pain on her right foot. MRI and FDG-PET/CT suggested multiple osteomyelitis in her limbs. Bone biopsy revealed no presence of bacterial and malignant bone inflammation, suggesting non-specific osteomyelitis. We diagnosed the CRMO, and started NSAIDs and Bisphsphonate. The combination therapy successfully improved her clinical symptom, laboratory abnormalities, and MRI imaging. We need to know CRMO, encountering multiple osteomyelitis caused by unknown origin.

P3-229

Validation of old and new Jones criteria in acute rheumatic fever and poststreptococcal reactive arthritis

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Conflict of interest: None

[Object] Both acute rheumatic fever (ARF) and poststreptococcal reactive arthritis (PSRA) are disease occurred after streptococcus infection and thought to be on the same spectrum. In 2015, Jones criteria for ARF was revised. We validated new and old Jones criteria on children with ARF and PSRA. [Methods] We investigated retrospectively children with ARF or PSRA who visited our hospital between 2010 and 2015. [Results] There were 3 cases with ARF and 2 cases with PSRA. ARF or PSRA was diagnosed by attending physicians in reference to old criteria. All patients satisfied 1 major and 2 minor manifestation of old criteria. Four of five patients met 1 major and 2 minor manifestation of new criteria, but one patient who was diagnosed as ARF by old criteria satisfied only 1 major manifestation. He had inflammatory manifestation, but grade of fever (less than 38.0 ˚C) and serum CRP level (2.58 mg/dL) did not meet new criteria that contained "Fever (≥38.5˚C)" and "ESR ≥60 mm/hr and/or CRP ≥3.0 mg/dL". Like in this case, it can be controversial how we deal patients slightly under value of criteria. [Conclusions] One ARF child who met old criteria did not satisfy new criteria. Newly revised Jones criteria is supposed to need validity among Japanese children.

P3-230

The myositis-specific autoantibody and myositis-associated autoantibody phenotypes of Japanese juvenile idiopathic inflammatory myopathies

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Conflict of interest: None

【Objective】Demographics, clinical features, and outcomes among myositis-specific autoantibody (MSA) and myositis-associated autoantibodies (MAAs) subgroups were assessed in children with juvenile idiopathic inflammatory myopathies (JIIM). 【Methods】MSAs (anti-TIF-1, anti-MJ, anti-ARS, and anti-MDA-5), and MAAs were evaluated with above clinical information. 【Results】Among 12 JIIM children, MSAs and MAAs were detected in 9 (anti-TIF-1 (n=3), anti-MJ (n=3), anti-MDA-5 (n=2), and anti-ARS (n=1))and 1 (anti-Ku). The other two were negative. Eleven except anti-Ku positive child were consistent with juvenile dermatomyositis. Three patients with anti-TIF-1 mainly had skin manifestations, 2 of the 3 were diagnosed clinically amyopathic dermatomyositis. Typical skin manifestations and myositis were noted in another 3 patients with anti-MJ. Of the two children with anti-MDA-5, 1 developed interstitial pneumonia successfully treated intravenous cyclophosphamide pulse therapy, and the other had arthritis intractable to conventional treatments and improved by adalimumab. 【Conclusion】The MSAs were highly detected in JIIM patients. Myositis was most severe in anti-MJ positive patients, whereas the skin and extra-skeletal muscles symptoms were mainly noted in patients with anti-TIF-1 and anti-MDA-5.

P3-231

National survey of childhood-onset rheumatic diseases followed up in the clinical departments except the pediatrics in Japan

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Conflict of interest: Yes

Objective: About juvenile idiopathic arthritis (JIA), systemic lupus erythematosus (SLE), juvenile dermatomyositis (JDM), Sjögren's syndrome (SS), Takayasu disease (TA) and polyarteritis nodosa (PN), we would like to know the actual situation of follow-up in clinical departments except pediatrics. Method: For the facilities in the e-mail address registrants of Japan College of Rheumatology, we performed the questionary survey for grasping the number of patients < 16 and ≧16 years about the above diseases with an electronic form. The answer period was from July 8 to August 31, 2016. Results: As for the answer from 83 facilities, the number of patients < 16 and ≧16 years were as follows; JIA: 29 vs 164, SLE: 23 vs 178, JDM: 4 vs 9, SS: 2 vs 15, TA: 1 vs 27 and PN: 1vs 1, individually. We compared the data from the Japan Pediatric Society specialist training facilities with these results. Conclusion: We finally reported the detail of the medical actual situation such as the enforcement systems of the transition medicine in the childhood-onset rheumatic diseases, based on 1) number of patients of capital way prefectures in Japan, 2) distribution of the rheumatic specialists, 3) cooperation with the core institutions of pediatric rheumatology in each medical area.

P3-232

Perception gap with parents is a latent burden for children with juvenileidiopathic arthritis

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Conflict of interest: None

Background / Purpose: We have been asking both children with juvenile idiopathic arthritis (JIA) and their parents to answer the Childhood Health Assessment Questionaire (CHAQ). Coincidence of the two questionnaires would be preferable, but a perception gap exists in some cases. So, we examined the gap and tried to find the way to bridge it. Methods: Retrospective observational study. With informed consent of the children with JIA and parents, CHAQ described by both children and parents were examined, with special attention to the gap. Data represented numerically were compared between patients and children. Descriptive data were also collected. Results: Three children with JIA and their parents were included. There was a perception gap between children and parents about what difficulty children have and how hard it is. The gap seemed to be caused by endurance of children, anxiety of parents, and so on. And the gap resulted in some burden for the children, such as excessive restriction of exercise, or spiritual pain, like "I am not understood". Through this study, most parents newly recognized the gap. Conclusion: Using CHAQ, the perception gap between children with JIA and their parents could be recognized. And it might be the first step to bridge the gap.

P3-233

Pregnancy and childbirth in juvenile idiopathic arthritis treated with etanercept

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Conflict of interest: None

[Object] The number of pregnant cases treated with biologicals is increasing. However there are not enough evidences about the safety of pregnancy with biologicals. Here we report the pregnancy and childbirth in juvenile idiopathic arthritis treated with etanercept for a long time. [Methods] The case was a 30 years old woman who developed RF positive juvenile idiopathic poly-arthritis (pJIA) at the age 15. Her arthritis could not be controlled by treatment with MTX because of its side effect. She participated in the etanercept trial at the age of 17. After the end of trial she received adalimumab instead of etanercept. However her arthritis became worse. So she received etanercept again at age26. [Result] She became pregnant at age 29. At that time she received etanercept 50mg/week, prednisolone 7.5mg once a day and loxoprofen 60mg 3 times a day. Etanercept and prednisolone were continued and we prescribed acetaminophen as needed instead of loxoprofen. Her arthritis was controlled during pregnant. She gave a birth to 2352g healthy boy at the gestational age of 35 weeks 5days. [Conclusions] In this case long term etanercept treatment for pJIA is safe for pregnancy and childbirth.

P3-234

A case of acute idiopathic pericarditis of which serum interleukin-18 measurement was useful to differentiate from relapse of systemic juvenile idiopathic arthritis

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Conflict of interest: None

The patient was diagnosed as sJIA when he was 5 years old. He had many relapses and developed macrophage activation syndrome four times, acute encephalopathy once, and acute pericarditis once. We started tocilizumab (TCZ) administration when he was 6 years old, and without any relapses, he was able to stop prednisolone (PSL) by 9 years old and TCZ by 11 years old. After a year of drug-free condition, he visited our hospital with a complaint of right shoulder pain and upper back pain which improved in sitting position, aggravated by recumbency. The electrocardiogram showed ST elevation and pleural effusions (PE) were seen on the chest X-ray. The echocardiogram showed pericardial fluid (PF), trivial mitral regurgitation and tricuspid regurgitation leading to the diagnosis of acute pericarditis. We started treatment with ceftriaxone, PSL, flurbiprofen, and NSAIDs, and his PE and PF had disappeared by the 6th hospital day. Since his serum IL-18 was in the normal range, it did not seem to be a relapse of sJIA. After denying infections, we diagnosed him as acute idiopathic pericarditis and withdrew PLS on 19th hospital day. Even after PSL was stopped soon, he is stable without a relapse of sJIA. Serum IL-18 was useful to differentiate the cause of pericarditis.

P3-235

Distinct subset of systemic juvenile idiopathic arthritis based on serum interleukin-18 at the onset of the disease

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Conflict of interest: None

We reported two subset of s-JIA patients with certain distinct clinical feature can be identified on the basis of their serum IL-6 and IL-18 levels. However, some patients treated with steroid are included in our previous study. In this study, to validate our previous study, we analyzed serum levels of IL-6 and IL-18 in patients with s-JIA during acute phase without any treatments at the onset of their diseases. We divided s-JIA patients into two subsets: high or low IL-18, high or low IL-6 group, based on the median values of serum IL-18 (37,000pg/ml) or IL-6 (44.5pg/ml), and furthermore, IL-18/IL-6>1000 (IL-18 dominant group) or IL-18/IL-6<1000 (IL-6 dominant group). We compared them with the clinical features of s-JIA. Sixty six patients were analyzed. Serum IL-6 and IL-18 levels were quantified by ELISA. As well as our previous study, the IL-6 dominant group and low IL-18 group had a significantly greater number of joints with active disease, whereas IL-18 dominant group and high IL-18 group showed was more likely to develop MAS. These findings indicate that two subsets of patients with s-JIA, one which is prone for arthritis and another with prone for MAS, can be identified on the basis of their serum IL-18 levels or IL-18/IL-6 ratio.

P3-236

Relapse of systemic-onset juvenile idiopathic arthritis (s-JIA) after influenza vaccination in a patient receiving tocilizumab (TCZ)

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Conflict of interest: None

【Case】6-year-old-girl. She was initially diagnosed with having s-JIA at 4 year of age. She was initially treated with 3 kur of mPSL pulse, but MAS was occurred. DexP and cyclosporin subsided MAS, then TCZ was initiated, leading to remission. Maintenance therapy was PSL (3mg/day) and TCZ at 5 year of age. During almost same condition, she was given 0.25ml of flu shot three times, but no side effect occurred. Then, she was given 0.5ml of flu shot, and 2 days after the shot, she had urtica-like rash and blood examination showed coagulation abnormalities. With suspicion of relapse, she was treated with PSL (10mg/day) and H1 blocker. The treatment improved the rash and normalized lab data. Moreover, elevated serum level of IL-18 was confirmed, suggesting relapse of s-JIA for the patient.【Clinical importance】There is a paper reporting the effectiveness of influenza vaccine for patients with s-JIA by confirming elevation of antibody titer against influenza. However, there are some reports describing relapse of s-JIA after the vaccination. In this case, increased dosage of the vaccine caused a relapse of s-JIA, suggesting some amount of adjuvant in the vaccine may affect the activity of s-JIA. In conclusion, a dosage of influenza vaccine may be important for patients with s-JIA.

P3-237

A retrospective study about the first induction of remission of adult onset Still disease in our institution

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Conflict of interest: None

OBJECTIVE: Adult onset Still disease (AOSD) is an autoinflammatory disease by the activation of reticuloendothelial system. The main features of AOSD are a high spiking fever, polyarthralgia, evanescent rash. A corticosteroid is usually used in the induction of remission, but the treatment reactivity varies by a case. We investigated the first induction of remission in our hospital. **METHODS:** We retrospectively analyzed the medical records of fourteen AOSD patients who received treatment in our hospital after 2006. **RESULTS:** Five of 14 cases were men, and one of 14 cases was not inducted in remission. Mean follow-up period is 41.3 months. Five patients received only corticosteroid therapy, four patients corticosteroid with cyclosporine, four patients corticosteroid with methotrexate, and one patient corticosteroid with TNF-α blockers (etanercept) respectively. The significant difference was not seen in clinical features in each group. Six patients received steroid pulse therapy. The period to induction of remission by the treatment with cyclosporine was longer than other drugs in our institution. There was a correlation with significant difference between the age and the period to induction of remission. **CONCLUSION:** We reported the fourteen AOSD patients in our institution.

P3-238

A case of elderly-onset AOSD in which TCZ was effective

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Conflict of interest: None

Case: 85-year-old female. **Chief complaint**: fever **History of present illness:** She was examined for the chief complaint of fever of 38 degrees or higher and was hospitalized for further examination. **Clinical course**: Her fever persisted after admission, and she began to complain of joint pain and rash on the breast. Blood test results indicated that WBC was 44420/μL and serum ferritin levels were elevated at 58106 ng/ml, leading to suspicion of adult-onset Still's disease (AOSD). Based on the above, AOSD was implicated and she was begun on a course of steroid pulse therapy, but she suffered recurrence of fever after completion of the pulse therapy. Then 8 mg/kg Tocilizumab (TCZ) was added to her treatment regimen. This resulted in prompt improvement in fever, WBC, and ferritin level. **Discussion**: TCZ is one treatment option for AOSD, and based on the fact that it was effective we came to believe that in fact she was suffering from hypercytokinemia caused by the abnormal activation of her natural immune system, including macrophages. **Conclusion**: We experienced a case of elderly-onset AOSD in which TCZ was extremely effective.

P3-239

Tocilizumab therapy for Adult Still's disease: four case reports

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Conflict of interest: None

Tocilizumab (TCZ) appears a key drug that enables a rapid reduce in steroid doses for treating adult Still's disease (ASD) and leads the steroid-free remission. We report a combination therapy with prednisolone (PSL) and TCZ in our serial four cases of ASD. Case 1: A 60-year old man had 6 month-persistent ASD despite 30 mg/day of PSL therapy. Intensive therapy by 1.6 mg/kg/day of PSL and following biweekly TCZ led to remission of ASD. Case 2: A 41-year old woman had repeated ASD flares for 10 months. PSL therapy at our division up to 2mg/kg/day showed no response. Additional TCZ therapy resolved her ASD for the first time and resulted in adverse event, retroperitoneal abscess formation. The drainage, antibiotics, and PSL monotherapy for the ASD succeeded. The remitted ASD is now maintained by low dose PSL and adalimumab. Case 3: A 42-year old man had flared ASD during PSL therapy with methotrexate. His ASD remitted by 0.5 mg/kg/day of PSL and TCZ therapy. Case 4: A 46-year old man was diagnosed with ASD three weeks after the onset. PSL plus TCZ therapy was effective and PSL dose was successfully reduced from 70 to 20 mg/day for 14 days. In summaries, TCZ therapy for ASD was effective even in our most severe case, and enabled a rapid PSL reduce in stable cases.

P3-240

A case of juvenile idiopathic arthritis presenting recurrent eruption with tocilizumab

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Conflict of interest: None

【Case】A 16-year-old female complained of many arthralgia of the large joint predominance. There were synovitis findings in echo. She was diagnosed with JIA, and started of therapy with TCZ8mg/kg subcutaneous injection, and MTX4mg/week. Her symptoms were under good control, but after 2 month later erythema developed several hours after TCZ subcutaneous injection. Eosinophil counts was 2226mg/dl. We thought a side effect of TCZ, and changed to the intravenous drip of TCZ. We used PSL before the administration of TCZ. After 3 month later erythema appeared again just after the administration of TCZ. We thought infusion reaction of TCZ, and changed to GLM. We used PSL before the administration of GLM. After use of GLM, the course of her desease is good, and side effects are not appeared. 【Discussion】We report a patient with JIA who developed eosinophilia with skin symptoms while being treated with TCZ. Interestingly, marked eosinophilia and skin symptoms were not observed in this patient for a half year switching to GLM. GLM is a fully human antibody produced in a human immunoglobulin transgenic mouse. That is why GLM is a lower immunogenicity. We thought switching to a biologic with a lower immunogenicity was effective for the case of eosinophilia and skin symptoms related to biologics.

P3-241

A case of Suspected Systemic Juvenile Idiopathic Arthritis with Macrophage activated syndrome observed Langerhans Cell proliferation in Lymph Nodes

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Conflict of interest: None

[Introduction] Some cases of systemic Juvenile idiopathic arthritis (sJLA) with Kawasaki disease-like symptom are recently diagnosed based on serum cytokine level, however, the pathophysiology is unknown. [Case] A 8-year old boy was transferred to our hospital due to fever, rash, hyperferritinemia and thrombocytopenia. He was diagnosed as Kawasaki disease and Macrophage activation syndrome (MAS). Intravenous immunoglobulin and plasmapheresis was performed to bring down fever. Prednisolone (PSL) was administrated by a dose in a gradual reduction manner but developed fever again. After a cervical lymph node biopsy, mPSL pulse therapy and plasmapheresis were performed. Subsequently, the remission was achieved. At the onset of symptoms, serum IL-18 level was high, and cytokine profile shows a pattern of sJIA with MAS. While a growth of CD1a+ S-100+ Langerhans cells in lymph node were recognized, however, clinical findings were different from typical Langerhans cell histiocytosis. [Discussion] MAS is understood as disease based on activated macrophage proliferation, the findings of this case were distinctive. An abnormal differentiation and proliferation of Langerhans cells may be associated with the pathophysiology in a part of cases diagnosed as sJIA with MAS.

P3-242

Successful treatment with etanercept (ETN) in a case of a familial Mediterranean fever (FMF) variant complicated with refractory aseptic meningitis

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Conflict of interest: None

A 66 years old male developing polyarthralgia and fever visited our clinic. A diagnosis of rheumatoid arthritis was made by positive test for ACPA and bone erosions then therapy with sulfasalazine was initiated. The patient also diagnosed as bullous pemphigoid and administration of prednisolone (PSL) was additionally started. In February, 2014, severe headache and periodic fever had emerged and the patient presented to a neurologist. Meningitis was suspected, however, anti-microorganism agents did not dissolve the symptoms. Methylprednisolone at a dose of 250mg/day improved the symptoms. The meningitis was relapsed when PSL was tapered to 15 mg/day. Copresence of an old pleuritis prompted us a diagnosis of FMF. Sequence analysis of MEFV gene revealed a heterozygous mutation causing S503C amino acids substitution. Administration of colchcine and PSL improved the symptoms, however protein level in cerebrospinal fluid was not decreased. We did not find genetic mutations in other autoinflammatory syndromes-related genes. The patient was tentatively diagnosed as refractory FMF variant. Application of ETN (50 mg/wk) ameliorated the disease course so that PSL dose could be reduced. This might be one of a few cases of meningitis in FMF successfully treated with ETN.

P3-243

Clinical characteristics of late-onset familial Mediterranean fever in Japan

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Conflict of interest: None

【Objectives】We aim to evaluate the demographic and clinical characteristics of late-onset Japanese familial Mediterranean fever (FMF) patients. 【Methods】We analyzed clinical pictures and genetic mutations of the *MEFV* gene in 373 patients clinically diagnosed with FMF based on Tel-Hashomer diagnostic criteria. Patients were divided into three groups by the age of onset; group I: under 19 years old (early onset group), group II: 20 ~ 39 years old, group III: over 40 years old (late-onset group). 【Results】There were 57 patients (15.3%) who experienced their first FMF attacks at over 40 years of age. Among them, high fever (86.0%) was the most common clinical finding. In contrast, peritonitis (66.4% in group I, 69.7% in group II, 38.6% in group III) and pleuritis (47.7% in group I, 35.9% in group II, 24.6% in group III) were less frequent compared with early-onset patients. In late-onset groups, the fre-

quencies of p. Met694Ile mutation (12.3%) inducing severe clinical FMF phonotype was low, and the response to colchicine therapy was relatively good (88.9%). 【Conclusion】In Japan, a number of FMF patients with late-onset exist. Our observation indicates that they has milder form of disease for less frequent of peritonitis and pleuritis.

P3-244

The case that merged Extranodal NK/T-cell lymphoma after a diagnosis of the familial Mediterranean fever

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Conflict of interest: Yes

The case is 28-year-old woman who had a fever, stomachache, and exanthem. She had periodic fever, an abdominal pain symptom from 19 years old. The period of the symptom gradually shortened, and so she consulted our hospital on the suspicion of familial Mediterranean fever (FMF) at 27 years old. Because E148Q heterozygote of exon2 was detected by gene analysis, an attack symptom disappeared by taking colchicine, and her clinical manifestations were equal with typical FMF, we gave her a diagnosis of FMF. Erythema developed to her both legs from the same year, and the exanthem accepted expansion and an ulceration. And she did not eat by the result that high heat and abdominal pain lasted several weeks. During hospitalization we increased colchicine to her and gave a steroid pulse, but the symptom was not improved. Because a period of the fever and a form of the exanthem were not equal with FMF, we enforced skin biopsy for diagnosis. She had a diagnosis of EB virus-related NK/T-cell lymphoma from a pathology organization. The malignant lymphoma does not have the sign which is specific like FMF. In having experienced this case, we tried FMF and the differentiation of the malignant lymphoma.

P3-245

Mevalonate kinase deficiency with severe neurological involvement possibly caused by secondary mitochondrial dysfunction

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Conflict of interest: None

Mevalonate kinase deficiency (MKD) is a multisystemic inflammatory disorder caused by a mutation of *MVK* gene that severely reduces mevalonate kinase activity. Mevalonic aciduria (MA) is severe phenotype of MKD characterized by serious neurologic abnormalities as well as recurrent fever with poor prognosis. The pathogenesis of neurologic impairment of MA is not yet clear. One hypothesis is that neurodegeneration is linked to intrinsic apoptosis pathway triggered by mitochondrial damage. We present a case of MA with severe neurological involvement, mimicking Leigh encephalopathy, which is neurodegenerative disorder associated with dysfunction in mitochondrial energy metabolism. Laboratory data showed elevation of blood lactate and pyruvate concentration with mild lactic acidemia. The lactate to pyruvate ratio of blood and cerebrospinal fluid increased, which suggested mitochondrial dysfunction. Magnetic resonance imaging of brain showed symmetrical T2 and FLAIR hyperintensity of basal ganglia, severe brain atrophy and thinning of corpus callosum, which resembled to Leigh encephalopathy. It was suggested that neuropathology of severe phenotype of MA might be related to secondary mitochondrial dysfunction due to deregulation of mevalonate pathway.

P3-246

A case of infancy-onset mevalonate kinase deficiency which had a good response to canakinumab administration

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Conflict of interest: None

Mevalonate kinase deficiency (MKD) in early infancy is likely to develop fatal complication. We will report a case of infancy-onset MKD that repeated fever attack and ileus, which was uncontrollable with glucocorticoid, but after canakinumab administration, not only her fever attack relieved but also physical growth and development has improved. The patient was a 1 year-old girl with no significant perinatal events and no familial history of periodical fever. She had periodical fever from 3 days old, accompanied by skin rash and abdominal symptoms. Her urinary mevalonate acid was elevated, MVK gene mutation (MVK c.613A>G hetero, c.382_383 del AG hetero) was detected with low mevalonate kinase activity (1.3%) leading to the diagnosis of severe MKD. By the age of 2 months, her fever became persistent and small dose of oral prednisolone was started making her condition good. However, by the age of 8 months, she became to repeat fever attacks accompanied by ileus, and her symptoms were exacerbating gradually. After the Ethics Committee approval was obtained, we started to administer canakinumab 2mg/kg/month when she was 1 year old. Since after, she had no more fever attacks and ileus, and also her height, body weight and physical development is catching up readily.

P3-247

New Gene Mutation Report in TNF Receptor-Associated Periodic Syndrome (TRAPS)

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Conflict of interest: None

Tumor necrosis factor receptor-associated periodic syndrome (TRAPS) is an autosomal dominantly inherited autoinflammatory syndrome caused by mutations in *TNFRSF1A.* We report here three cases of one family of TRAPS. One case was a thirty-four years old woman. She had suffered from recurrent episodes of intermittent fever and abdominal pain lasting one month. Laboratory examinations suggested systemic inflammation, but no abnormalities were observed in imaging studies. The patient responded well on corticosteroids. The investigation of family history revealed that her mother and cousin had the similar symptoms of intermittent fever. The diagnosis of TRAPS was strongly suspected by the patient and family's medical history. Genetic tests showed the patient had a heterozygous mutation, G58V (p.G87V) in *TNFRSF1A*. There are fewer cases of TRAPS from Asian than Caucasians. In Japan, Only 30 familial cases have been reported. Some of disease associated mutations in *TNFRSF1A* were identified, and the symptoms and the complications appear to vary according to the site of mutations. The G58V mutation had not been reported in patients with TRAPS. We plan to perform the functional study using cells transfected with this mutation.

P3-248

A novel *TNFRSF1* gene mutation in a Japanese patient with tumor necrosis factor receptor-associated periodic syndrome

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Conflict of interest: None

[Background] Tumor necrosis factor receptor-associated periodic syndrome (TRAPS) is an autosomal dominantly inherited rare autoinflammatory disease. We present a sporadic case of TRAPS with a novel mutation. [Case] A 33-year-old Japanese woman presented with recurrent episodes of fever, myalgia, and joint pain. Before this visit, she experienced five febrile episodes associated with increased CRP, which persisted for a few weeks (in 14, 15, 20, 22, 29 years old). At the time of her

fifth attack, she had bilateral conjunctivitis. She was completely healthy in attack-free intervals. She has no family history of TRAPS or periodic fever. The analysis of *TNFRSF1* genes revealed a heterozygous V2A on exon 2. Her clinical manifestation fulfilled the Hull's criteria for TRAPS. Finally, the diagnosis of TRAPS was made. [Discussion] It is unclear how a V2A mutation functions for disease processing of TRAPS. But, in Japan, periodic fever syndrome is still underestimated among clinicians. Although rare, clinicians should be astute and consider TRAPS when they see a difficult case with fever of unknown origin. [Conclusion] Our case illustrated that a novel mutation V2A may play a role as an etiological factor and may be associated with a pathological process in a mild form of TRAPS.

P3-249

Exhaustive analyses of 11 responsible genes derived from autoinflammatory syndrome in the patients with unknown fever

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Conflict of interest: None

Purpose: Autoinflammatory syndrome is characterized by 1) the episodes of seemingly unprovoked inflammations, 2) the absence of high titer of autoantibody or auto-reactive T cell. Autoinflammatory syndrome is known to be important for the differential diagnosis of unknown fever. Methods: We examined the responsible genes including *MEFV*, *TNFRSF1A*, *NLRP3*, *MVK*, *NOD2*, *IL1RN*, *NLRP12*, *PSTPIP1*, *PSMB8*, *NLRC4*, and *PLCG2* in the genomic DNA derived from 255 patients with unknown fever using the next-generation sequencer (MiSeq). Results: 1) We diagnosed as FMF (M694I) in 10 patients (3.9%) and detected another *MEFV* mutations, such as E84K, R202Q, E225K, R304R, R354Q, P369S, and R408Q in 61 patients (23.9%). 2) We identified *TNFRSF1A* mutations, such as V125M in 8 patients. 3) We identified less than 1% of frequency of mutations derived from East Asia healthy individuals in 9, 8, 12, 7, 5, and 3 location of *NLRP3*, *NOD2*, *NLRP12*, *PSTPIP1*, *NLRC4*, and *PLCG2*, respectively, in the patients with unknown fever, however, none of patients has clinical symptoms in eachautoinflammatory syndrome. Conclusions: These exhaustive analyses suggest that we could find the *MEFV* mutations from 11 responsible genes derived from autoinflammatory syndromes in 29.8% of the patients with unknown fever.

P3-250

A case of TAFRO syndrome developed with central nervous system disorder during the disease course

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Conflict of interest: None

A 61-year-old man presented with fever from the mid-June X year. He has been diagnosed with pleurisy in a previous doctor. He was transferred to our hospital at the beginning of July of the same year because the disease condition worsened. As a result of various examinations including lymph node biopsy, we diagnosed as TAFRO syndrome. The disease rapidly worsened during admission in our hospital and presented with respiratory and renal failure. So we administered steroid pulse therapy, tocilizumab, cyclosporine, rituximab but either drug was not effective. A consciousness disorder with bilateral abductive nerve paralysis appeared on the 58 th disease day. Although the brain MRI was normal, the cerebrospinal fluid test showed prominent rise of protein (4636 mg / dl). We suspected opportunistic infection, but various microbial tests were negative. Then we diagnosed central nervous system disorder by TAFRO syndrome, steroid pulse therapy and following prednisolone 0.8mg / kg / day were started. It was effective and respective disorder were improved. He was resistant to various therapeutic drugs, successfully treated with oral glucocorticoid therapy. Reported cases of TAFRO syndrome are rare, it is necessary to accumulate the symptom progression and an effective treatment regimen.

P3-251

Novel SNP mutation in NLRC4 in 1-year old girl with CAPS-like symptoms of fever and urticarial rash

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Conflict of interest: None

We report a one- year old girl with CAPS-like symptoms due to NLRC4 gene mutation by novel SNP mutation (p.P338S). Her father had episodes of unexplained skin rash in his early childhood. Her skin rash appeared at 1 year 4 months old, fever around 38 ° C began several times a week in the next month and continued every day thereafter. She referred to several hospitals but fever and rash did not improve with antibiotics. She was admitted to the previous hospital at 1 y7m of age. PSL was administered under a diagnosis of polymorphic exudative erythema, however, even 1.2mg/kg/day of PSL was ineffective. She was admitted to our Hospital. No abnormalities were found by bone marrow examination and any imaging studies. Drug fever was also denied. CAPS was finally suspected, and genetic examination was underwent at Kyoto University. As the result, novel SNP mutation (p.P338S) in NLRC4 was found without NLRP3 mutation. Even now symptoms have been repeated, her general condition remains well. Several reports have indicated that CAPS-like symptoms occur due to NLRC4 gene mutation, but the SNP mutation in our case has not been reported. Our case has pathological significance which may lead to one of new autoinflammatory syndrome.

P3-252

Functional effects of a *PYCARD/ASC* variant lacking exon2 in NLRC4 inflammasome activation

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Conflict of interest: None

[Objectives] We previously found the *PYCARD/ASC* variant mRNA lacking exon2 in Japanese patients with palindromic rheumatism (PR). We also reported that this variant PYCARD/ASC might interfere the NLRP3 inflammasome activation, at JCR2016. To investigate the effect of this variant in NLRC4 inflammasome activation, we compared IL-1β production of PBMCs and THP-1 cells expressing PYCARD/ASC wild type or the variant lacking exon2, which were stimulated by using flagellin as NLRC4 inflammasome activator. [Methods] PBMCs were obtained from six healthy donors expressing heterozygous *PYCARD/ASC* variant or homozygous wild type. THP-1 cells were expressed recombinant PYCARD/ASC wild type or the variant lacking exon2. These cells were primed by using PMA (0.5 μM), followed by stimulation with 100ng/ml flagellin. IL-1β concentrations in conditioned medium were measured by using ELISA. [Results] Activation rates in NLRC4 inflammasome showed lower trends in case with wild type. [Conclusion] Our results suggest that the variant *PYCARD/ASC* interfere with the NLRC4 inflammasome activation.

P3-253

Functional analysis of a *PYCARD/ASC* variant lacking exon2 in inflammasome activation

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Conflict of interest: None

[Objectives] We previously found a *PYCARD/ASC* variant mRNA lacking exon2 in Japanese patients with palindromic rheumatism (PR). To investigate the contribution to the pathogenesis of PR of this variant, we compared IL-1β production in PBMCs and recombinant THP-1 cells expressing variant or wild type PYCARD/ASC. [Methods] PBMCs were obtained from three healthy donors expressing heterozygous PYCARD/ASC variant and four healthy donors expressing homozygous wild type. We generated recombinant THP-1 cells expressing variant or wild type PYCARD/ASC. These cells were primed by 0.5 μM PMA, then stimulated with 100 μg/mL MSU. IL-1β concentrations in conditioned medium were measured by using ELISA. [Results] IL-1β concentrations without stimulation were 40.77±13.00 and 6.15±1.02 (pg/mL) in heterozygous and wild type homozygous PBMCs, respectively. The activation rates of inflammasome were 178±46 and 164±45 (%), in heterozygous and wild type homozygous PBMCs, respectively. Although IL-1β concentrations in THP-1 cells without stimulation were the same, concentrations with stimulation were 693.4±14.8 and 812.7±43.2 (pg/mL) in the case with variant and wild type, respectively. [Conclusion] Our results suggest that the variant PYCARD/ASC interferes with inflammasome activation.

P3-254

A case of periodic fever with trisomy 8

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Conflict of interest: None

【Clinical meaning】A 50 years old man developed periodic fever which was similar to familial Mediterranean fever (FMF), but he didn't have MEFV mutation. Bone marrow test showed he had trisomy 8. Plasma inflammatory cytokines were markedly elevated at attack phase. Treatments with colchicine, PSL, tacrolims and tocilizumab were ineffective, so we started to treat with azacitidine. This case is valuable in finding out a mechanism of the periodic fever.【Case】We report a 50 years old man who has developed periodic fever once in a few weeks for one year. He has been repeatedly hospitalized due to poor systemic condition with systemic arthralgia, myalgia and painful erythema at attack phase, though his condition is extremely good during the interictal period. Blood test showed elevation of inflammatory cytokines at attack phase. There was no mutation in his MEFV gene. We identified trisomy 8 in his bone marrow cells (19 of 20) but his blood profile did not fit for MDS. Several reports described that existence of trisomy 8 might trigger cytokine storm. Treatments with colchicine, PSL, tacrolims and tocilizumab were ineffective. Therefore, treatment with azacitidine, a drug for MDS, was initiated because it is reported that it reduces the production of inflammatory cytokine.

P3-255

Rheumatoid arthritis with latent tuberculosis infection presenting as eosinophilic pneumonia in a 65-year-old male patient

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Conflict of interest: None

The patient is a 65-year-old male who started having cough, sputum and slight fever from April, received antibiotic treatment without relief of symptoms. He was also suffering from multi joint pain from May. His physical examination revealed 12 tender joint counts, 5 swollen joint counts and normal lung sounds. Laboratory tests revealed uric protein (-), occult blood (-), CRP 6.66 mg/dL, WBC 11100 /μL, Eosinophil 33%, MPO-ANCA (-), PR3-ANCA (-), IgE 43 IU/mL, anti-CCP antibody 819.1 U/mL and RF 130 IU/mL. Computed tomography showed reticular shadow, infiltrative shadow and frosted glass shadow in his both sides lung. He also received bronchoscopy, his bronchoalveolar lavage fluid (BALF) had 25.0% eosinophil, so he was diagnosed with eosinophilic pneumonia. On the other hand, he complicated with latent tuberculosis infection (LTBI) because his laboratory data showed T-SPOT was positive, but smear staining and polymerase chain reaction of acid-fast bacilli with sputum and BALF was negative. So he was finally diagnosed with rheumatoid arthritis (RA) complicated with eosinophilic pneumonia and LTBI. It is important to treat RA carefully because of complication with eosinophilic pneumonia, and this is rare case of RA with LTBI presenting as eosinophilic pneumonia.

P3-256

A case of multiple arthritis with Multiple Myeloma which was first diagnosed as seronegative Rheumatoid Arthritis

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Conflict of interest: None

[Case] A 52 years old man, diagnosed with seronegative Rheumatoid Arthritis (RA), was introduced to our hospital. He had been treated with methotrexate and prednisolone, without effectiveness. Clinical examination and ultrasonographic assessment of joints revealed multiple arthritis which met the diagnostic criteria for RA. Two hours after first infusion of infliximab he developed fever which had continued for 2 weeks, and multiple arthralgia worsened. Further investigation of Laboratory data showed elevation of serum TP/Alb, hypercalcemia, decreased IgA and IgM level, and positive urine protein. Serum and urine protein electrophoresis revealed Bence Jones protein. We performed bone-marrow puncture and found increased number of plasma cells, thus he was diagnosed as Multiple Myeloma (MM). [Discussion] Some MM patients develop synovitis due to AL amyloidosis. Its clinical examination and laboratory findings are similar to those of seronegative RA, leading to difficulty differentiating diagnosis. Abnormal laboratory findings including immunoglobulin test, renal function, and electrophoresis, radiological imaging tests, and biopsy can be useful to find hidden MM.

P3-257

Three cases of rheumatoid arthritis patients with adult T-cell leukemia

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Conflict of interest: None

Clinical meaning: We report three cases of rheumatoid arthritis (RA) patients who developed adult T-cell leukemia (ATL) in the course of RA treatment in one hospital for 5 years. Immunosuppressant and biological agent has been introduced into RA treatment, and reactivation of various viruses has become an important problem. It is strongly suggested that immunosuppression by biological and conventional DMARDs may become the key mechanism of the emergence of ATL in our 3cases. Case1:

A 71-years-old woman was diagnosed with RA in 1993 and treated with abatacept and iguratimod. She later presented with lymphadenopathy and was diagnosed as lymphoma-type ATL in 2015. She has maintained partial remission after chemotherapy. Case2: A 52-years-old woman was diagnosed with RA in 2000 and treated with PSL, methotrexate (MTX) and tocilizumab. Abnomal lymphocytes appeared in his peripheral blood, and he was diagnosed as chronic-type ATL in 2011. He has maintained remission after chemotherapy and bone marrow transplant. Case3: A 72-years-old man was diagnosed with RA in 2011 and treated with PSL and MTX. Multiple masses appeared in his liver in April 2015. Liver biopsies revealed acute-type ATL. He was treated with chemotherapy, but later died of pneumonia.

P3-258

A case of malignant lymphoma presenting with multiple arthritis and peripheral edema, which misled to the diagnosis of RA or RS3PE

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Conflict of interest: None

Case: A 75-year-old woman presented with pain and stiffness of the shoulders and back of neck 3 months before admission, and subsequently developed multiple arthritis, pitting edema at bilateral dorsum of hands and foots, and an intermittent fever. After admission, treatment with Celecoxib, PSL, and MTX which had been prescribed at the outside hospital was continued while close examination was performed with a mind to rheumatoid arthritis (RA) and remitting seronegative symmetrical synovitis with pitting edema (RS3PE) syndrome as differential diagnosis. However, she became worse and had severe fever with pancytopenia and serum CRP, LDH and ferritin elevation two weeks after admission. Bone-marrow biopsy revealed a diagnosis of malignant lymphoma with hemophagocytic syndrome. Chemotherapy was started, resulting in resolution of all symptoms including arthritis and edema. Conclusion: We experienced the case of malignant lymphoma presenting with multiple arthritis and peripheral edema, which misled to the diagnosis of RA or RS3PE. A careful attention is necessary in diagnosing and treating patients with multiple arthritis and peripheral edema because paraneoplastic syndrome can show RA-like or RS3PE-like symptoms.

P3-259

An IRIS-like phenomenon after recovery from febrile neutropenia in a patient with RA on MTX and tocilizumab

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Conflict of interest: None

A 73-year-old woman, treated for rheumatoid arthritis with MTX and tocilizumab since 2012 was transferred to our hospital because of agranulocytosis and acute renal failure. Antimicrobial therapy was initiated immediately and blood culture grew *E. coli*. A CT scan subsequently revealed iliopsoas abscesses and bacterial spondylodiscitis. Despite recovery from agranulocytosis in a week and effective antimicrobial therapy, high fever continued and her condition deteriorated clinically. After confirming that bacterial spondylodiscitis was under control and excluding other possibilities of high fever such as miliary tuberculosis and lymphoma, low dose steroid therapy was initiated. Soon after that her general status was dramatically improved. Immune reconstitution inflammatory syndrome (IRIS) is a collection of inflammatory disorders associated with paradoxical worsening of preexisting infectious processes after the initiation of anti-HIV therapy in HIV infected patient. In this case, we speculate that excessive immune response similar to IRIS was induced against bacterial infection under unbalanced restoration of the immune system after severely immunosuppressed state with IL-6 suppression by tocilizumab and agranulocytosis due to MTX use in acute renal failure.

P3-260

Management of patients with rheumatoid arthritis and an active malignant disease

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Conflict of interest: None

【**Objective**】When rheumatoid arthritis (RA) and malignant disease occur concurrently in the same patient, this sometimes poses a therapeutic challenge to either the rheumatologist or the oncologist. We reported the current management of RA patients with an active malignancy in a cancer center hospital.【**Methods**】Patients with RA and active malignancies who were referred to the department of musculoskeletal oncology between January 2015 and October 2016 were included in this study. We surveyed the management of those patients focusing on cancer treatment, RA treatment, and final outcome according to a retrospective review of medical records.【**Results**】Ten patients (7 females and 3 males, median age of 68.5 years) were available for the analysis. The somatic symptoms were directly related to RA in 5 patients and to malignancy in another 5. Two patients had never been previously diagnosed as RA. Of the 8 patients with history of RA, 5 discontinued all DMARDs. After the withdrawal of DMARDs, two patients required glucocorticoid therapy. At last oncological follow-up, 2 patients were DOD, 7 were AWD, and 1 was CDF.【**Conclusion**】In RA patients with active malignancies, treatment decisions should be a shared decision between the rheumatologist, the oncologist, and the patient.

P3-261

Symptomatic diversity of AA amyloidosis secondary to rheumatoid arthritis

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Conflict of interest: None

Prevalence of AA amyloidosis secondary to rheumatoid arthritis (RA) has decreased recently thanks to the remarkable advances in treatment, management, and so on, with RA. In a real daily practice, however, we rheumatologists will encounter patients with AA amyloidosis secondary to RA, whose symptoms are so different from each other clinically in the process of the disease state. From the symptomatic point of view under developed medical milieu, we defined the following five types of AA amyloidosis secondary to RA in clinical symptoms;(1) asymptomatic AA amyloidosis, (2) overt AA amyloidosis without inflammatory activity, (3) amelioration in AA amyloidosis, (4) silent AA amyloidosis with adverse effects of advanced biological treatments, (5) AA amyloidosis in extreme terminal stage. We must take measures depending on each type when seeing a patient with AA amyloidosis secondary to RA, with keeping our eyes on multiple organ functions without losing point of no return in daily practice, within watching out over-suppression among immunological states in each case of AA amyloidosis secondary to RA.

P3-262

Possible involvement of interleukin 6 signaling in two cases of AA amyloidosis nephropathy complicated in Rheumatoid arthritis

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Conflict of interest: None

Case one is a 70 years old man. He had been treated for rheumatoid arthritis for more than 30 years, though kidney dysfunction progressed. Etanercept or abatacept was not effective for arthralgia, and he was reffered to our hospital at the age of 67. Serum creatinine level was already

as high as 2.68 mg/dl. AA amyloidosis of the kidney was diagnosed by kidney biopsy, and Tocilizumab was started. Serum creatinine level is maintained around 2.69 mg/dl four years after the initiation of Tocilizumab. Case two is a 62 years old woman. She had developed RA when she was 20 years old, and had developed bucillamine induced kidney injury during the therapy course. When she was referred to our hospital her serum creatinine level was as high as 4.4 mg/dl. In spite of etanercept induction serum creatinine increased to 6.0 mg/dl. Next we applied Tocilizumab, and creatinine dropped to 3.7 mg/dl. We diagnosed by kidney biopsy as AA amyloidosis being the cause of kidney dysfunction. Eight years after initiation of Tocilizumab, her serum creatinine is maintained around 4.4 mg/dl. The two cases showed the possibility that underlying mechanism concerning deterioration of renal function is related to interleukin 6 signaling in AA amyloidosis.

P3-263

A simple detection test for AA amyloid in abdominal fat

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Conflict of interest: None

Background. Detection of AA amyloid in the biopsy materials is not difficult with the use of histological methods. However, there is some material like abdominal fat aspirates, which are not easy to process into histology specimens. Here, we introduce a simple method for suspecting the presence of AA amyloid. **Materials and methods.** Two monoclonal antibodies, anti-SAA30 and anti-SAA90, were utilized. The number indicates the epitope region in SAA molecule. Since AA amyloid usually defects the carboxyl terminal region beyond the residue 77, the positive reaction with anti-SAA30 and the negative reaction with anti-SAA90 may suggest the presence of AA amyloid. The antibodies were conjugated to gold colloid particle. The biopsy materials were sonicated and mixed with the antibody-particle solution. **Results.** The detection sensitivity for both the systems was approximately 10 ng/mL when rSAA76 was used as the sample. When reacted with anti-SAA30 and was 10 ng/mL when recombinant SAA was reacted with anti-SAA90. Gastric mucosa samples from AA amyloidosis patients resulted in positive with anti-SAA30 and negative with anti-SAA90. **Conclusions.** The test was simple and easy to use. The combined use of the two antibody system may avoid the contamination of SAA-high blood.

P3-264

A case recurring arthritis due to Calcium pyrophosphate deposition disease (CPPD) with Familial hypocalciuric hypercalcaemia (FHH)

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Conflict of interest: None

A 79-year-old woman developed rapidly progressive right-side foot swelling. Antibiotics were administered by first-aid medical doctor and made her symptoms better. She had one kidney removed for kidney transplantation and had lumbar spondylolisthesis, lumbar spinal canal stenosis and cervical disc herniation as a medical history. After 10 days hospitalization, bilateral knee revealed a new swelling. Intra-cartilage calcification with active synovitis was depicted in shoulder, knee and wrist joint by musculoskeletal ultrasound. The Calcium pyrophosphate crystals were confirmed by synovial fluid obtained by means of joint aspiration. It was diagnosed as CPPD and the medical treatment was carried out with analgesics. However colchicine treatment was required because of the recurring arthritis due to CPPD. In addition, hypercalcemia was presented and FHH became clear by examination of secondary CPPD. Although it is well known that hypercalcemia is one of the causes of CPPD, FHH induced hypercalcemia finally led to recurring CPPD. Here we report a valuable case of CPPD with FHH based on consideration from literatures.

P3-265

A rheumatoid arthritis patient complicated with adenine phosphoribosyltransferase deficiency and unilateral renal agenesis

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Conflict of interest: None

A 40-year-old woman with unilateral renal agenesis (URA) and a history of urolithiasis was diagnosed with rheumatoid arthritis (RA). Since her arthritis was refractory to methotrexate and she developed urolithiasis twice within two years, she was admitted to our hospital. She showed typical RA manifestations and her symptoms was resolved by adalimumab. Moreover, we revealed that her urolithiasis was caused by adenine phosphoribosyltransferase (APRT) deficiency, which is a rare autosomal recessive inherited metabolic disorder leading to renal stones, crystal nephropathy, and renal failure. For prevention of urolithiasis and those complications, we immediately administered a xanthine oxidase inhibitor febuxostat and urolithiasis has not relapsed for more than a year. This is a first case report of RA patient complicated with URA and APRT deficiency. Since renal involvements often worsen prognosis and hamper aggressive immunosuppressive treatment for RA, immediate diagnosis and treatment of such rare but treatable extra-articular involvements contribute to better management of RA. Recently, epistatic gene interactions are going to be known to account for the susceptibility of certain diseases, this case might be of genetic importance to consider the role of URA and APRT in RA.

P3-266

Characteristics of avascular necrosis in rheumatic disease

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Conflict of interest: None

[Object] Avascular necrosis (AVN) is a serious complication in patients receiving corticosteroid. The aim of this study was to clarify the characteristics of AVN in rheumatic disease. [Methods] 17 patients (3 men and 14 women) who developed AVN in 2004 to 2016 were analyzed retrospectively. AVN was diagnosed by MRI abnormality or radiographical change. [Results] Underlying diseases were followed: 10 SLE, 4 PM/DM, 1 MCTD, 1 Takayasu arteritis, 1 rheumatoid vasculitis. The mean age of underlying disease onset was 31.9 years, and the age of AVN onset was 37. Only 1 patient developed unilateral AVN, 9 were performed surgery. 7 patients were cigarette smoker, 9 patients had dyslipidemia, antiphospholipid antibodies were detected in 3 patients. The mean maximum dose of prednisolone was 52.1 mg, and the dose at the onset of AVN was 13.4 mg. 14 patients received steroid pulse therapy and 8 required more than twice. In 14 patients, 3 were received heparin in the course of steroid pulse therapy. 7 were administered antiplatelet agent, and 2 were administered anticoagulant agent. [Conclusions] SLE was the most common disease in AVN patients, and steroid pulse therapy was a risk factor of AVN. Even though administered anticoagulant or antiplatelet agent, AVN was developed.

P3-267

A Case of Symmetric Ankle Arthritis Diagnosed with Löfgren's syndrome

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Conflict of interest: None

[Introduction] Between 15% and 25% of patients with sarcoidosis have arthritis. Symmetric ankle arthritis is observed characteristically in sarcoidosis. Löfgren's syndrome is characterized by bihilar lymphadenopathy, arthritis and erythema nodosum. It was reported that among patients with sarcoidosis suffering from arthropathy, a quarter of them had clinical manifestations of Löfgren's syndrome. We report a case of symmetric ankle arthritis diagnosed with Löfgren's syndrome. [Case] A 39 year-old woman presented with swelling and pain of bilateral ankles lasting for a month. Physical examination revealed symmetric ankle arthritis and tender subcutaneous nodules in both pretibial locations. She had no respiratory symptoms. Chest radiograph and CT showed bihilar lymphadenopathy and multiple nodules in both lung fields. A skin biopsy of lower leg was consistent with erythema nodosum. A diagnosis of Löfgren's syndrome was made based on these findings. Results of spirometry test and echocardiogram were normal. She was treated with oral naproxen which resulted in a rapid clinical response. [Conclusion] It is important to examine skin lesion and perform chest images on patients with symmetric ankle arthritis for ruling out sarcoidosis regardless of absence of associated symptoms.

P3-268

Genetic diagnosis of familial juvenile hyperuricemic nephropathy

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Conflict of interest: None

Familial juvenile hyperuricemic nephropathy (FJHN) is an autosomal dominant disease characterized by juvenile-onset hyperuricemia due to decreased urate excretion, gout, and interstitial nephritis that progresses to end-stage renal failure (ESRD). Although no effective medical treatment has not yet been developed, renal transplant is curative. Four causative loci of FJHN are reported so far. The most prevalent one is FJHN1 that locates on the chromosome 16p, Uromodulin gene (UMOD). Here, we report our experiences of the genetic testing for FJHN at our institution. 【Subjects and Methods】The subjects are 72 cases among 40 families, who were clinically suspected to had FJHN. The mutations were identified by UMOD sequencing, and confirmed by PCR-RFLP when possible. 【results and discussion】We detected causative mutations of the UMOD gene in 14 cases among 6 families. 14 cases consisted of 9 men and 5 women, aged 5 to 41 at the time of genetic diagnosis. all the patients had hyperuricemia. Two cases experienced gouty attacks. The identified mutations were all missense mutations, and cysteine residues were involved among 5 families. The study shows that FJHN is important as one of the causes of juvenile-onset hyperuricemia and female hyperuricemia/gout.

P3-269

Prognosis for interstitial lung disease with connective tissue disease

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Conflict of interest: None

[Objectives] To investigate the prognosis of interstitial lung disease (ILD) with dermatomyositis (PM/DM), rheumatoid arthritis (RA), systemic sclerosis (SSc), and microscopic polyangiitis (MPA). [Methods] Of patients with CTD who were attend to our hospital between 2003 and 2012, the subjects examined prognosis and prognostic factors using the clinical data. [Results] There were 267 patients with CTD-ILD, consisting 71of 267 males and 196 females, with a mean age of 67 years. The most poor 1-year survival rates after the treatment of PM/DM was 79%. The 5-year of RA and PM/DM were 81% and 79%, respectively. The 10-year of RA and MPA were 69% and 69%. The best 10-year of SSc was 92%. There were many UIP in the RA and MPA, and NSIP in the SSc. [Conclusion] RA and MPA with UIP become a problem in the long-term survival rate of 5 - 10 years, and treatment devises are required in the future.

P3-270

Clinical profile of rheumatoid arthritis patients with obstructive sleep apnea syndrome

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Conflict of interest: None

<Purpose>The exacerbation of pain and fatigue by sleep disorders in rheumatoid arthritis (RA) and the risk of obstructive sleep apnea syndrome (OSAS) in patients of rheumatic disease has been reported. We aimed to clarify the clinical profile of RA complicated by OSAS. <Methods>We examined AHI by polysomnography in OSAS suspected objects in our hospital in 2008-2015, of which objects, RA was complicated by OSAS in 14 cases. We evaluated the relationship between AHI (apnea hypopnea index)/JESS (Japanese version of the Epworth Sleepiness Scale) and RA Stage/disease duration by correlation analysis. <Results>The age of the patients was 64.6±8.6 years, disease duration was 11.4±11.9 years, and RA was at the early to advanced stage (Steinbrocker Stage),5 in I,3 in II,2 in III and 4 in IV. AHI was 51.0±22.5 and JESS was 5.08±2.91. AHI showed a positive relationship tendency and JESS showed a negative relationship tendency with RA Stage and disease duration, without significant difference. <Conclusions>The study showed the possibility that the higher RA stage is, the higher OSAS severity is in RA patients. We suggest that we investigate the complication of OSAS by polysomnography and examine the introduction of therapy in RA patients, as joint findings and sleep disorders influence each other.

P3-271

Successful treatment of organizing pneumonia with low-dose steroid in a patient with rheumatoid arthritis

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Conflict of interest: None

A 75-year old man was diagnosed as rheumatoid arthritis (RA) in 1998 and had been good condition treated with 2.5mg/day prednisolone (PSL) and 50mg/day bucillamine until the beginning of February 2016. He admitted to our hospital for fever and arthralgia in February 17. Chest CT shows multiple consolidations and ground glass opacities (GGO) in the left lung. After tuberculous and bacterial pneumonia were denied, organizing pneumonia (OP) was clinically diagnosed. PSL12.5mg/ day with 3 days of methylPSL 125mg/day was started and PSL reduced on 16th day to 5mg/day for 2 months and maintained. There being no relapse for 8 months, a low-dose PSL is considered effective. As for the treatment of cryptogenic OP (COP), PSL0.5 - 1mg/kg/day (more than moderate dose) is recommended. OP with RA differs from COP clinically just in this point, so we call it Rheumatic OP (ROP). COP is an inflammation having essentially fibrous elements as idiopathic interstitial pneumonias (IIPs) but ROP an inflammation which fibrosis occurs when postponed. Also, GGO is an interstitial pneumonia (IP) and effective with a low-dose PSL, so IP with RA differs from an idiopathic pulmonary fibrosis. As for the clinical significance, OP and IP with RA differ from IIPs and could be treated with a low-dose steroid.

P3-272

A case of steroid-resistant organized pneumonia

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Conflict of interest: None

<Case>A 78-year- old man with dry cough was diagnosed as interstitial pneumonia (IP) by local doctor, and administered 20mg of Predonine (PSL), which didn't work. Rheumatoid arthritis (RA) was suspected due to the positive rheumatoid factor and the patient was referred to our hospital. His chestCT scans showed non-segmental infiltrative shadows, which led to the diagnosis of organized pneumonia (OP). The case seemed to be lack for feature of RA. PSL was increased to 40mg, then cough disappeared and CRP turned to negative, while CT findings improved partially though still remained. After administration of PSL 40mg for 4 weeks, he was left hospital. 4 weeks later, he was re-hospitalized after developing fever and dyspnea. His blood test showed hypoxemia and increases in CRP and SP-D levels, as CT exhibited interstitial shadows and infiltrative shadows scattered over the total lung field. PSL was increased to 60mg, which resulted to be afebrile and CRP turned negative. Since OP remained while the interstitial shadows vanished, cyclosporineA (CyA) was administered. 6 monthslater, pneumonia improved and PSL 10mg and CyA 100mg has been continued. <Discussion> OP is considered to be steroid-responsive disease. We had better try early administration of CyA to steroid-resistant cases.

P3-273

The safety and efficacy of therapy with certolizumab pegol for early rheumatoid arthritis patients of childbearing age

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Conflict of interest: None

Women of child-bearing age with rheumatoid arthritis (RA) often question the use of medications. We assessed the efficacy and safety of certolizumab pegol (CZP) for early RA in patients of childbearing age. [Material and Methods] Two patients with early RA were evaluated. Case 1: A 36-year-old female with ACPA > 150. She stopped using 1 mg of tacrolimus (TAC) when intending a second pregnancy, and started using CZP. Case 2: A 29-year-old female with ACPA > 200. She will have marriage and hopes to have a child; she started using CZP. Effectiveness was evaluated using EULAR improvement criteria, DAS28-CRP scores, and CDAI results assessed at introduction, compared with the last observation. Safety was assessed by monitoring adverse events. [Result] A good response was observed in the EULAR improvement criteria, and DAS28-CRP and CDAI scores decreased in both cases. Case 1 was pregnant 3 months after CZP was started; CZP was stopped, and there has been no exacerbation of arthritis. The pregnancy has proceeded without problems. Adverse events were not observed in either case. [Conclusion] For patients desiring to bear children, it is important to control disease activity before pregnancy. CZP has low placental permeability, and is useful for patients with RA who wish to bear children.

P3-274

Rheumatic disease medical treatment at the time of hope for the pregnancy

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Conflict of interest: None

[Background] "Japanese RA medical treatment guideline (2014)" is announced, and we can treat RA patient using Treat to Target strategy with MTX and/or biologics. Also, we can control disease activity of SLE (and other connective tissue diseases) patients with corticosteroid and immune-suppressive drugs. Treatment of the pregnant woman and the lady planning pregnancy, is always a difficult problem. [Objects and Method] There were 15 women planning pregnancy (RA 10 and SLE 5) at my clinic (about 5 years). And, I reviewed clinical information about these 15 cases. [Result and Discussion] I changed the RA treatments at the time of a pregnancy request. Case (1) ETN→ETN, (2) MTX+GLM→GLM, (3) MTX→none, (4) PSL5mg→PSL5mg, (5) ETN+PSL2mg→ETN+PSL2mg, (6) MTX→none, (7) ETN→ETN, (8) MTX→ETN, (9) MTX+PSL5mg→CZP (10) Bucillamine→GLM. There were five childbearing in RA patients. About SLE 5 cases, (a) PSL10mg→PSL10mg, (b) PSL10mg→PSL10mg, (c) no medication→no medication, (d) PSL15mg→PSL15mg, (e) PSL13mg→PSL13mg. There were three childbearing and one artificial interruption. I will contrive about pregnancy patient (RA and SLE) treatment using "BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding".

P3-275

The outcome of 15 patients with connective tissue disease associated pulmonary arterial hypertension (CTD-PAH) in our hospital

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Conflict of interest: None

[Object] CTD-PAH has a lower survival rate compared with idiopathic PAH. Furthermore, recent studies have suggested that PAH associated with SSc is more severe than PAH associated with other CTDs. [Methods] Fifteen CTD-PAH patients diagnosed by right heart catheterization (RHC) received follow-up RHC from April 2008 to October 2016. We analyzed the difference in mean pulmonary artery pressure (mPAP) between pre-treatment and the most recent measurement values to assess the efficacy of treatment, depending on the primary disease. [Results] Primary diseases were SSc (including CREST) in 6 patients, SLE in 4, MCTD in 1, and SjS in 4. There was a significant difference in mPAP between the pre-treatment (39.3 ± 13.2 mmHg) and most recent values (28.5 ± 10.3 mmHg). Mean PAP of 10 cases decreased, and that of 7 cases fell to within normal limits. Mean PAP of SSc patients was not significantly different after the treatment. Moreover, ΔmPAP of SSc patients did differ significantly from that of non-SSc patients. [Conclusion] Active therapy for PAH was effective for CTD-PAH patients. However, in SSc patients, there was no difference in mPAP before and after the treatment. We concluded that the pathology of SSc-PAH may be different from that of PAH associated with other CTDs.

P3-276

Two cases of protein-losing gastroenteropathy associated with rheumatic diseases

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Conflict of interest: None

Case 1: In 2015, a 77-year-old woman was referred to our department because of hypoalbuminemia. She had a diagnosis of rheumatoid arthritis in 1996, and she had been treated with methotrexate and prednisolone (PSL 2.5 mg/day). Serum albumin (Alb) level was 0.9 g/dl. Protein-losing scintigraphy revealed that Tc-labeled Alb was accumulated to the small intestine, and α1-antitrypsin clearance test was positive. She had a diagnosis of protein-losing gastroenteropathy (PLGE). After increasing the dose of PSL up to 30 mg/day, Alb level was elevated to 2.7 g/dl. Case 2: In 2015, a 71-year-old woman was referred to our department because of hypoalbuminemia. She had been suffering from dry eye and dry mouth for a year. Serum Alb level was 1.0 g/dl. Sjögren's syndrome was diagnosed because anti-SSA antibodies, Schirmer's test and Saxon test were positive. Protein-losing scintigraphy revealed that Tc-labeled albumin was accumulated to the stomach and the colon, and α1-antitrypsin clearance test was positive. She had a diagnosis of PLGE. Af-

ter treatment with PSL of 40 mg/day and tacrolimus, Alb level was elevated to 3.4 g/dl. Discussion: Both patients did not complain diarrhea. PLGE should be considered as a differential diagnosis when patients with rheumatic diseases have hypoalbuminemia.

P3-277

NSAID ulcer prevention in elderly patients with collagen tissue disease (CTD) and no history of gastrointestinal ulcers

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Conflict of interest: None

[Objective] NSAID treatment is becoming more prevalent because the number of the elderly with CTD has increased recently. They often affect NSAID ulcers, even when used in the short-term (Intern Med. 2014; 53: 1107-11). Currently, patients with a history of gastrointestinal ulcers are administered acid inhibitors during NSAID therapy, but those without controversial. [Methods] We examined patients with CTD, aged ≥65 years, without a history of ulcers who were prescribed NSAID for over a week from January 2014 to December 2014 at our hospital. 117 patients were included, and 70% of them had rheumatoid arthritis. We analyzed their baseline characteristics and the incidence of NSAID ulcers during an observational period until September 2016. [Results] Loxoprofen was the most used drug, followed by celecoxib. For long-term use, celecoxib was the most widely prescribed NSAID. The rate of concurrent use of steroid, anticoagulant or antiplatelet drugs, and acid inhibitors was 66%, 13%, and 46%, respectively. NSAID ulcer developed only in one case during the observation. [Conclusions] In the elderly with CTD and no history of ulcers, if a high risk of gastrointestinal bleeding is not considered, we do not necessarily have to cope with NSAID ulcers using acid inhibitors.

P3-278

A case of rheumatoid arthritis with methotrexate-induced multiple organ failures

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Conflict of interest: None

A 66-year-old woman was admitted to our hospital due to pyelonephritis. She has been suffering from rheumatoid arthritis (RA) for 9 years and treated with methotrexate (MTX). Recent her condition of RA has been stable by weekly MTX therapies (12mg/week). After hospitalization, she showed severe oral mucositis, renal dysfunction, and hepatotoxicity. These symptoms were rapidly worsening. Leucovorin therapies were started on 7th day because of an increase of her serum concentration of MTX (0.07 μ mol/L). In spite of this treatment, her creatinine and total bilirubin levels were increased to 1.61 mg/dl and 24.8 mg/dl on 12th day, respectively. Pancytopenia were also observed on 9th day. Furthermore, pleural effusion and ascites were accumulated drastically, thus she showed multiple organ failure. Because her pancytopenia was not improved even after a decrease of serum MTX concentration (0.02μ mol/L), treatments of granulocyte colony stimulating factor (GCF) and blood transfusion were performed. These treatments were effective for her pancytopenia, and other symptoms were improved before 50th day. This case was MTX-induced refractory multiple organ failure. We report this case and nine other cases of MTX-related pancytopenia in our hospital with literature considerations.

P3-279

Analysis of clinical features for venous thromboembolism in patients with systemic autoimmune disease

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Conflict of interest: None

<Objectives>The objective of this study was to evaluate clinical characteristics of autoimmune disease with VTE, including deep vein thrombosis (DVT) and pulmonary embolism (PE), in our institute. <Methods>This was a retrospective observational study performed at our institute on patients admitted from January 2009 to September 2015. All 49 patients in which VTE (10DVT/39PE) was highly suspected were diagnosed by enhanced computed tomography scanning (CT). <Results> Sixteen patients with autoimmune disease and 33 patients with non-autoimmune disease in our institute were enrolled in this study. The Plasma D-dimmer value at the onset of VTE was significantly lower in the autoimmune disease group than in the non-autoimmune disease group (P <0.05). The period from the diagnosis of autoimmune disease to the onset of VTE was 56% of the total 24 months. Oral prednisolone was administered at 20.5 mg/day on average in 12 cases of the autoimmune disease group. <Conclusion> The D-dimmer value at the time of VTE onset was significantly lower in the autoimmune disease group than in the non-autoimmune disease group. This suggests that the risk of VTE increases in high-dose steroids users with autoimmune diseases, particularly from onset to several years later.

P3-280

A case of sarcoidosis with variety of organ lesion which include extraocular muscle and ureter, and a pathological change of caseous granuloma

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Conflict of interest: None

We report a case of sarcoidosis which include a variety of organ lesions such as ocular muscle, ureter, skin, skeletal muscle and bilateral hilar lymphadenopathy at the same time. The case is 74-year-old man who had been diagnosed as thyroid gland ophthalmopathy and treated by corticosteroid. However, his double vision got worse when the corticosteroid was less than 5 mg/ day. From the biopsy of bilateral hilar lymphadenopathy, noncaseous granuloma was found, but from the right eye orbit, caseous granuloma was found. We had a differential diagnosis of sarcoidosis, tuberculosis, non-tuberculous mycobacteriosis, malignancy, malignant lymphoma and ANCA associated disease. We underwent as much of the biopsy as possible and we conclude that diagnosis is sarcoidosis. We start to treatment of corticosteroids and methotrexsate and he has a good clinical course.

P3-281

A case of acute onset sarcoidmyopathy

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Conflict of interest: None

Sarcoidosis is a rare disease characterized by granulomatous lesions of multi-organ involvement, especially lymphoid organs and lungs. It's muscle involvement is relatively uncommon and classified into three types of chronic, nodular and acute myopathy. The last one is the least common. Here, We show a 60 year old female with sarcoidosis which presented acute onset high grade fever, myalgia and sever muscle weakness on admission. On the laboratory study, creatine kinase level was elevated, and MRI T2 fat suppression image showed high signal of her proximal muscles reflecting inflammatory changes. We performed muscle biopsy and it revealed non-caseous granuloma around damaged muscle fibers. After infectious causes ware excluded, she was diagnosed acute type sarcoidomyopathy, that's it's the rarest type, and started to treat with glucocorticoid. Her clinical course is good.

P3-282

Ostitis in the vertebral body and humerus by Treponema pallidum

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Conflict of interest: None

(Case) 22 year old Japanese female (Chief complain) Elbow pain, back pain, oral and genital ulceration (History of present illness)One month bofore admission, the patient had left elbow pain which was diagnosed as muscle strain by an orthopedist. After that, the patient felt back pain gradually. Two weeks later, the patient had painful oral and genital ulcers, which was diagnosed as infection of herpes virus and was prescribed bidarabin ointment by a gynecologist but the genital ulcer didn't improve. (Clinical course) On admission day, physical examination showed circular desqumating skin rush with pigmentation at bilateral palms and soles. Also she had local thoracic vertebral pain. We re-evaluated her symptoms and all syphilis test, which are RPR, TPHA and FTA-ABS showed all high-positive. Thoracolumbar spine MRI revealed ostitis lesion (high signal on STIR and low signal on T1WI) at the second and sixth thoracic vertebras. We diagnosed ostitis and ulceration caused by secondary syphilis. The patient was treated with 3 million unit of intravenous aqueous penicillin G every 4 h for 14 days, followed by 3000 mg/day of amoxicillin p.o. (Summary)We report a case of secondary syphilis presenting ostitis at thoracic vertebra with some literature review.

P3-283

Adalimumab improved erythema nodosum conbined with Takayasu arteritis and Crohn's disease

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Conflict of interest: None

Background: Autoimmune diseases sometimes are overlapped, however, there has been few reports about the overlap of Takayasu areteritis (TKA) and Crohn's disease (CD). Case: A 45-year-old woman was admitted to our department due to the deterioration of erythema nodosum (EN), arthritis, and colitis. She repeated EN on her legs until 21 years old. At the age of 30, she presented diarrhea and was diagnosed CD, and mesalazine was started. At the same time, loss of pulsation was noticed on her left arm. At the age of 33, she was diagnosed TKA. High dose of prednisolone (PSL) (1mg/kg) was started, and other immmunosupressants (MTX and CyA) were added. At the age of 41, EN on her legs sometimes relapsed and remitted. On admission, serological inflammation (CRP 2mg/dL, ESR 80mm/h) continued, and EN and arthritis on the lower legs was were deteriorated. Radiological studies revealed that there was no apparent progression of vascular lesions caused by TKA. However, thickening of gut wall and inflammatory view of gut lumen was observed, which indicated that CD was active. After adalimumab was started, these symptoms were clearly improved. Here, we report this rare overlap case with some literature review.

P3-284

Overlap syndrome of SSc and MPA complicated with TMA successfully treated with rituximab : A case report

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Conflict of interest: None

A 81-year-old woman with a 11-year history of systemic sclerosis was admitted to our hospital with leg edema, pleuroperitoneal effusion and proteinuria. She was diagnosed as microscopic polyangitis (MPA), based on glomerulonephritis, interstitial pneumonia and MPO-ANCA positivity. It was pulmonary and kidney type, but each were mild activity, 0.8 mg/kg of PSL has been begun. After that, hypertension and hypercreatinemia led to the diagnosis of sclerotic renal crisis (SRC), furthermore thrombocytopenia and erythrocyte fragmentation were suggestive of appearance of thrombotic microangiopathy (TMA). The immediate initiation of ACE inhibitor and plasma exchange (PE) therapy was not effective. We tried steroid pulse therapy and got improvement, but relapse was occurred soon. We thought immunosuppressant also became good coarse, we tried weekly Rituximab and achieved complete remission. TMA has various cause, explication of the new pathological mechanism were being developed such as complement related aHUS and anti CD36 antibody in recent years. It is necessary to be reconsidering the cause and the treatments while estimating the condition accurately, we reported including new knowledge.

P3-285

Adverse outcome after infectious hospitalization in patients with systemic lupus erythematosus

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Conflict of interest: Yes

Background: The outcomes after infectious hospitalization in patients with systemic lupus erythematosus (SLE) were not completely understood. The purpose of this study is to evaluate the risk of complications and mortality after infectious hospitalization in patients with SLE. **Methods:** We conducted a retrospective cohort study of 289167 people with infectious hospitalization (due to pneumonia, urinary tract infection, septicemia, or cellulitis) and identified 5591 of them had history of SLE using Taiwan's National Health Insurance Research Database 2008-2013 claims data. Logistic regression was used to calculate the odds ratios (ORs) and 95% confidence intervals (CIs) of complications, intensive care, and mortality associated with SLE after the admission. **Results:** Hospitalized patients with SLE had higher risks of post-infection acute renal failure (OR 1.34, 95% CI 1.10-1.63), intensive care (OR 1.19, 95% CI 1.06-1.35) and mortality (OR 1.47, 95% CI 1.21-1.79) compared with non-SLE patients. SLE patients also had higher medical expenditures during infectious hospitalization than non-SLE group (2865±4797 vs. 2458±3795 US dollars, p=0.0002). **Conclusion:** Patients with SLE showed more adverse events after infectious hospitalization compared with non-SLE people. These findings suggest the need to revise the protocols for infectious admission care for this population.

P3-286

Can zolendronic acid use lead to impair renal function in osteoporosis patients?

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Conflict of interest: None

Objectives: Bisphosphonates are recommended in patients with osteoporosis patients. clinical concerns had been considered in kidney safety. This study investigated the safety of bisphosphonate effects on renal function in patients with magnetic resonance imaging (MRI)-proven acute osteoporotic vertebral fractures after vertebroplasty. **Methods:** This retrospective study was conducted in osteoporotic patients with acute vertebral fractures treated with vertebroplasty between January 2001 and December 2015. Their gender, age, body mass index (BMI, kg/m^2), comorbidities were recorded, as well as their use of zolendronic acid. Those with increase in creatinine was defined as progress of renal function. Logistical regression was used to adjust the variables. **Results:** There were 989 patients (783 females; mean age, 74.08±9.26 years). 71patients accepted zolendronic acid, the others accept other anti-osteoporotic agents. 35 (49.3%) of zolendronic acid had increased creatinine, while 379 (41.3%) of non-zolendronic acid had creatinine changes (p=0.117). After

adjust variables, zolendronic acid did not increase creatinine (p=0.291; OR: 0.750; 95% CI: 0.440-1.279). (Table 1) **Conclusion:** Zolendronic acid use did not lead to increase in creatinine as compared with the control group. However it need more cases to confirm this findings.

P3-287

The use of hand perfusion scintigraphy to assess Raynaud's phenomenon associated with hand-arm vibration syndrome

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Conflict of interest: Yes

Purpose This study aimed to evaluate the hand perfusion scintigraphic features of hand-arm vibration syndrome (HAVS) and to compare these with the features of primary and secondary Raynaud's phenomenon (RP) associated with rheumatic diseases. **Patients and Methods** Hand perfusion scintigraphy was performed in 57 patients with primary RP, 71 patients with HAVS-related RP, and 36 patients with rheumatic disease-related RP. Patients' clinical details were collected by a retrospective review of medical records. We calculated 6 ratios by using the time-activity curve and static blood pool images, the chilled to ambient hand and wrist ratios of the first peak height, initial slope, and blood pool uptake. We analysed 3 morphologic characteristics: slow progress pattern, paradoxically increased uptake pattern in the time-activity curve, and the inhomogeneous radioactivity uptake in the blood pool image. **Results** All of the 71 patients with HAVS-related RP were mine workers. The onset of RP after exposure to vibration was at 21.8 ± 7.3 years, with 26.3 ± 7.0 years of vibration exposure time. The chilled to ambient hand ratios of the first peak height and the initial slope were significantly lower in patients with HAVS-related occupational RP than in patients with primary RP. The presence of a paradoxically increased uptake pattern was significantly lower in HAVS than in primary RP. **Conclusions** There were significant differences in hand perfusion scintigraphic features between primary RP and HAVS. These results suggest that the underlying pathophysiology of the two diseases differs; thus, different criteria might be applied for their evaluation.

P3-288

A case of relapsing polychondritis showing personality changes and cognitive impairment

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Conflict of interest: None

Relapsing polychondritis is a rare, multisystem autoimmune disease. It is characterized by recurrent inflammation of the cartilage and connective tissues in the body. In this paper, we describe a case of relapsing polychondritis initially diagnosed as leptomeningeal meningitis with symptoms of cognitive dysfunction and personality changes. A 63-year-old male developed cognitive impairment and fever. Brain magnetic resonance imaging revealed leptomeningeal and periauricular hyperintensities. A cerebrospinal fluid exam showed aseptic meningitis. As he developed hearing difficulties, audiometry showed sensory neural hearing loss. On physical examination, erythematous swollen auricles were noted, consistent with inflammation with perichondritis on auricle biopsy. He was diagnosed with relapsing polychondritis accompanied by leptomeningeal meningitis and treated with methylprednisolone (62.5mg/day for 3 days) followed by prednisolone 60mg/day and methotrexate 7.5mg/week. Fever and painful swellings on both ears subsided. He showed improvement in cognitive function and personality. Although relapsing polychondritis is rare, it should be considered to be a possible cause of leptomeningeal meningitis.

P3-289

The pathogenic mechanisms of atypical femoral fractures depend on the fracture site; from our case series

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Conflict of interest: None

To elucidate the pathogenic mechanism of atypical femoral fractures, we compared the clinical features and laboratory findings depending on the fracture sites, which were 6 subtrochanteric and 4 diaphysic fractures. In subtrochanteric group, age was younger (53 years old versus 77 years old on average), and bisphosphonate duration was longer (5.9 years versus 2.6 years on average) compared to diaphysic group, but no significant difference was detected. The daily dose of methylprednisolone was significantly higher (11 mg/day versus 2.3 mg/day on average) in subtrochanteric groups, and 25-hydroxy vitamin D (25-OH-D) was significantly lower (17.8 mg/ml versus 25.6ng/ml) in subtrochanteric group. In addition, diaphysic group showed higher incidence (100% versus 54%) of femoral lateral bowing "positive" though no significant difference. Bone parameters isolated from iliac bones demonstrated that almost all osteoid parameters were lower than reference values. However, bone resorption parameters indicated not all cases showed decreased. Three cases showed both osteoid and resorption parameters were low, suggesting severely suppressed bone turnover (SSBT). Four cases demonstrated contralateral beaking finding on X-ray and all cases are symmetrical. These data indicated that not all cases of atypical femoral fractures showed SSBT and that pathogenic mechanism of AFFs is different depending on the fracture sites.

P3-290

Efficacy of multi-target therapy in anti-melanoma differentiation-associated gene 5 (MDA5) positive dermatomyositis with early stage interstitial lung disease

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Conflict of interest: None

Objective: Anti-melanoma differentiation associated gene 5 (MDA5) autoantibody is detected in patients with dermatomyositis (DM) and strongly associated with rapidly progressive interstitial lung disease (RP-ILD) and high mortality rate. The treatment strategy to prevent fulminant ILD in anti-MDA5 positive dermatomyositis has not been established. The objective of this study is to evaluate the efficacy and safety of multi-target therapy with tacrolimus and mizoribine in patients with anti-MDA5 positive DM and early stage ILD. Method: We treated two amyopathic dermatomyositis patients: one was 45-year-old male and the other 63-year-old female. They both had characteristic skin rash, polyarthritis, and mild ILD on chest CT with elevated anti-MDA5 titer (more than 150 unit in both patients; cutoff: 32 unit) and elevated ferritin (365.6 and 306.3 ng/ml respectively). They did not have respiratory symptoms, muscle weakness, or elevated creatinine kinase. Pulmonary function test (PFT) was normal for both of them. They received Multi-target therapy with tacrolimus 3mg/day and mizoribine 300mg/day along with prednisolone (0.5mg/kg every other day and 1mg/kg every other day, respectively). Results: Both patients had gradual improvement in skin rash, arthritis. After 6 month of treatment, FRN was 163 and 389 ng/ml respectively. Consecutive chest CT showed very mild progression of ILD, and PFT had no interval change in both of them. PSL was successfully tapered to 12.5 mg every other day in former patient and 20 mg every other day in the latter. Neither of them had serious adverse event related with the drugs, such as opportunistic infection, diabetes, hypertension, renal impairment, cataract, osteoporotic fracture. Conclusion: Multi-target therapy with alternative day steroid may be effective and safe in the treatment of patients with anti-MDA5 positive DM and early stage ILD.

P3-291

Salmonella-related mycotic pseudoaneurysm of the superficial femoral artery in a systemic lupus erythematosus (SLE) patient without vascular procedure: A case report

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Conflict of interest: None

【Case】A 50-year-old female with systemic lupus erythematosus (SLE)presents with poor appetite and body weight loss about 8kg within one year. She notices that the inguinal region of right thigh has became gradually swelling with mild tenderness during the same period. The laboratory data was as follows: WBC: 4200/CUMM with Seg/Lym: 88.5/5.6%, platelet: 129000/CUMM, Cre 0.78mg/dl, albumin: 3.0 g/dl, Ca 8.0mg/dl, C3: 55.8 mg/dl (normal range:80.0 ~ 193 mg/dl), CRP: 1.88mg/dl, and Anti-dsDNA was negative. The 24-hour urine protein was 0.296 g/day. The CXR, panendoscope, and colonscope revealed all negative finding of malignancy. The Doppler sonogram of low extremities revealed one large cystic structure about 5.2 x 4.3 cm in medial aspect of right distal thigh with yin-yang sign. The pseudoaneurysm of right femoral artery was diagnosed, and the angiogram during operation revealed perforation with contrast extravasation over middle to distal superficial femoral artery. The stent graft with Gore Viabahn 7mm/100mm was performed over middle to distal right superficial femoral artery. The culture of hematoma removed during operation showed Salmonella group D. 【Clinical significance】For the etiology of femoral artery pseudoaneurysm in SLE patient without vascular procedure, Salmonella infection should be considered.

P3-292

Evaluation of IgG4-related disease with multiorgan involvement using fluorodeoxyglucose-positron emission tomography and comprehensive diagnostic criteria

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Conflict of interest: None

Objectives The present study aimed to the diagnostic utility of the CDC IgG4-RD (comprehensive diagnostic criteria for IgG4-related disease) with that of the classical organ-specific criteria and to determine the usefulness of FDG-PET (fluorodeoxyglucose-psitron emission tomography) in evaluating the extent of IgG4-RD **Methods** This retrospective study included 240 patients suspected of having IgG4-RD at 9 institutions in Japan between 2009 and 2015. Serum IgG4 levels were measured in these patients. We applied the CDC IgG4-RD and classical organ-specific criteria to these patients, and determined the diagnostic rates. We evaluated the number of involved lesions using FDG-PET in patients with IgG4-RD. Additionally, we examined the relationship between serum IgG4 titers and the number of involved lesions. **Results** Using the CDC IgG4-RD, of the 240 patients, 49 were serum IgG4 -positive, 16 had definite IgG4-RD, and 25 had possible IgG4-RD. Therefore, 41 patients were diagnosed as having IgG4-RD, with a diagnostic rate of 17.1%. Using the classical criteria, of the 240 patients, 2 were diagnosed with AIP, 10 with MD, and 3 with IgG4-related KD, with a diagnostic rate of 6.3% FDG-PET scans were performed in 29 of the 41 IgG4-RD patients. We found a correlation between serum IgG4 titers and the number of involved lesions (correlation coefficient = 0.89). In IgG4-RD patients with several involved organs, FDG uptake into the lesions was relatively mild and the serum IgG4 levels were remarkably elevated. However, in non- IgG4-RD patients, FDG uptake was not clearly detected and the serum IgG4 levels were remarkably elevated. **Conclusions** The CDC IgG4-RD is more appropriate than the classical organ-specific criteria for the diagnosis of IgG4-RD. FDG -PET is useful to evaluate the extent of IgG4-RD. Additionally, analysis of FDG uptake and serum IgG4 titers might be useful for differentiating IgG4-RD from other diseases.

P3-293

The sternoclavicular and sternocostal joints chroniditis show as the initial presention of granulomatosis with polyangiitis: A case report

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Conflict of interest: None

【Case】The 64-year-old male had been healthy in his usual status until 2 months before admission. He has been intermittent fever, chest tightness, and general weakness for 2 months. The several episodes of near syncope are noted during the same period, and the dyspnea with hoarseness was in progression. The patient notices the soreness was around the bilateral sternoclavicular and sternocostal joints, multiple arthralgia of bilateral hands, and rhinorrhea with nasal congestion. The physical examination shows no tenderness, no limited of range of motion of bilateral hand joints, and no pitting edema. The laboratory data was as follows: Cr: 2.37mg/dl (Cr:1.01mg/dl on July, 2016), Ferritin: 2650.2 ng/mL, ESR:119 mm/hr, CRP:27.09 mg/dl, and urine routine:3+/HPF. The thorax MRI showed subchondral bone edema and mild joint effusion at bilateral sternoclavicular joints and SPECT/CT revealed increased uptake over sternoclavicular joints and PIP joints of bilateral hands. The finding of MRI and SPECT/CT was compatible with arthritis and chroniditis of sternoclavicular joints. The progressive impaired renal function was from 2.37 mg/dl to 4.54 mg/dl. The antineutrophil cytoplasmic antibodies (ANCA) showed C-ANCA:126 IU/ML (positive) and p-ANCA: negative. The renal biopsy arranged for rapidly progressive glomerulonephritis (RPGN) showed pauci-immune type and necrotizing crescentic glomerulonephritis. The granulomatosis with polyangiitis (GPA) with RPGN was the diagnosis. The progressive dyspnea with hoarseness and impaired renal function was quickly improved after methylprednisolone pulse therapy with cyclophosphamide infusion, and the level of c-ANCA was decreased to 26 IU/ML (positive). 【Clinical significance】The clinical presentations of Granulomatosis with Polyangiitis and relapsing polychondritis are overlapping. The c-ANCA level should be considered as a marker for following treatment efficacy for positive ANCA in patient of GPA.

P3-294

Systemic Lupus Erythematosus accompanied with acute Type A aortic dissection and non-infective endocarditis : Myxomatous degeneration of aortic wall provides the link of SLE and aortic dissection

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Conflict of interest: None

【Case】A 53-year-old female complained of easy fatigue, mild fever and dyspnea on exertion for about 2 days. She had past history of systemic lupus erythematosus (SLE) 33 years ago and received prednisolone therapy with 20 mg /day since then. A chest x-ray did not show abnormal finding. The rapidly progressive respiratory failure was noted and status post endotracheal intubation with ventilator support. The computed tomography of chest revealed acute type A aortic dissection with pericardial effusion. The emergent Bentall's operation + total arch replacement was performed smoothly without surgical complication. The vegetation about 0.5x0.5cm2 in size at non-coronary cusp (NCC) of aortic valve was also found during operation. The pathology revealed myxomatous degeneration and non-infective endocarditis of aortic valve and myxomatous degeneration of aortic wall.【Clinical significance】 Aortic dissection in patients of SLE is extremely rare, and the myxomatous degeneration of aortic wall this case provides the link of SLE and aortic dissection.

P3-295

New-diagnosed systemic lupus erythematosus (SLE) after complete remission of gastric diffuse large B cell lymphoma after Rituximab-base chemotherapy : A case report

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Conflict of interest: None

【Case】The 54-year-old female presents with general weakness and poor healing of oral ulcer for about one month. The anemia, thrombocytopenia and acute kidney injury was found in clinic. She was diagnosed with gastric diffuse large B cell lymphoma (DLBCL) four years ago, and the disease status was in complete remission after rituximab-based chemotherapy. The panendoscope and bone marrow biopsy do not showed evidence of recurrence of DLBCL. The blood examination showed low C3/4, elevation of LDH (270 U/l), positive of Coombs' test, high titer of ANA (1:1280), positive of anti-dsDNA (444 IU/ml) and anti-RNP antibody. The urine routine revealed proteinuria and hematuria. The pathology of renal biopsy was diffuse glomerulonephritis, ISN/RPS class IV-G (A), and compatible with lupus nephritis. The SLE was diagnosed according to 2012 Systemic Lupus International Collaborating Clinics (SLICC) SLE Criteria. 【Clinical significance】The case with diagnosis of diffuse large B cell lymphoma preceding SLE was few. The selfantigens, including DNA and nucleoprotein, may be exposed and accumulated due to chemotherapy and immunotherapy.

P3-296

An IgG4-related disease case with two episodes of lymphoma history

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Conflict of interest: None

Objective: To report a patient diagnosed as IgG4-related disease (IgG4-RD) with prior and subsequent lymphoma history and explore the association between IgG4-RD and lymphoma. **Methods:** To report an IgG4-RD case with a prior history of small cell lymphoma, died of diffuse large B cell lymphoma (DLBCL) in the end. We also performed a literature review of close relationship between IgG4-RD and lymphoma. **Results:** A 60 year-old female who presented diffuse superficial lymphadenopathy 17 years ago, diagnosed as small cell lymphoma by cervical lymph node biopsy. After topical radiotherapy, chemotherapy and autologous stem cell transplantation, the patient got a 6 years' remission. Then she gradually suffered from lacrimal and submandibular glands enlargement, obstructive jaundice and hydronephrosis, all of which were well responded to glucocorticoids and immunosuppressive agents. An biopsy specimen from one submandibular gland showed a dense IgG4 positive lymphoplasmacytic cells infiltrate (85/HPF) and the ratio of IgG4- to IgG-positive cells was 48.6%, without storiform fibrosis or obliterative phlebitis. The serum IgG4 level was normal, however, measured after glucocorticoid treatment. The diagnosis of IgG4-RD was confirmed by the typical clinical and histopathologic findings. Two months ago, the patient developed growing high fever, myalgia and weakness. The PET scan showed diffuse increased FDG uptake of most lymph nodes, nasopharynx and bone marrow. The histopathologic findings of nasopharynx confirmed a diagnosis of DLBCL. The patient died 3 weeks later unfortunately. **Conclusions:** Several studies have shown that IgG4-RD is associated with an increased risk of lymphoma, and a lymphoma history is associated with subsequent development of IgG4-RD. This is the first IgG4-RD case combined with two different types of lymphoma reported in China. The appearances of two diseases may mimic each other very much, which calls for a timely and accurate histopathologic evaluation.

P3-297

Clinical features and outcome in patients with anti-MDA-5 antibody-positive dermatomyositis: a single center experience

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Conflict of interest: None

Objective: To evaluate whether anti-MDA-5 antibody-positive dermatomyositis actually shows specific clinical features as previously reported, such as increased skin manifestations, interstitial lung disease (ILD) and decreased myositis activity at Fukushima Medical University Hospital. Methods: Twenty-four dermatomyositis (DM) patients measured in sera of anti-MDA-5 antibodies in our institute from January 2012 to August 2016 were included in this study. These patients were divided into 2 groups: anti-MDA-5 positive (+) and anti-MDA-5 negative (-) patients and we retrospectively reviewed their clinical records. The clinical features compared were as follows: age, sex, from disease onset to diagnosis, skin manifestations, myositis symptoms, laboratory data, and outcome. Results: Anti-MDA-5 (+) DM showed significantly increased lung complications (ILD, rapidly-progressive ILD), skin manifestations (heliotrope rash, palmar papules, periungual erythema, $p < 0.05$) and lack of malignancy compared to anti-MDA-5 (-) DM ($p = 0.03$). Anti-MDA-5 (+) DM patients had a tendency of increased clinically amyopathic DM than anti-MDA-5 (-) DM (50% vs 12.5%, $p = 0.07$). In laboratory data, significantly decreased WBC counts and increased percentage of anti-SS-A antibodies were found ($p < 0.05$). Kaplan-Meier analysis revealed anti-MDA-5 (+) DM patients showed significantly lower overall survival than anti-MDA-5 (-) DM ($p < 0.01$). Conclusion: Our study shows that anti-MDA-5 (+) DM patients in our institute had similar clinical features as previously described, except for increased frequency of heliotrope rash, anti-SS-A antibody positive, and decreased WBC counts. These results indicate that autoantibodies and complications can affect the clinical features of anti-MDA-5 antibody-positive DM.

P3-298

Assessment of subclinical tophi and erosions in patients with gouty arthritis using a dual-energy computed tomography

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Conflict of interest: Yes

Objectives Joint damage in gout is a consequence of deposition of monosodium urate (MSU) crystals as tophi. Detection of tophi before they become clinically apparent and optimizing urate lowering therapy is important for minimizing joint damage. The aim of our study was to evaluate the utility of dual-energy CT (DECT) in detecting subclinical tophi and erosion in patients with gouty arthritis. **Methods** DECT scans of feet were performed in 71 gouty arthritis patients without apparent clinical tophi. For each patient, 28 joints were evaluated for presence of tophi and erosion. Total volumes of tophi in both feet were quantified using an automated software program of DECT. Clinical and laboratory data were obtained simultaneously at the time of the DECT evaluation. **Results** The mean age of gout patients was 47.3 ± 14.8 years, and median disease duration was 2.6 (range 0-20) years. Subclinical tophi were detected in 70 (98.6%) patients and in 793 (39.9%) joints, and median 9 (0 to 26) joints per patient were positive for tophi. The most common sites for tophi were first metatarsophalangeal joints (93%), followed by interphalangeal joints (74.6%) and ankle joints (66.2%) in patients. Tophi in Achilles tendons were present in 50.7% of patients. The mean total volume of tophi per patient was 1.14 ± 1.20 (0.05-4.86) cm^3. Erosions were found in 18 (25.4%) patients and in 38 (1.9%) joints, and 31 (81.6%) of the joints with erosion were combined with tophi within the joints. The presence of erosion did not correlate with volume of tophi but was significantly correlated with disease duration ($p = 0.027$). **Conclusions** Tophi frequently occur in both intra- and extra-articular structures of gouty arthritis patients despite absence of clinically apparent tophi. Presence of tophi increases the likelihood of erosion. DECT is an excellent imaging modality for detection of subclinical tophi.

P3-299

Different responses to treatment in two onset categories of lupus nephritis

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Conflict of interest: None

[Objectives] To study the clinical features in two onset categories of lupus nephritis (LN): LN that developed as a flare of systemic lupus erythematosus (SLE) after treating the prior non-renal SLE conditions successfully (delayed, D-LN) and LN manifesting at the time of SLE onset (early, E-LN). We previously reported more frequent flares and higher serum titers of anti-dsDNA antibody during the active LN phase in D-LN compared with E-LN. This study further analyzed the different clinical features, particularly the response to treatment between E-LN and D-LN. [Methods] We retrospectively examined 118 LN (60 E-LN, 58 D-LN) patients who attended our hospital between January 1991 and May 2016. We compared the proportion of renal biopsy histological types, the extent of proteinuria, the proportion of induction therapy options at LN onset and flares, and the response to therapy at 24 weeks between E-LN and D-LN. The response was classified into complete response (CR; the urinary protein [UP] to urinary creatinine [UC] ratio was <0.2 and there were no active urine sediments), partial response (PR; the UP:UC ratio was 0.2−2.0 or there were active urine sediments), and insufficient response (IR; anything else). [Results] The proportion of histological types and induction therapy options, and the extent of proteinuria at LN onset were similar between the two groups, but the response to induction therapy for LN onset was better in E-LN than D-LN (CR/PR/IR: 46/13/1 *vs*. 24/29/5, p<0.001). A greater number of E-LN patients achieved CR by glucocorticoids monotherapy compared with D-LN at LN onset (34/40, 85.0% *vs*. 14/37, 37.8%, p<0.001). LN flares were observed in 15/60 E-LN and 24/58 D-LN patients, and IR was observed in 13.3%(2/15) of E-LN and 41.7%(10/24) of D-LN patients. [Conclusion] The relatively poorer treatment response in D-LN compared with E-LN patients is consistent with our previous report that suggested that D-LN might reflect intractable SLE conditions.

P3-300

Application of 2016 ACR/EULAR macrophage activation syndrome classification criteria on adult-onset Still's disease

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Conflict of interest: None

【Objectives】Classification criteria for macrophage activation syndrome (MAS) for juvenile idiopathic arthritis (JIA) have recently reported. However, clinical relevance of its application on adult-onset Still's disease (AOSD) is uncertain. To evaluate the difference between "MAS group" and "non-MAS" in AOSD, we applied this criterion on our AOSD patients.【Methods】We retrospectively extracted patients who had the diagnosis of AOSD from our computerized clinical records. We manually evaluated their records and judged whether the patients fulfilled Yamaguchi's classification criteria for AOSD. These selected patients were further applied to MAS criteria and subdivided into 2 groups. We included their age, gender, disease duration, new-onset or relapse, clinical symptoms (joint pain, rash, sore throat, lymph node swelling, and splenomegaly), leucocyte count, ratio of neutrophil, liver enzymes, inflammatory markers, soluble IL-2 receptor, and thymidine kinase, and treatment regimen, for the analysis. Logistic regression analysis was used to evaluate the difference among the 2 groups.【Results】Thirty-eight patients who fulfilled Yamaguchi's AOSD classification criteria were included in the analysis (mean age 44.0, male n=12, female n=26). Mean disease duration was 14.0 months. Fourteen patients (male n=3, female n=11) were included in MAS group, whereas 24 patients for non-MAS group (male n=9, female n=15). Logistic regression analysis showed that ESR (mean ESR in MAS / non-MAS group = 41.9mm/h / 79.0mm/h, respectively) were significantly lower in MAS groups (p=0.035, OR=3.21) No other clinical symptoms were different among the 2 groups. We will present our data and literature-based consideration.【Conclusion】We could not identify clinical significance of applying MAS criteria on our AOSD patients. However, due to small sample size, further enrollments of patients are necessary to deliver confident conclusion whether the MAS criteria is useful in AOSD.

P3-301

Disseminated *Mycobacterium marinum* Infection complicated by infliximab in patients with psoriatic arthritis

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Conflict of interest: None

A 58-year-old man presented with a 4-week history of fever, multiple ulcers on both legs, and vesicles on the left side of his face. He had a 30-year history of psoriatic arthritis treated with infliximab for 5 years and with low dose prednisolone for 2 months. Physical examination revealed a nodule on his left hand and cervical lymphadenopathy. The facial vesicles were diagnosed as herpes zoster. *Mycobacterium marinum* was detected by culture of leg ulcers and pus from the nodule on his hand and a cervical lymph node, confirming a diagnosis of disseminated *M. marinum* infection. He regularly went fishing at sea. We treated him with acyclovir, clarithromycin, rifampicin, and ethambutol. The skin lesions resolved after 4 weeks. Use of biologic agents for psoriatic arthritis has increased recently, but more attention should be paid to side effects like immunosuppression, which led to herpes zoster and disseminated *M. marinum* infection in our patient.

P3-302

Familial granulomatosis with polyangiitis in two sibling cases with similar clinical features

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Conflict of interest: None

Introduction: The aetiology of granulomatosis with polyangiitis (GPA) is likely a complex interplay between environmental triggers and genetic predisposition. There are a few cases of familial GPA in the literature, however, we report here the rare scenario of two sibling cases of GPA, showing closely similar clinical courses. Case presentation: Patient 1 was a 73-year- old female with previous rheumatoid arthritis and Sjögren's syndrome, suffering from refractory otitis media. She was found to be PR3-ANCA positive (492 U/ml), and serum creatinine and CRP levels were elevated (1.79 mg/dl and 5.4 mg/dl, respectively). Her renal function remained stable, at which time her creatinine rose slowly in conjunction with a rise in PR3-ANCA. The renal biopsy revealed a pauci immune focal and segmental glomerulonephritis, leading to a diagnosis of GPA. She was started on high dose steroids and rituximab (375 mg/m^2, once weekly), then converted to maintenance oral prednisolone. Her PR3-ANCA and CRP levels improved. Patient 2 was patient 1's sister, a 63-year-old female with no previous disease, developing new onset hearing loss associated with intractable otitis. A CT scan of her chest demonstrated nodules in the bilateral lungs, and she was found to be PR3-ANCA positive (>3,000 U/ml). Serum creatinine and CRP levels were elevated (1.79 mg/dl and 26.3 mg/dl, respectively). She underwent renal biopsy which confirmed a diagnosis of GPA. She was treated with high dose steroids in combination with intravenous cyclophosphamide, on which she made a symptomatic improvement and a rapid decrease in PR3-ANCA. Following reduction of immunosuppression she relapsed twice and was treated with intravenous cyclophosphamide. She remains well in remission. Conclusion: Our reported family is two siblings both of whom presented with hearing loss and renal dysfunction. They shared a remarkably similar disease phenotype and may have important implications for understanding of the genetics of GPA.

P3-303

Long term exsistence of lymphadenopathy prior to the onset of IgG4 related disease

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Conflict of interest: None

«Case presentation» A 67-year-old man was admitted to our hospital, because of bilateral blepharoptosis for one year. He had a medical history of duodenal ulcer with H. pylori infection nine years prior. An abdominal CT at that time had showed multiple peritoneal lymphadenopathies (1cm in diameter) with unknown etiology, which had not been reexamined. As he began having pollakiuria six months before, he started to take medicine for prostatic hypertrophy, which was ineffective. On admission, bilateral swollen parotid glands and submandibular glands were noted. MRI revealed remarkable swelling of bilateral lacrimal glands with thickened infraorbital nerves. Results of laboratory tests follows; WBC 6200/μl, eosinophil 13.6%, CRP 0.10 mg/dl, total protein 9.5g/dl (polyclonal hypergammaglobulinemia), IgG 4137 mg/dl, IgG4 2050 mg/dl, IgE 28.7 IU/l, CH50 55 U/ml, C3 73.3 mg/dl, C4 11 mg/dl, ANA < x40, anti-SSA Ab negative, and amylase 88 IU/l. CT of the abdomen showed retroperitoneal thickening and multiple swollen lymph nodes in the peritoneum without pancreatic abnormality. Precise examination of lymph nodes on CT image convinced that each swollen node had been existed for nine years with some increment of diameters. With the diagnosis of IgG4 related disease, 40mg of PSL were started, resulting good response. Serum IgG4 decreased to 314 mg/dl. All swollen organ including salivary glands, lacrimal glands, infraorbital nerves, and prostate promptly shrank. Interestingly, peritoneal lymph nodes also shrank to smaller than those of nine years ago, suggesting that the lymphadenopathy was due to IgG4 related disease. «Discussion» Long term natural course of IgG4 related disease is not well known. In this case, peritoneal lymphadenopathy presumably due to IgG4related disease existed at least nine years prior to the onset of IgG4 related disease, without causing any symptoms. Long term H. pylori infection might have some causative role by molecular mimicry.

P3-304

Evaluation of noninvasive clinical samples for detection of *Chlamydia trachomatis* infection in undifferentiated spondyloarthropathy patients

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Conflict of interest: None

Objectives: Undifferentiated Spondyloarthropathy (uSpA) constitute a significant proportion of patients in rheumatology clinics. Infection with *Chlamydia trachomatis* may be etiologic in uSpA. However, the possible role of *C. trachomatis* in uSpA is not well studied in India. As joint material cannot always be obtained in uSpA, hence, an attempt was made to detect the presence of *C. trachomatis* infection in noninvasive samples for an improved diagnosis. **Methods:** Prospective study was conducted in uSpA (n,35) and control patients comprising of Rheumatoid Arthritis (RA; n,35) and Osteoarthritis (OA; n,35) attending major tertiary hospital in New Delhi. First void volume (FVU) of urine and nonheparinized blood were collected for detection of chlamydial pathogen by Fluorescence Assay (FA), PCR and elisa for antichlamydial antibodies by commercially available kits. Data were statistically analyzed. **Results:** *C. trachomatis* plasmid was detected in urine by PCR in 17.3%(6/35) uSpA ('p'= 0.02 vs RA/OA) while chlamydial antigen was localized in urine cells of 22.8%(8/35) patients by FA ('p'= 0.03 vs RA/OA). Anti *C. trachomatis* IgM/ IgG/ IgA were detected in 11.4%(4/35; 'p'= 0.1 vs RA/OA), 22.8%(8/35; 'p'= 0.007 vs RA/OA and 25.7%(9/35; 'p'= 0.01 vs RA and 0.003 vs OA), respectively. There was moderate kappa agreement between PCR and anti *C. trachomatis* IgA findings (k=0.44) while fair agreement was observed between IgG antibodies and DFA (k=0.32). only 1 RA patient showed the presence of both *C.trachomatis* antigen and IgA antibodies, however, none of the OA patients was found to be positive. **Conclusions:** Our findings indicate that detection of secretory antiC. *trachomatis* IgA antibodies in serum may be useful for initial diagnosis of infection in uSpA patients who are otherwise asymptomatic for genitourinary infection and lack effusions.

P3-305

Successful Treatment of refractory Lupus Nephritis with Secukinumab in a patient complicated with Psoriasis Vulgaris

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Conflict of interest: None

We report the case of a 62-year-old woman. Psoriasis Vulgaris (Psoriasis) was diagnosed in X-31 year and also Systemic Lupus Erythematosus (SLE) with nephritis (WHO IIIA) in X-11. She was treated with high-dose methylprednisolone and cyclosporine A (CsA) to achieve remission. Methylprednisolone was reduced to 4 mg/day. Because of renal dysfunction, although CsA was discontinued in May X, psoriasis, renal dysfunction and proteinuria became further worse, she was admitted to our hospital in July X. She was diagnosed with SLE flare with class IV-G (A/C)+V lupus nephritis (INS/RPS) and associated psoriasis. The SLEDAI score was 16 and psoriasis area and severity index (PASI) score was 16. Although high-dose corticosteroid (1 mg/kg/day) and a concomitant first dose of biweekly IV cyclophosphamide (IVCY) 15mg/kg were started, anasarca was still observed and S-Cr was increased from 1.98 to 2.85 mg/dL. Because proportion of activated Th17 cells were increased in peripheral blood, and the infiltration of many lymphocytes and IL-17-positive cells in renal interstitium, secukinumab, an antibody against IL-17A, was administered. Then, anasarca and nephrosis was improved and S-Cr was decreased to 1.20 mg/dL in proportion to the reduction in activated Th17 cells in peripheral blood. Although recent studies have begun to shed light on the role of IL-17 in the pathogenesis of SLE, there is no convincing evidence in actual patients. In this case, improvement of disease activity of SLE was correlated with the decrease of activated Th17. This is the first report that the IL-17-targeted therapy for SLE was shown to be effective in a patient skewing towards Th17-phenotype.

Luncheon Seminar

LS1-1

Important thigs for the treatment of psoriatic arthritis; not to overlook various symptoms

Yuho Kadono
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Conflict of interest: Yes

Because there are a lot of similarities in the clinical symptoms or response to medicine, psoriatic arthritis (PsA) and ankylosing spondylitis (AS) are considered as a part of the comprehensive clinical concept, so called spondyloarthritis (SpA). SpA is roughly classified in axial SpA which is mainly involved sacroiliac joint or spine like AS, and in peripheral SpA which is involved peripheral joints like PsA or reactive arthritis. Since PsA sometimes shows axial symptoms, we should not think that these two are totally different, but they are overlapped. SpA is known to present various symptoms, such as inflammatory back pain which is worsened at rest and relieved on exercise, arthritis of spine and limbs, enthesitis of Achilles' tendon, dactylitis, psoriasis, inflammatory bowel diseases such as Crohn disease or ulcerative colitis, uveitis. It is important that we should plan a strategy under comprehensive viewpoint based on discussion with several departments. CASPAR classification criterion is often used for a diagnosis of PsA. The existence or past of skin psoriasis, and the nail psoriasis are the key for diagnosis. It is also known that many comorbidities are seen in PsA patients. Lifestyle diseases such as diabetes mellitus, hypertension or hyperlipidemia are commonly seen, and they sometimes result in life-threatened cardiovascular or cerebrovascular disease. According to the GRAPPA recommendation, the first choice for the treatment of PsA is NSAIDs. If it is not sufficient, csDMARDs such as methotrexate followed by bDMARDs such as TNF inhibitor should be used for peripheral symptoms. For axial symptoms, bDMARDs comes the second. The concept of treat to target (T2T) is established in the treatment of PsA, and minimal disease activity (MDA) is shown as useful target. I will comment that it is important to treat various symptoms of PsA comprehensively, with eyes on long-term prognosis.

LS1-2

Latest Therapies for the management of Psoriatic arthritis − focus on IL-17A inhibitors (secukinumab)

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Conflict of interest: None

Recent advances in the understanding of the pathogenesis of Psoriasis (PsO) & and Psoriatic Arthritis (PsA) have demonstrated a critical role of IL-17A in both disorders, as well as highlighted that the pathophysiology of PsA is distinct from Rheumatoid Arthritis (RA). While TNF inhibitors (TNFi) have been established as biologic treatment in PsA, there remains unmet therapeutic need as TNFi demonstrate achieves minimal disease activity in only half of patients, demonstrate loss of efficacy is some patients and the safety profile includes serious adverse events and contraindications. This review will detail: 1. The pathophysiological role of IL-17A in PsO & PsA, with differences from RA 2. The development of IL-17A inhibitors secukinumab, ixekizumab & IL-17 receptor inhibitor brodalumab, focusing on secukinumab 3. The phase 3 study results out to two years for secukinumab demonstrating efficacy on signs and symptoms, patient reported outcomes and the prevention of radiological progression 4. The safety profile of secukinumab 5. Discussion of implication to the current treatment algorithm of PsA and whether it should be reconsidered in the light of efficacy-safety balance of this therapy, as well as increased responsiveness to secukinumab in TNF-naïve patients compared with patients previously exposed to TNFi.

LS2-1

Treatment strategy for tocilizumab from the standpoint of EULAR recommendations and SURPRISE study

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Conflict of interest: Yes

The great advance in the management of rheumatoid arthritis have made clinical remission the first goal to achieve. After achieving remission, whether continuing the treatment or reducing it has been debated. While easing the burdens patients with rheumatoid arthritis have had, the physical one, the financial one and the temporal one, is definitely blessing to the patients and also to the society, it at once increases the risk of flare, which might not be subdued by the same treatment or lead to the joint damage or physical functional impairment. In this seminar, I would like to dicuss the best treatment strategy regarding biologic agents including tocilizumab from several latest evidence.

LS2-2

The best use of tocilizumab for rheumatoid arthritis indicated by cohort studies

Motomu Hashimoto
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Conflict of interest: Yes

Anti-IL-6 receptor antibody, tocilizumab (TCZ), has a good clinical effect for rheumatoid arthritis (RA) as is shown by many clinical trials. It also shows the better drug retention rates in the real world database, even for patients with various disease backgrounds. It is well known that IL-6 causes cartilage destruction via induction of osteoclast differentiation and production of matrix metalloproteinases. In addition, IL-6 has a pleotropic effect that is responsible for various symptoms of RA patients. For example, IL-6 contributes to the production of serum amyloid A (sAA), which is a precursor protein of AA amyloidosis. IL-6 is also responsible for the production of hepcidin, which is a major cause of anemia of chronic diseases (ACD). IL-6 also promotes cachexia and sarcopenia with muscle weakness and exhaustion at the increased risk of falls and fractures. Thus, considering the unique effects of IL-6, ADL and QOL of certain RA patients can be best improved by TCZ. Cohort studies of daily clinical practice help reveal the clinical characteristics of the patients who will benefit from the use of TCZ.

LS3

Management of osteoporosis in rheumatoid arthritis

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Conflict of interest: Yes

Rheumatoid arthritis (RA) is a systemic disorder characterized by inflammatory synovitis. When the disease progresses, it results in the joint destruction and attenuates ADL and QOL of the patients. It has been recognized that RA patients are frequently suffered from osteoporosis. The osteoporosis in RA patients exhibits a complicated pathology of combined local periarticular osteoporosis and general osteoporosis. Periarticular osteoporosis is caused by the excessive bone resorption caused by inflammatory cytokines such as TNF-α and IL-6. General osteoporosis is also caused by the cytokine-induced inflammation, but it is also related to the steroid usage, inactivity and vitamin D deficiency. Although osteoporosis in RA patients is correlated with disease activity and some studies reported the relationship between bone destruction and osteoporosis, antirheumatic drugs including biological agents are not enough to recover the reduced bone mineral density in RA patients. Anti-resorptive agents such as bisphosphonates increased not only bone mineral density (BMD) but also bone strength in RA patients. In contrast, they are not enough to suppress bone destruction. Recently, it was reported that anti-RANKL antibody, denosumab, not only increased BMD and suppressed osteoporotic fractures in postmenopausal women, but also increased BMD in RA patients. Combination of these anti-osteoporosis drugs and anti-rheumatic drugs will be useful for the proper management of osteoporosis in RA patients.

LS4

Evidence based discussion in RA and SpA – what we need to figure out next?

Arthur Kavanaugh
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Conflict of interest: None

In recent years, the introduction of biologic disease-modifying antirheumatic drugs (bDMARDs) in the treatment of rheumatoid arthritis (RA)and systemic inflammatory autoimmune rheumatic diseases has enabled achievement and maintenance of sustained clinical remission, with significant improvement in the patients' long-term quality of life (QOL). In particular, the combination therapy with bDMARDs such as tumor necrosis factor (TNF) inhibitors and methotrexate (MTX) is for many patients at present the most efficacious method of treatment. There has been a wealth of clinical evidence accumulated supporting this, and the profile of anticipated adverse event has been well elucidated. Accordingly, with improvement of the global classification criteria for RA by the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) etc., treatment guidelines for RA have been updated to recommend early intervention with appropriate treatment. In addition to TNF inhibitors, a variety of other bDMARDs and more recently Janus kinase inhibitors (jakinibs) have been developed, enablingd physicians and patient to have multiple treatment options. Such treatments are effective not only in patients with RA but also in those suffering from psoriatic arthritis (PsA), ankylosing spondylitis (AS), or spondyloarthritis (SpA), thereby providing benefits to more patients.

LS5

The role of interferon gamma release assay for the diagnosis of Latent Tuberculosis -Infection in immunocompromised host-

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Conflict of interest: None

Latent tuberculosis infection (LTBI) World health organization defined Latent tuberculosis infection (LTBI) as follows, "Latent tuberculosis infection (LTBI) is a state of persistent immune response to stimulation by Mycobacterium tuberculosis antigens without evidence of clinically manifested active TB." The lifetime risk of reactivation for a person with documented LTBI is estimated to be 5-10%, with the majority developing TB disease within the first five years after initial infection. However, the risk is considerably higher in the presence of predisposing factors. (http://www.who.int/tb/challenges/ltbi/en/) Interferon gamma release assay Interferon-Gamma Release Assays (IGRAs) (QuantiFERON TB Gold in tube:QFT and Tspot.TB:TSPOT) are currently available for the diagnosis of LTBI. The risk of developing active tuberculosis (TB) The risk of developing active TB has been analyzed. (Landry J, Menzies D. IJTLD. 2008;12:1352) AIDS and HIV infection was very high risk, and relative risk (RR) was 110-170, and 50-110, respectively. Diabetes mellitus, hemodialysis and steroid therapy had been known as a kind of compromised host, and its RR is 2.0-3.6, 10-25, and 4.9, respectively. The RR of TNFαblocker, biological agents, was estimated to be1.5-4. The role of IGRAs The Japanese Society for Tuberculosis published two guideline associated with LTBI and IGRA. One is "Treatment Guidelines for Latent Tuberculosis Infection" in 2014 and the other is "GUIDELINES FOR USING QuantiFERON TB Gold In-Tube" in 2013, and revised in 2014 after TSPOT was available in JAPAN. The role of IGRAs was described in both guidelines for practical use. There is not "Gold standard for the diagnosis of LTBI", however we can use many evidences associated with LTBI and IGRA. Especially, Sensitivity, specificity, positive predictive value and negative predictive value are very useful information. There are many difficulties for the estimation of compromised host. The physicians for compromised host need to understand the characteristics of IGRAs, and make final diagnosis.

LS6

Treatment of Pulmonary Hypertension Associated with Connective Tissue Disease from a Perspective of Cardiologists

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Conflict of interest: Yes

Prognosis of pulmonary arterial hypertension associated with connective tissue disease (CTD-PAH) is poorer than other causes of PAH and 5-year survival rate in patients with CTD-PAH is approximately 40%. Therefore, the importance of early diagnosis has been emphasized recently and examinations or algorithms such as exercise echocardiography and DETECT algorithm for screening of PAH associated with scleroderma (SSc-PAH) have become widespread. On the other hand, the differential diagnosis for pulmonary hypertension of unknown etiology is usually performed by cardiologist. In the differential diagnosis, CTD may be overlooked as a possible cause of PAH by cardiologist if the patient have little typical physical findings of CTD. For example, Sjogren's syndrome (SS) patients without complaint of sicca syndrome sometimes go undiagnosed as a cause of PAH by non-rheumatologist because antinuclear antibody is negative in approximately 20% of them and anti SS-A/SS-B antibody is not measured for usual screening of PAH. Although the complication rate of PAH in patients with SS was considered to be rare, Shirai et al reported that 10% of patients with CTD-PAH were SS recently. In our institute, 4 patients (8%) among 48 consecutive patients without any obvious cause of PAH at the time of PAH diagnosis were diagnosed as SS. Two of four patients were not diagnosed as SS at initial diagnosis of PAH and were diagnosed as idiopathic PAH. If they were diagnosed as SS at initial diagnosis, the indication of immunosuppressive therapy had to be considered. In addition, although SSc-PAH has been usually developed long time after diagnosis of SSc, some SSc patients with minimal dermal sclerosis have not been diagnosed as SSc until onset of PAH. Therefore, the differential diagnosis of PAH should be performed with the participation of rheumatologists. In the treatment of PAH, there is little specific evidence of PAH specific agents for CTD-PAH. However, the results of subgroup analyses for CTD-PAH were published in some clinical trials. In this seminar, we will discuss about optimal treatment strategy for CTD-PAH based on the latest findings.

LS7

Musculoskeletal ultrasound optimizes management of rheumatic diseases

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Conflict of interest: Yes

Musculoskeletal ultrasound visualizes synovial inflammation (i.e. synovitis, tenosynovitis, bursitis), enthesitis, crystal deposition, and bone surface abnormalities (i.e. erosion, osteophyte), and thus contributes to accurate diagnoses of rheumatic diseases such as rheumatoid arthritis (RA), psoriatic arthritis, crystal-induced arthritides, and osteoarthritis. Ultrasound also ensures the accurate assessment of RA disease activity by the accurate assessment of synovitis/ tenosynovitis. This allows for the accurate assessment of drug effectiveness and remission, which is expected to improve the clinical outcome of RA. Furthermore, ultrasound helps rheumatologists perform arthrocentesis/ injection, understand the pathophysiology, improve skills, and establish optimal patient-physician communication, and thus contributes to the improved quality of RA management. The "precision medicine" in RA that is already achievable with ultrasound in real patients will be discussed.

LS8-1

Inflammatory memory in rheumatoid arthritis

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Conflict of interest: Yes

In rheumatoid arthritis (RA), a representative inflammatory disease, autoimmune abnormality in the synovial tissue elicits the production of various inflammatory mediators and matrix metalloproteinases (MMPs)

by the synovial resident macrophages and fibroblast-like synoviocytes (FLSs), as well as the differentiation induction of macrophages into osteoclasts, leading to bone and cartilage destruction. Treatment with biologic DMARDs targeting inflammatory cytokines has markedly increased the remission induction rate, but there is a so-called "window of opportunity" that limits the therapeutic effect when the initiation of treatment is delayed. This suggests that the continuation of the inflammatory environment itself induces abnormality in the epigenetics of various cells in the living body, causing deterioration of a refractory nature. In recent years, abnormality in DNA methylation in various cells, including peripheral blood mononuclear cells and FLSs, has also been reported in patients with RA. Our research group and several others have shown a disease-specific DNA methylation pattern in RA patient-derived FLSs (RA FLSs) using non-biased comprehensive genome DNA methylation analysis, suggesting that many genes with abnormal methylation are deeply involved in the pathological condition of RA. Namely, continuation of the inflammatory environment itself can cause changes in the DNA methylation pattern of the synovial resident FLSs as an inflammatory memory, which makes the disease intractable. Early and potent therapeutic intervention to prevent such inflammation memory from leaving a permanent mark could be a key to finding a cure for RA.

LS8-2

Therapeutic strategy for rheumatoid arthritis beyond remission

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Conflict of interest: None

More than fifteen years have passed since introduction of the first biological DMARD (bDMARD) in Japan. To date, several types of biological DMARDs (bDMARDs) for rheumatoid arthritis (RA) with different mode of actions have been available, resulting in a large proportion of patients with RA to be able to acquire clinical remission with various investigation of therapeutic strategy to maximize the effect on disease activity. Maintenance of a good condition if a patient achieve to remission is quite important. The most reliable way to maintain remission is to continue the therapy, however, long lasting treatment with bDMARDs have concerns regarding safety and medical economy. Thus, reduction or discontinuation of bDMARDs beyond the target to treat has been globally expected, leading to domestic and international investigation of therapeutic strategy. RRR study and HONOR study were reported as pioneering evidence from Japan indicating possible successful discontinuation of infliximab and adalimumab. Mainly from Europe, randomized control trials (RCTs) to investigate the therapeutic strategy of reduction or discontinuation of bDMARDs with minimized risk of flare were actively conducted, including PRESERVE study, comparing reduction and discontinuation of etanercept, or STRASS study, assessing stepwise spacing of etanercept or adalimumab. For non-TNF drugs, DREAM study and ACT-RAY study were conducted for tocilizumab, and ORION study was performed for abatacept. In this lecture, accumulated evidences of therapeutic strategy beyond remission, mainly focusing on reduction or discontinuation of bDMARDs, will be reviewed. In addition, a newly reported data of certolizumab pegol from C-OPERA study will be introduced.

LS9-1

Aging issues in RA patients: Use of DMARDs in patients aged 80 years and above

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Conflict of interest: None

(Background) In the NinJa (National database of Rheumatic disease by iR-net in Japan) study, RA patients in Japan have aged in the last 11 years. In addition to the increased age at death, age at onset has also increased. Conventional synthethic DMARDs were commonly used 20 years ago, and csDMARDs were not recommended for elderly patients in our hospital. In this study, Use of DMARDs in elderly RA patients aged over 80 years were examined, based on our cases and the NinJa2015. (Subjects) 63 patients aged over 80 years (53 females, age 83.1 years, RA disease duration 19.0 years, Stage 1, 2, 3, 4 in 8, 5, 11, 39, elderly-onset RA 35, RF positive 46) received treatment. 24 patients underwent joint arthroplasty, and many patients had progressive disease. Medical treatment, SDAI, m-HAQ, concomitant diseases, and nursing care levels were studied transversally. (Result) Regarding anti-inflammatory analgesics, NSAIDs, Tramcet and none were used in 9, 13 and 41. PSL was in 26 (46%) including 6 who received only steroids without DMARDs. DMARDs were used in 55 (87%), and csDMARD alone were used in 27 (43%) (MTX, TAC, SSZ, IGU, BUC, MZB in 9,7,4,4,2,1), and csDMARDs combination were used in 4. Biological DMARD was used in 23 (37%) (ETN, ABT, TCZ, GLM in 10, 7,4,2), and 17 received monotherapy. 2 patients did not receive medicinal treatment. SDAI was high disease activity in 3, moderate in 20, low in 31, and remission in 9. Low disease activity or better was achieved in 63% of patients and the clinical remission rate was 14%. mHAQ was ≤ 0.5 in 18 (29%), 0.5-1 in 18 (29%), 1-2 in 15 (24%), and 2-3 in 4 (6.3%); however, mHAQ was increased in 21 (33%) compared to scores 1 year ago. Concomitant diseases were osteoporosis 60%, renal dysfunction 53%, anemia 43%, low back pain 41%, pulmonary lesion/lung infection 29%, knee pain (OA) 21%, cardiovascular diseases 19%, diabetes mellitus 11%, and malignant tumor 9.5%.27 patients (43%) needed nursing care/assistance for hospital visits/admission. (Discussion) In elderly RA patients aged over 80 years, considering concomitant diseases or general residual function and risk management, I suggest that DMARDs therapy is not necessarily for "tight control" but for "soft and mild control". Especially, aspects such as "to let patients enjoy good health and take care of themselves" and "to functionally support patients not to require nursing care (encouragement/compliment)" are important. Disease activity was good and safe with csDMARD in half of the patients; however, initial symptoms of dementia that may affect medication compliance should not be overlooked.

LS9-2

Tailor Made Medicine

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Conflict of interest: None

We are now in the forefront of the medical revolution from the conventional uniformed medicine to the tailor-made one. On January 20, 2015, President Obama announced the Precision Medicine Initiative (PMI), in his State of the Union address. As part of PMI, the NIH is leading the effort to build a national, large-scale research enterprise with one million or more volunteers to extend precision medicine to all diseases. Personalized medicine is a medical procedure that separates patients into different groups—with medical decisions, practices, interventions and/or products being tailored to the individual patient based on their predicted response or risk of disease. We, Japanese Clinician Biologics Research Group, have been continuing the study named SARABA Study (which means "SNP Analysis of Responsiveness and Adverse Events of Biologic Agents") for several years. We have produced the results of prediction about effectivity and adverse events approximately at 90% of accuracy. This is one of the most effective and useful methods in choosing relevant Biologics for the particular patient.

LS10

Possible role of iguratimod in the treatment of rheumatoid arthritis (RA)

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Conflict of interest: Yes

Conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) have a central position in RA treatment. Among csDMARDs, MTX is considered as the first line drug and anchor drug. However, about 20~40% of patients experience inadequate response to MTX and require further therapy. Furthermore, we need several therapeutic options for not only patients of MTX contraindications or early intolerance but also for patients who have low renal function, risk factors of infection, and a his-

tory of lymphoproliferative disorders (LPD) Iguratimod (IGU) is a novel DMARD that is a chromone derivative and is classified to immunomodulatory drugs. IGU inhibits the production of immunoglobulins and various inflammatory cytokines by inhibiting the nuclear transcription factor NFκB, but does not inhibit the proliferation of lymphocytes. Clinical efficacy and tolerability are comparable to salazosulfapyridine when used as monotherapy and combination with MTX is synergic. The rates of remission and low disease activity were 48% and 26%, respectively in patients inadequate response to high-dose MTX. In patients responding insufficiently to combination of MTX and biologics, the addition of IGU as the 3rd DMARD could be a therapeutic option to not only achieve remission but also to reduce or discontinue biologics. Recently safety concerns such as opportunistic infections and LPD due to long-term immunosuppression have been regarded as a problem in RA patients. IGU is considered as a substitutional drug in patients with non-tuberculosis mycobacterial infection or patients developed LPD under treatment of immunosuppressive drugs. In this lecture, I discuss the possible role of IGU in the treatment of RA.

LS11-1

The progress of the treatment in patient with rheumatoid arthritis

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Conflict of interest: Yes

Rheumatoid arthritis (RA) is an autoimmune disease characterized by synovitis and joint destruction. With the development of biological disease-modifying antirheumatic drugs (bDMARDs), clinical remission has become the primary goal in the treatment of the disease, and both structural and functional remissions have become possible. Based on these evidences, both the ACR and EULAR introduced the treat-to-target concept. Treatment of RA with bDMARDs or tsDMARDs is designed to achieve this goal. Meanwhile, no preference of one over another biological agent should be expressed in the 2016 update of the recommendations. Current research focuses on how to use these biological products. On the other hand, the high cost of some bDMARDs and concern about long-term safety through the inhibition of particular molecules, may limit the use of bDMARDs and can lead to discontinuation after persistently long remission. Previous studies on TNF inhibitors, such as infliximab and adalimumab, in combination with MTX, demonstrated that treatment with these agents reduced disease activity allowing their discontinuation without clinical flare. To date, we have conducted several studies from the cohort of more than 2500 patients treated with bDMARDs (the FIRST registry), such as study regarding clinical effects of abatacept (ALTAIR study) and comparison using propensity score matching among biologics. In these studies, differences were found in factors predictive for efficacy. Moreover, we reported the diversity of immunopathogenesis in patients with RA using the immunophenotypic analysis and identified the phenotypes that could predict the response to bDMARDs. Despite of these studies, there is no established evidence to guide drug selection. Meanwhile, studies from our laboratories and several other investigators have previously suggested discontinuation of bDMARDs such as TNF inhibitors, but the consequences of discontinuation of abatacept and tocilizumab were uncertain. Accumulation of further evidence is needed to resolve these two clinical questions in the next decade.

LS11-2

Optimized rheumatoid arthritis treatment strategy and the its practice -based on balance with the effectiveness and safety-

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Conflict of interest: Yes

The aim of rheumatoid arthritis (RA) treatment at the present is actually clinical remission by the development of the drug including the biological agents and the appearance of the treatment concept of treat to target (T2T). How should we perform T2T with a disease activity index by reviewing treatment? Guidelines for the management of RA, Japan College of Rheumatology 2014 suggested the treatment strategy and the effectiveness of drugs, but not how to select drugs in the poor evidence of the direct comparison of their effectiveness. It seems that there are still problems how we should select drugs and practice this optimized treatment strategy. Therefore, following a principle and treatment policy of this guideline, it is important that we should prevent or reduce side effects of drugs by appropriate use controlling complication of RA, and to decide a therapeutic drugs based on a shared decision including medical costs between the patient and the rheumatologist Key drugs in the treatment of RA in daily practice are methotrexate (MTX) and biological reagents. If RA was diagnosed in early phase, we can control the disease activity only by MTX, but the effectiveness of biological reagents leading to remission and bone destruction is higher than MTX. Furthermore, MTX use is becoming difficult because of increase on a side effect and compliance with the aging of RA patents. In this sense, usefulness of biological reagents which have not liver kidney metabolism becomes higher if we can avoid the infection risk and reduce the cost. The reduction or discontinuation of biological reagents and MTX will be necessary in future. Abatacept is different from the drug which targeted conventional cytokine in action mechanism. It (called T-cell co-stimulation modulator) inhibits the costimulatory signal between an antigen presenting cell and the T cell, leading to suppress inflammatory cytokine production mediating the downstream. So abatacept can control the basic factor of the immune disease to control antigen-antibody reaction including the indirect action to B cells. The superiority of this reagent is to reduce the side effect and secondary failure, but to keep the efficacy after drug withdrawal because of its low immunogenicity. More recently, the direct action to osteoclast is shown in the mechanism of the suppression of bone destruction. In this seminar, I would like to give an outline about a role of abatacept in the current RA treatment strategy on the basis of the balance of effectiveness and safety.

LS12

The changing landscape of biosimilars in rheumatology

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Conflict of interest: Yes

Biosimilars represent a new opportunity for lowering the cost of treatment with biological disease-modifying antirheumatic drugs (bDMARDs). Reduced costs of bDMARDs should potentially lead to better access of this important therapy for more patients and reduction of the current inequity in the access to these drugs across countries. The regulatory agencies in Europe and in US have set up strict guidelines for approval of biosimilars. Three biosimilars have till now been approved in Europe. CT-P13 is a biosimilar infliximab which was approved in the fall 2013 (marketed in most EU countries from 2015). SB4 (biosimilar etanercept) and SB2 (biosimilar infliximab) were also recently approved. Most rheumatologists will consider biosimilars on the same level as originator products when treatment are started or changed for medical reasons. However, replacing originator product by a biosimilar in patients on stable treatment is more controversial, but is important because of the large cost-savings. Switch data from extension studies and from registries have not raised any major concerns about switching (also called transition). In the NOR-SWITCH trial – totally funded by the Norwegian government – 482 patients on stable treatment with reference infliximab across the 6 indications (RA, SpA, PsA, UC, CD, PsO) were randomized to continued treatment with the reference product or switch to CT-P13 and followed for one year (Jørgensen KK et al, Lancet, in press). The primary endpoint was occurrence of disease worsening which occurred in 26.2% of patients who continued treatment with reference infliximab and in 29.6% of patients who switched to CT-P13. The adjusted treatment difference (95% CI) was -4.4%(-12.7 – 3.9) which was within the prespecified non-inferiority margin of -15%. There were no differences between the two groups in secondary endpoints including time to study drug discontinuation, remission rates, CRP levels, adverse events, formation of anti-drug antibodies and drug trough levels. In conclusion, the NOR-SWITCH study demonstrated that switching to CT-P13 was not inferior to continued treatment with reference infliximab supporting that switching for non-medical reasons is safe and efficacious.

LS13

Strategy of osteoporosis treatment using long-acting bisphosphonate

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Conflict of interest: Yes

Japan is one of the most aging countries in the world, and the proportion of people aged over 65 years old in the total population is highest in the world. The aging of the society results in the increase in the number of osteoporosis patients, and around 15 million osteoporosis patients exist in Japan, which is an economic burden for the society. The treatment of osteoporosis by anti-resorptive agents such as second and third generation bisphosphonates successfully reduces the osteoporotic fractures. However, oral bisphosphonates are associated with complicated dosing regimens because of poor absorption, resulting in poor adherence. Zoledronic acid (ZOL) 5 mg, a once-yearly intravenous bisphosphonate, is approved for the treatment of osteoporosis, and ensures adherence and persistence over the entire 12-month dosing interval. In Once Yearly-Pivotal Fracture Trial (HORIZON-PFT), intravenous injection of ZOL 5 mg showed an increase in bone mineral density (BMD) and decrease in morphometric vertebral fractures (70%), clinical vertebral fractures (77%), non-vertebral fractures (25%) and hip fractures (41%) compared to the placebo in 36 months. The fracture prevention and safety of once-yearly intravenous infusion of ZOL was also analyzed in Japan (ZONE study), and ZOL treatment significantly reduced vertebral fractures (65%) and non-vertebral fractures (45%) compared to the placebo in 24 months. Adverse events such as acute phase reaction, osteonecrosis of jaw and kidney injury should be carefully monitored.

LS14

Perspective of the treatment of rheumatoid arthritis

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Conflict of interest: Yes

Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by synovial inflammation and joint destruction. However, the combined use of methotrexate (MTX), a synthetic disease-modifying anti-rheumatic drug (DMARD), and biologic DMARD has revolutionized treatment of RA. Clinical remission is now realistic targets, achieved by a large proportion of RA patients, and rapid and appropriate induction of remission by intensive treatment with biological DMARD and MTX is prerequisite to halt joint damage and functional disabilities. However, biological DMARD is limited to intravenous or subcutaneous uses and orally available small but strong molecules have been developed. The multiple cytokines and cell surface molecules bind to receptors, resulting in the activation of various signalling, including phosphorylation of kinase proteins. Among multiple kinases, Janus kinase (JAK) plays pivotal roles in the pathological processes of RA. Oral administration of JAK inhibitors is significantly effective than placebo with or without methotrexate in active RA patients with methotrexate-naïve, inadequately responsive to methotrexate or TNF-inhibitors. Their therapeutic efficacy was observed in a short term after administration and was as strong as adalimumab, a TNF-inhibitor. However, because the association of JAK inhibitors with carcinogenicity and infections remains debated, further investigation on post-marketing survey would help us understand the positioning of this drug.

LS15

Selexipag for the Treatment of connective-tissue disease associated Pulmonary Arterial Hypertension

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Conflict of interest: Yes

Although recent progress of pulmonary vasodilator therapies, the prognosis of pulmonary arterial hypertension associated with connective tissue diseases is still poor. Lung disease, left ventricular disease, and pulmonary venous involvement has been reported in patients with connective tissue disease associated pulmonary hypertension, especially in patients with systemic sclerosis, and may also be the risk of development of pulmonary edema after starting pulmonary vasodilator therapies. Current recommendations support the combination therapies that target the endothelin, nitric-oxide, and prostacyclin pathways. Epoprostenol has been shown to decrease the mortality in PAH patients when used in combination with other drugs. Despite the benefits of intravenous prostacyclin therapy, its short half-life turned out to be its main disadvantage as an intravenous catheter is required for its continuous delivery. Selexipag is an oral prostacyclin (PGI2) agonist. In the multi-centered Phase 3 study (GRIPHON), selexipag has been shown to reduce the death and hospitalization due to PAH significantly, and the beneficial effect was showed in the patients with connective tissue associated pulmonary arterial hypertension. In this seminar we review the comprehensive information on screening, diagnosis, and therapy of connective tissue associated pulmonary arterial hypertension. We also discuss the effect of selexipag to the connective tissue associated pulmonary arterial hypertension, showing the case of SSc-PAH patients treated with selexipag.

LS16

New wave in management of Sjögren's syndrome

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Conflict of interest: None

Recently, new wave in management of Sjögren's syndrome (SS) is generated. First, SS has been targeted for medical expenses subsidy as specify incurable disease from January 2015 in Japan, if patients satisfy the diagnostic and disease severity criteria. Then, new ACR-EULAR classification criteria was published in 2016. Finally, in 2017, the evidence-based practice guideline for SS will be published by the research team of Ministry of Health, Labour and Welfare. SS is a chronic inflammatory autoimmune disease primarily characterized by lymphocyte-mediated destruction of the exocrine glands, resulting in dry eye and dry mouth. The inflammatory process can affect any extraglandular organ. Therefore, in addition to the common dryness signs and symptoms, systemic manifestations may occur during the evolution of the disease. SS is associated with other autoimmune rheumatic diseases, such rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). When extraglandular manifestations developed, the distinction between SS-induced and other connective tissue disease-induced may be difficult in some patients. Thus, SS has various clinical conditions. The therapeutic management for patients with SS is based on the management of both sicca and systemic manifestations. The management of extraglandular manifestations must be tailored to organs involved. Adequate understanding and best use of diagnostic criteria and disease activity assessment indexes is necessary for accurate grasping clinical conditions and therapeutic planning. Besides, appropriate researches require them. In this seminar, I will introduce "the new wave in management of SS" such as actual state of SS in Japan, diagnostic / classification criteria, disease activity assessment by ESSPRI and ESSDAI, characterization of glandular and extraglandular manifestations and efficacy of biologics, based on evidences which formed practice guideline for SS.

LS17-1

Management of Lupus nephritis

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Conflict of interest: Yes

Amongst the organ diseases in patients with systemic lupus erythematosus (SLE), lupus nephritis (LN) is one of the most common and important manifestations. Treatment guidelines for LN have recently been issued by American College of Rheumatology and European Renal Association-European Dialysis and Transplant Association. A number of im-

munosuppressants has been used for the treatment of systemic lupus erythematosus in daily practice, and they contribute to improve the prognosis of the affected patients. Recently we (Lupus 23, 1124-32, 2014) reported that clarify the long-term outcome in patients with lupus nephritis (LN) according to the International Society of Nephrology and Renal Pathology Society classification. This retrospective analysis comprised 186 Japanese patients given a diagnosis of LN by renal specimen with a mean observation period of 12 years. Kaplan-Meier analysis revealed a 10-year overall survival of 95.7%. However, ADL in patients with LN have not been well preserved. The maintenance therapy is as important as the remission induction. In any case, active LN should be treated using effective immunosuppressants, according to the LN classification. Mycophenolate or cyclophosphamide are the most recommended for active class III/IV nephritis. Patients with class V LN are in general poor responders. For difficult LN, steroid pulse and/or tacrolimus may be used as well. The management of the LN patients as chronic renal diseases should be seriously considered. Proteinuria, urine-sediment and blood pressure should be monitored as well as immunological biomarkers. Anti-infection is the most important in the remission induction phase. In contrast, anti-osteoporosis and/or anti-cardiovascular diseases should be carefully considered during the maintenance phase.

LS17-2

Current therapeutic strategies for lupus nephritis

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Conflict of interest: Yes

Systemic lupus erythematosus (SLE) has mainly been treated with steroids for the past few decades. Particularly in patients with life-threatening visceral lesions, high-dose steroid therapy is selected to induce remission, while the main issue regarding therapeutic strategies is which type of immunosuppressive agents is added to the therapy. Steroids have an immediate and reliable effect, which other drugs do not have. However, a high incidence of various complications due to long-term use of steroids has been recognized in recent years, and treatment with steroids at the lowest possible dose is required from a long-term perspective. Although clinical studies aiming to reduce steroid doses have lately been conducted on many drugs with therapeutic targets that differ from previously used targets, no satisfactory results have been obtained. At present, a practical therapeutic strategy to minimize the steroid dose would be a combination therapy with existing drugs. One of the advantages of combination therapy is the beneficial synergistic effects of concomitant drugs. A problem with the treatment of SLE is its various pathological conditions. No drug is effective for all conditions, and particularly drugs targeting specific molecules are often effective for only specific pathological conditions. The concomitant use of drugs with different mechanisms of action can compensate for such a disadvantage of monotherapy. In terms of safety, combining drugs with different profiles of adverse reactions would allow doses to be set aiming at maximum effect. As for the treatment of lupus nephritis, immunosuppressive agents with abundant evidence are IVCY and MMF, and an option of multidrug therapy with one of them as a mainstay should be considered. Currently available drugs that can be used in combination with these drugs with myelosuppressive effects include calcineurin inhibitors. In Europe and the United States, these inhibitors are not commonly used, with limited evidence in the literature. However, calcineurin inhibitors are frequently used in Asia and many specialists acknowledge their usefulness. Further studies are needed to investigate the therapeutic targets to be set, treatment protocols, safety concerns, etc., for combination therapy with these drugs.

LS18-1

The treatment of the latest psoriatic arthritis (PsA) −From a viewpoint of internal medicine−

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Conflict of interest: None

PsA is systemic disease characterized by multiple enthesitis, arthritis, and spondylitis. These symptoms tend to repeat exacerbation and remission in the early stage therefore dermatologists should be careful about systemic physical symptoms and the cooperation with rheumatologists for early diagnosis. There is distinct characteristic in PsA. Because of inflammation sites is where mechanical stress is concentrated, the whole finger may be swollen as dactylitis as well as small joints. The differential diagnosis with the tender points of fibromyalgia is necessary. As a lesion appears in the axis joint in addition to a peripheral symptom, PsA is classified as one of the spondyloarthritis. It is difficult to diagnose the inflammatory back pain resulting spinal and sacroiliac ankylosis. Because PsA presents with polyarthritis, differential diagnosis with the RA is important. The joint synovium is the main lesion in RA, on the other hand the enthesis is the main lesion of inflammation in PsA. The proliferative changes of bones after inflammation improvement in addition to osteoclastic progress in PsA, and causes spur formation and ankylosis are the major difference with RA. In psoriasis patients as well as RA with systemic inflammation, cardiovascular complications due to arteriosclerosis and poor vital prognosis. Furthermore, the frequency of the metabolic syndrome is higher in the psoriasis patients, therefore it is necessary to pay more attention in PsA, severe condition of psoriasis. The treatment with new anti-IL-17A antibody presents a good effect for a skin symptom including a nail lesion besides all of peripheral arthritis, dactylitis, enthesitis, and the axial arthritis. It can be the good treatment choice for the secondary failure case for anti-TNF treatment, the case with demyelinating diseases or the antinuclear antibody-positive case. It is necessary to build clinical evidence for this new therapy.

LS18-2

Psoriatic arthritis and its treatment by biologics −A dermatologist's view

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Conflict of interest: Yes

Psoriasis is a chronic inflammatory disease mainly involving skin and joints. Skin symptoms of psoriasis varies greatly from tiny scaly plaque to gigantic plaques covered by coarse scale. All of the patients who have such lesions are diagnosed as having psoriasis, hence, the diagnosis covers wide variety. In other words, diagnosis of psoriasis consists of qualitative feature. This is a difference in diagnosing diseases in other field of medicine, where most of the diseases have quantitative diagnostic criteria. Psoriatic arthritis (PsA), one of the major part of spondyloarthritis, are usually diagnosed by CASPAR criteria. Fukuoka University Psoriasis Registry (FUPR) is a ongoing registry of psoriatic patients starting at 1998, and currently 1,188 patients are registered. Male/female ratio is 797/391≒2.03. The histogram stratified by onset age of psoriasis show two peaks at 30s and 50s. Very few disease show this skewed onset ages, hence, this observation may suggest that clinical diagnosis of psoriasis contain heterogenous sets. PsA shares 12.2% of men, 10.5% of women, and 11.6% of total. When PsA+ patients are compared with PsA- ones, there reside no difference in male/female ratio, severity of skin symptoms, body mass index, and age of onset. This result means that PsA is evenly distributed in any psoriatic patients. However, if we assume there are different set of patients in psoriasis, there may be a phenotype that contains more PsA+ patients. In this seminar, I will discuss this issue based on case control studies within FUPR. In Japan, there are six biologics of four different classes are available, namely two anti-TNF-α antibodies (Abs), one anti-IL-12/23p40 Ab, two anti-IL-17A Abs, and one anti0IL-17RA Ab. Furthermore, additional three anti-IL-23p19 Abs are on the pipeline. By bringing dramatic improvement of skin and joint symptoms of psoriasis, biologics have changed the treatment of psoriasis dramatically. In FUPR, 16.0% of the patients are receiving biologics. The proportion of biologics is 12.9% in PsA negative patients, while it is 39.9% in PsA+ patients, showing that biologics are employed much frequently in PsA+ patients. I also discuss the effectiveness of biologic treatment on PsA in FURP.

LS19

Management of RA after clinical remission from the aspects of pain, deformity and body image

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Conflict of interest: None

The control of systemic inflammation of rheumatoid arthritis (RA) has dramatically improved with new treatment strategies and introduction of biologic DMARDs. In this seminar, we will focus on the treatment strategy from the view of patients' pain, deformity, and psychological aspect after calming down their inflammation. Synovitis localized in the single joint may cause nociceptive pain. Intra-articular injection of corticosteroid is often effective for the joint with minimal structural damage, not only for knee joint, but other joints such as shoulder, elbow, wrist and fingers, and foot and ankle joints. Arthroscopic synovectomy is a useful option for the joint with steroid-resistant inflammation. Severe pain may be induced by mechanical stimulation by loss of joint congruity or stability, and bony protrusion in the late stage of joint destruction. For these conditions, surgical intervention would be required with appropriate timing. In cases to whom surgical treatment cannot be indicated, pharmacologic therapy for pain should be considered. COX-2 inhibitor or acetaminophen for nociceptive pain, tramadol for chronic and more severe pain and pregabalin for neuropathic pain are options for secondary osteoarthritis with RA patients with low disease activity. The number of total joint arthroplasty for hip and knee has been declined, whereas surgery for hand and foot has been increasing in our institute. Patients require surgery for finger deformity with cosmetic problem and functional disability, and foot surgery with pain in walking, even after the clinical remission. In our institute, disease control of patients before the surgery has been improving during these 10 years. In this line, joint preserving surgery has been much more indicated for finger and foot joints, expecting preservation of inflammation-free condition after the surgery. With effective pharmacological management of RA, patients' body image has been changed. Our recent study indicated surgical intervention can improve the patients' body image, and there are characteristic surgical site-related pattern in the improvement of body image. We should not expect RA patients "happy" because they manage to do in their daily lives.

LS20-1

Current conditions and problems of the elderly patients with rheumatoid arthritis registered in NinJa

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Conflict of interest: Yes

We have constructed a nationwide database of rheumatoid arthritis (RA): NinJa (National Database of Rheumatic Diseases in Japan) and have been collecting data since 2002. This data shows that medical care for RA is going in the better direction, such as a decrease in disease activity, an improvement in physical function, a decrease in RA-related surgery, and an increase in the mean age at the time of death. However, their mean age / mean onset age of RA has increased year by year (60.2yrs/46.6yrs in 2002 and 63.3yrs/50.9yrs in 2014, respectively) and the proportion of late elderly patients (over 75 yrs) has also significantly increased (8.3%/1.6% to 18.9%/5.3%). As RA patients get older, disease activity deteriorated and the remission rate (by SDAI) also decreased (35.4% in 60-64yrs, 31.0% in 70-74yrs, and 24.8% in 80-84yrs), the use of MTX (70.1%, 61.3%, 44.0%) and biologics (27.9%, 25.2%, 20.6%) reduced, and the use of csDMARDs other than MTX and oral corticosteroid (36.5%, 45.0%, 53.6%) elevated. It is suggested that sufficient disease control cannot be achieved because of complications or aging (such as deterioration of renal function), or that treatment is not strengthened more than necessary as the treatment targets are set to mild. In addition, physical function worsened (mHAQ>0.5: 24.7%, 33.0%, 49.7%) and the rate of patients requiring hospitalization also increased (13.6%, 19.0%, 22.9%) as RA patients get older, which should be interpreted by taking account of aging itself. "Age" is not considered in the current guideline for RA treatment and also in the strategy of T2T. Even composite measures themselves, which are the indices of disease activity, don't also consider "age". There are many factors relating to age affecting the components of composite measure (ESR, VAS, and so on), so their disease activities may be overestimated in the elderly patients with RA. For further aging of RA patients, it should be necessary to formulate the therapeutic strategies and the goals of treatment for RA considering age.

LS20-2

Treatment strategy of elderly patients with RA in the super-aging societies

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Conflict of interest: Yes

Elderly rheumatoid arthritis (RA) is classified into 2 clinical subsets, elderly-onset RA (EORA) and younger-onset elderly RA. EORA is a progressive disease similar to younger-onset RA. To prevent progression to irreversible geriatric syndromes, patients with EORA may undergo intensive treatment using a treat-to-target strategy. The treat-to-target strategy has been established in middle-aged patients with RA. TNF inhibitors, tocilizumab or abatacept are slightly less or equally effective in reducing disease activity in elderly patients with RA than in younger patients, and disease duration may have a greater impact on disease outcomes than age. Biological disease-modifying antirheumatic drugs are indispensable in the achievement of good outcomes on the treatment strategy of patients with EORA. However, the growing number of patients with EORA and younger-onset elderly RA poses a challenge to implementation of the treat-to-target strategy in the super-aging societies. Elderly patients with RA had multiple risk factors for serious infections, since they had multimorbidities and increasing age, chronic lung diseases, and physical dysfunction are independent risk factors for serious infections. Multi-morbidities, patient factors, and treatment-related risks make it difficult to establish a treatment strategy for EORA. Evidence-based treatment strategy for this patient population should be established in the next decade with special emphasis on the benefit-risk balance of various treatments. Do achieving low disease activity and functional remission are realistic goals in elderly patients with early RA? We will discuss the treatment strategy of elderly patients with RA in this seminar.

LS21

Clinical pearls for improving outcomes of patients with CTD-PH

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Conflict of interest: Yes

Prognosis in patients with connective tissue disease complicated with pulmonary hypertension (PH) used to be very poor, with a survival of <20% at 3 years after diagnosis. Recent introduction of molecular-targeting pulmonary vasodilators has improved functional capacity and hemodynamics as well as survivals in patients with pulmonary arterial hypertension (PAH), but a long-term survival of CTD-associated PAH still remains unsatisfactory even in recent cohorts. To further improve outcomes, it is imperative to pursue personalized medical approach by appreciating complex nature of PH in patients with CTD. In PAH associated with systemic lupus erythematosus, mixed connective tissue disease, or Sjogren's syndrome, pulmonary vascular remodeling is often reversible, especially in early disease phase. In this case, intensive immunosuppressive treatment should be initiated in combination with pulmonary vasodilators to achieve remission, which is normalization of exercise capacity and hemodynamics. In contrast, SSc patients with PH often have complex pathophysiology consisting of PAH, pulmonary veno-occlusive disease, myocardial involvement (usually diastolic dysfunction), and interstitial lung disease, leading to an inadequate response to pulmonary vasodilators or even unfavorable responses, such as pulmonary edema and worsening oxygenation. Since information obtained from echocardiogram is very limited, comprehensive assessment involving right heart catheterization, left heart catheterization with or without fluid challenge, chest high-resolution CT scan, pulmonary function test, and perfusion-ventilation scintigram, is mandatory. Pulmonary vasodilators should not be initiated without such detailed assessment. In addition, patients suspected to have PH should be referred to experienced specialized centers promptly. This lecture features clinical pearls useful for improving outcomes of PH in daily clinical practice taking care of CTD patients.

LS22

How the management of RA may change by the introduction of tofacitinib ?

Hisashi Yamanaka
Institute of Rheumatology, Tokyo Women's Medical University

Conflict of interest: Yes

Along with the progression of basic medical science, drugs targeted to the molecules which are deeply involved in the pathogenesis of rheumatoid arthritis (RA) or cancer have been developed. Many biological DMARDs (bDMARDs) have been developed, and tofacitinib is the first drug in the next stage, the first targeted synthetic DMARD (tsDMARD) that inhibits JAK1/3 molecule intracellularly. Tofacitinib was approved in Japan in 2013, and all case PMS study is now conducted. When the safety profile is confirmed, tofacitinib will be more frequently used. I would like to consider how the management of RA may change by the use of tofacitinib, especially in comparison to bDMARDs. First, the efficacy of tofacitinib is numerically similar to bDMARD by a clinical study and it is also effective to anti-TNF refractory patients. The safety profile should be carefully investigated since tofacitinib belongs to the news drug category, but by the preliminary report of the ongoing PMS study, the safety profile will be confirmed shortly. However, we have to aware the cytotoxicity of tofacitinib, since tofacitinib acts intracellularly, compared to bDMARDs which act extracellularly. Tofacitinib is an oral medicine, thus, there is no need for the hazardous effort and time for the infusion or injection that were required for bDMARDs, and it is the great advantage for the medical staffs as well as patients. On the other hand, we should take account of adherence of patients. Regarding the medical costs, it is comparable to bDMARDs, thus, pharmacoeconomical analysis of tofacitinib will be necessary. As the results, oral use of tofacitinib has a comparable efficacy to bDMARDs, but the burden of infusion or injection will be largely reduced. It means that this drug may be widely used not only by the rheumatology specialists but also by non-specialists. Thus, we need to implement the precise knowledge and the information for the proper use of this drug to the wide variety of medical staffs.

LS23

Patient-related factors associated with treatment optimization in patients with rheumatoid arthritis

Takao Fujii
Department of Rheumatology and Clinical Immunology, Wakayama Medical University

Conflict of interest: Yes

In patients with rheumatoid arthritis (RA), conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) including methotrexate (MTX) are usually selected for the first line treatment. In case of insufficient response of MTX monotherapy, however, biological DMARDs (bDMARDs) may be required. Unfortunately, the Japan College of Rheumatology RA guideline 2014 showed no recommendation regarding the bDMARD selection and there are few evidences about the best choice especially for biologic-naïve patients. In pharmacological factors, 1) the right target molecule (e.g., TNF-α, IL-6, and others), 2) serum trough levels of bDMARDs superior to the minimum levels of effective concentration, and 3) preferable transmigration to target organs, should be critical, but these information are not available in clinical practice. Rather, it may be more important for optimal bDMARD selection to consider patient-related factors; 1) patient age, 2) disease activity including bone damage, 3) disease duration, 4) autoantibody positivity, 5) body weight, and 6) comorbidity. Additionally, patient-related factors associated with efficacy may be different by treatment targets; ·A) clinical remission, B) imaging remission, and C) achievement of treatment holiday. The GO-FORTH study clearly indicated that 100 mg of golimumab (GLM) + MTX was more preferable than 50 mg of GLM + MTX for imaging remission in high-CRP level and/or high disease activity patients whereas clinical remission was equally recognized between in both patients receiving 50 and 100 mg of GLM with MTX. Achievement of treatment holiday by infliximab (the RRR study), however, was associated with younger age, shorter disease duration, and lower total Sharp score, but not with CRP value and disease activity at baseline. Thus, predicting factors are quite different by clinical setting of treatment targets. In this seminar, patient-related factors associated with bDMARD efficacy will be shown from the previous studies and the optimal bDMARD use in RA may be discussed.

LS24

Pain care in the rheumatic diseases

Yuho Kadono
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Conflict of interest: Yes

Recently, we are able to hold down disease activity of rheumatoid arthritis (RA) using biological DMARDs and methotrexate, and it became the treatment goal to protect joint destruction. Although many patients can achieve remission, it is a fact that there are patients who cannot. Sometimes patients drop out because of the secondary failure even if they achieved remission. We often see patients who suffer side effects or complications. It is still difficult to maintain remission throughout the life. Under such an inflammatory situation, the joint destruction gradually progresses. In addition, even if we maintained remission and protect joint destruction for several years, we could not protect degenerative osteoarthritis or spondylosis for several decades. The chief complaint of the patient of not only RA but also other many rheumatic diseases, is 'a pain'. Patients visit clinic to get reduce a pain. Pain leads to ADL limitation, or psychological stress. Pain care is 'a key' for treatment and it is the start. We should distinguish nociceptive pain because of joint inflammation or deformity, from neuropathic pain due to the compression of nerve. It is necessary to prescribe an appropriate medicine. It is sometimes difficult to control the sharp pain at the time of the exercise using only medicines. In such a situation, it is required orthosis or surgery to get rid of pain due to deformity or instability of joints. The cause of the pain greatly varies according to an individual, and it is important to approach it from many aspects.

LS25

Pathophysiological mechanisms and treatments of pulmonary arterial hypertension with systemic sclerosis

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Conflict of interest: None

Pulmonary arterial hypertension (PAH) with systemic sclerosis (SSc) complicates several mechanisms of PH, leading to difficulties in diagnosis and treatments. Its prognosis is worse than those of idiopathic and non-SSc-PAH. Whereas improved prognosis after a trial of early detection and intervention was reported (Humber, 2011), unimproved prognosis was also reported (Rubenfire, 2013), suggesting that the efficacy of pulmonary vasodilators on SSc-PAH is relatively low. A recent topic in the area is "Death in SSc-PAH is not caused by PAH". Some pointed out the deaths brought by pulmonary or gastrointestinal lesions, another reported that even the heart-associated deaths occurred in the cases with well-controlled pulmonary arterial pressure (PAP) and declining left heart function (Dohi, JPCPHS 2016). The mechanisms of SSc-PH are complexed; there are very few cases with pure PAH (Group 1) without cardiac (Groups 2) and pulmonary (Group 3) lesions. In this seminar, the author exhibits his cases and explains 4 factors, which can interfere PAH: Group 2, Group 3, venous lesion, and volume retention by pulmonary vasodilators. Three open-label trials for SSc-PAH by bosentan showed only trivial effects, while an open-label trial for SSc-PAH by initial combination therapy with ambrisentan and tadalafil showed a significantly-decreased PAP (Hassoun, 2015). Sequential combination therapy can be also selected in the treatment of SSc-PAH in view of safety. Because a part of SSc patients with borderline PAP (20-25 mmHg) advance to real SSc-PAH, bosentan (Kovac, 2012) or sildenafil + beraprost (Yasuoka, JPCPHS 2016) have been tried in patients with borderline PAP. Use of pulmonary vasodilators are indicated in the treatments of SSc-PAH after meticulous assessment of complexed mechanisms. However, attention should be paid for the adverse events, and the ultimate prognosis remains poor with other causes of deaths. Development of anti-fibrotic agents is required.

LS26

Infectious disease management in rheumatoid arthritis therapy

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Conflict of interest: Yes

It is a giant leap that remission has become a real goal for rheumatoid arthritis (RA) treatment together with biological products. On the other hand, various infectious diseases sometimes result in lethal pathology. Major objective of this seminar is to review the background of infectious diseases since the introduction of biological products, the screening methodology and appropriate approach towards them. As Japan is still a medium-spreading country for tuberculosis (TB), TB screening and prophylaxis therapy has become mandatory together with tumor necrosis factor (TNF) inhibitor approval. Consequently, according to post marketing surveillance (PMS) of infliximab (IFX), we could successfully manage TB onset after 2000 cases and further. Currently, the guideline recommends the TB history inquiry, chest X-ray, Interferon gamma release assay (IGRA) screening even before methotrexate (MTX) administration. Due to the strong host immune response, pneumocystis pneumonia (PCP) in RA causes serious respiratory failure despite its small amount of bacteria. It is not rare to experience PCP not only during the administration of biological products but also in combination with anti-rheumatic drugs, and it is usually a big issue how to select the proper candidate for ST combination prophylactic therapy with many side effects. In HBV-infected cases, HBV-DNA titer sometimes increases with the immunosuppressive therapy, and trigger hepatitis onset, this is defined as “De novo hepatitis B”, and frequently becomes fulminant. Therefore, it is necessary to periodically measure the titer of HBV-DNA and to avoid fulminant episodes by proper administration of entecavir. Although it is rarely fatal, nontuberculous mycobacteria (NTM) disease is also a complication negatively affecting RA treatment. As it is difficult to distinguish between airway lesions associated with RA and NTM only with images, repeated sputum inspections are necessary. Although the use of biological products at the time of NTM bacterial shedding is contraindicated, it is necessary to understand what type of bacteria or whole body condition you can administer biological products. Herpes zoster is not a rare disease, however the incidence rate in Janus kinase (JAK) inhibitor therapy is higher than other anti-rheumatic drugs, furthermore, as it is apparent in Asians, inactivated vaccines need to be developed in the future. It is also necessary to watch for reactivation of Cytomegalovirus (CMV) and Epstein-Barr virus (EBV) belonging to herpesvirus family. For TB screening, two kinds of IGRAs, QuantiFERON -TB Gold (QFT) and T-SPOT. TB (T-SPOT) are currently used. Although our hospital has not experienced any case of TB onset during RA treatment, we have examined correlation between positive rates of each test and patient background. Furthermore, under the estimation that number of spots in T-SPOT positive control can possibly reflect the interferon productivity, we have examined the relationship between infectivity and disease activity of RA.

LS27-1

Advances in Rheumatological Treatment with High-Resolution Ultrasound Imaging: Excellent Results Obtained with and Strong Clinical Evidence for New Transducers

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Conflict of interest: None

The basic diagnostic methods that have been used by every physician since Hippocrates are inspection, auscultation, and palpation. However, in modern medical practice, we employ a wide variety of new technologies in addition to these basic methods, and the steady progress in diagnostic imaging has brought great benefits. As a physician specializing in rheumatology and connective tissue disease, I feel that ultrasound examination of the joints, which is attracting keen interest in Japan, is the ultimate example of such advanced technology. Joint ultrasound can be performed at any time and any place, allowing a multipronged clinical approach. Of course, there is no radiation exposure. The main benefit of joint ultrasound in the field of rheumatology is that subtle pathologic changes that cannot be detected by physical examination or plain X-ray can be clearly visualized. It is therefore indispensable for the early diagnosis of rheumatoid arthritis. In differential diagnosis, some diseases can be immediately diagnosed by simply applying the transducer to the target region. In addition, joint ultrasound is useful for evaluating treatment effects based on structural changes, and in many cases, it is useful for deciding whether to discontinue or reduce the dose of biologic agents. Joint ultrasound is commonly performed in Europe (as demonstrated by EULAR-OMERACT), and its clinical applications, effectiveness, and pitfalls are frequently reported in Japan. There are many highly skilled ultrasonographers in Japan whose excellent techniques are recognized around the world, and ultrasound systems with even higher resolution are being developed here. In rheumatology, such high-resolution ultrasound systems allow the detailed visualization of structures that cannot be evaluated by physical examination or other conventional means. This seminar focuses on the excellent results obtained with and strong clinical evidence for high-resolution transducers in routine clinical practice.

LS27-2

Current Expertise on Diagnostic Imaging for Rheumatoid Arthritis and Future Prospects

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Conflict of interest: None

Synovial hyperplasia due to inflammation and the development of vascular dilatation and neovascularization within the hyperplastic synovium resulting in joint damage are pathognomonic of the synovitis associated with rheumatoid arthritis. Ultrasound can be used to acquire blood flow signals from the extremely small abnormal blood vessels that have formed in the synovial membrane. Evaluation of synovial blood flow allows the presence of synovitis to be determined objectively, which is very useful for the diagnosis of rheumatoid arthritis. The Power Doppler method was specified as the gold standard by the Japan College of Rheumatology Committee for the Standardization of Musculoskeletal Ultrasonography in 2011, and it is now widely employed for the evaluation of blood flow. However, Toshiba Medical’s new Doppler technique “Superb Micro-vascular Imaging”(SMI) is also attracting attention. SMI can depict finer, lower-velocity blood flow due to its improved low-velocity flow detection capabilities, higher frame rate, superior resolution, and reduced motion artifacts. The low-velocity blood flow associated with inflammation can be observed in a stress-free examination, and synovial hyperplasia and blood flow in dilated vessels in surrounding tissues can be depicted with higher sensitivity, allowing the courses and extent of the vessels to be clearly visualized. Synovitis is usually evaluated using 2D images of planes that contain relatively severe inflammation, but SMI-3D volume images with low levels of artifacts can show the continuity of the blood vessels in the depth direction, making it easier to understand the overall anatomy. Image quality is dramatically improved in Aplio i800 due to its excellent spatial resolution and SMI’s ability to detect low-velocity blood flow with the 24-MHz high-frequency transducer PLI-2004BX. This seminar focuses on the added value provided by SMI as compared to the power Doppler method in the evaluation of synovitis in small joints.

LS28

Practical management strategy of interstitial pneumonia associated with polymyositis/dermatomyositis

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Conflict of interest: Yes

Polymyositis/dermatomyositis (PM/DM) is a heterogeneous disease spectrum consisting of inflammatory myopathy, skin lesions, and interstitial pneumonia (IP) in various combinations. Therefore, it is imperative to pursue management strategy based on prediction of future clinical course and prognosis. IP and malignancy are two major causes of death in patients with PM/DM. In particular, IP occurs in more than 40% of the patients, but clinical courses are highly variable: some represented progressive course leading to death, but others experience stable disease

course without progression for many years. Recently, a number of serum autoantibodies specific to PM/DM have been identified. They are shown to be useful in clinical subsetting because of their strong associations with clinical features and mutual exclusivity. Of those, anti-aminoacyl tRNA synthetase (ARS), anti-MDA5, anti-Mi-2, and anti-TIF1γ antibodies are currently measurable in routine clinical practice. Autoantibodies associated with IP include anti-ARS, which is often found in patients with acute or subacute IP showing a favorable treatment response but repeated recurrence, and anti-MDA5, which is associated with rapidly progressive IP refractory to immunosuppressive treatment. In clinical practice, it is necessary to consider other predictors, including anti-MDA5 antibody levels, skin ulceration, serum ferritin and CRP level, oxygen saturation on exercise, and chest high-resolution CT patterns. Corticosteroids plus immunosuppressants are the standard regimen, but intensity of the treatment is adjusted based on prediction of prognosis. Patients with multiple poor predictors should be treated with high-dose corticosteroids (including methylprednisolone pulse therapy) in combination with intravenous cyclophosphamide and calcineurin inhibitor, while treatment strategies considering both remission induction and maintenance phases are necessary to manage anti-ARS-positive patients who are likely to recur.

LS29

Hepatitis B Virus Reactivation during Immunosuppressive Therapies

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Conflict of interest: Yes

HBV itself is not toxic against hepatocytes. Liver injuries develop as a result of immune response against HBV. Clinical courses of patients with HBV infection are classified into immune tolerant, eradication and surveillance stages. Patients at immune surveillance stage in whom serum HBs-antigen disappeared are also diagnosed as having previously resolved HBV (prHBV) infection. Thus, patients with prHBV infection are classified into 2 types; patients after transient HBV infection and HBV carriers at remission stage. In these patients, liver injuries do not occur, since HBV proliferates minimally since nucleoside mutations occur. During immunosuppressive therapies, however, minor HCV strains possibly showing active proliferation may appear in the sera leading to development of liver injuries. The study group supported by the Ministry of Health, Labour and Welfare, revealed that the cumulative rate of HBV reactivation defined as serum HBV-DNA levels of 20 IU/mL or more was 3.2% at 6 months following the initiation/modification of immunosuppressive therapies, and HBV reactivation seldom developed then later. Moreover, serum HBV-DNA became undetectable without nucleoside/nucleotide analogs administration even when HBV reactivation occurred at 6 months or later. Thus, the guideline regarding HBV reactivation was revised in 2013; serum HBV-DNA measurements should be done every month within 6 months following the initiation and/or modification of the therapies, but the duration of the examination can be prolonged up to 3 months. Considering economic issues, the study is now conducting the prospective study to apply HBs-antigen measured by a high-sensitive method instead of HBV-DNA for monitoring of HBV reactivation. However, fatal cases with acute liver failure due to HBV reactivation were still enrolled in the nationwide survey by the study group, and the patients especially due to immunosuppressive therapies were increasing.

LS30-1

The concept of spondyloarthritis and its articular and extra-articular manifestations

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Conflict of interest: Yes

Spondyloarthritis (SpA) is characterized by axial joint inflammation, asymmetric peripheral arthritis, dactylitis and enthesitis. SpA includes predominantly axial SpA such as ankylosing spondylitis and non-radiographic axial SpA, and predominantly peripheral SpA such as psoriatic arthritis, reactive arthritis and SpA associated with inflammatory bowel diseases. As extra-articular manifestations, eye, skin, gut and urogenital lesions are frequently observed as compared with lung, kidney, heart and nerve disorders. Therefore, multidisciplinary approach to patients with SpA and systemic evaluation and monitoring are crucial. The American College of Rheumatology recommends non-steroidal anti-inflammatory drugs (NSAIDs), followed by anti- tumor necrosis factor (TNF) biological agents for axial SpA. The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) recommends conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) such as methotrexate and salazosulfapyridine, followed by biological agents including TNF inhibitors for psoriatic arthritis. Biological agents are also highly effective for extra-articular manifestations of SpA.

LS30-2

Inflammatory joint disease and eye

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Conflict of interest: None

Ocular problems are sometimes associated with systemic disorders, and various systemic illnesses, including inflammatory joint diseases accompany intraocular inflammation. Among them, uveitis, an inflammatory disease of uveal tract in the eye, is one of the most frequent ocular associations. Uveitis is anatomically classified into 4 categories;(1)anterior uveitis, (2)intermediate uveitis, (3)posterior uveitis and (4)panuveitis. Patients with inflammatory joint diseases, such as juvenile idiopathic arthritis (JIA), ankylosing spondylitis (AS), reactive arthritis, and psoriatic arthritis, develop anterior uveitis. Children with JIA sometimes develop chronic smoldering anterior uveitis with calcific band keratopathy, and visual prognosis may be poor due to secondary cataract or secondary glaucoma. Acute recurrent iridocyclitis is associated with AS. Sometimes, posterior segment intraocular inflammation such as macular edema and retinal vasculitis is also seen. In rheumatoid arthritis, scleritis or sclerouveitis is associated. On the other hand, Behcet's disease and sarcoidosis cause panuveitis. Visual prognosis used to be poor with conventional corticosteroid therapy or immunosuppressive drugs. However, recent new treatment with anti-TNFα agents is effective in maintaining good visual function. In this lecture, clinical features and new treatment of intraocular inflammation associated with inflammatory joint diseases will be presented.

LS31

The treatment strategies for Systemic Lupus Erythematosus in the past, present, and future

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Conflict of interest: None

Hydroxychloroquine (HCQ) and mycofenolate mofetil (MMF) were approved for the treatment of systemic lupus erythematosus (SLE) in 2015 and a new drug, belimumab, is expected to be approved in 2017. However, even these medications are incapable of curing SLE; although the 10-year survival is now higher than 90% the life-expectancy of SLE patients is still shorter than that of healthy individuals. The introduction of MMF and multi-targeted therapy has helped to achieve a higher remission rate but steroid- free remission remains difficult. Even low dose steroid (i.e. PSL 5mg/d) administered as maintenance therapy can increase the risk of osteoporosis, infection, and atherosclerosis. In contrast, HCQ is effective not only against symptoms of SLE such as rashes, arthralgia, and fatigue but also for the prevention of flare, organ damage, thrombosis, and death. Despite the recommendation in recent years of lupus experts worldwide that HCQ be administered to all SLE patients, this drug is still underused in Japan. It is important to be aware that HCQ can be administered safely over a lifetime as long as regular ophthalmologic screening is conducted.

LS32-1

Rheumatoid arthritis treatment - an update on joint surgery

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Conflict of interest: None

The role of the surgery in the treatment of Rheumatoid arthritis (RA) has dramatically changed over the last two decades. Since it has been difficult to control the disease activity only by conventional synthetic disease-modifying anti-rheumatic drugs previously, we have often performed synovectomy to control regional disease activity or total joint replacement for joint destruction. After the approval and the dose escalation of methotrexate and the launch of biological DMARDs for RA patients, outcome from RA treatment have improved dramatically. It is clear that the number of surgical interventions decreased by half compared with those in the early 2000's from our IORRA cohort data. However, surgery could still be a useful treatment option for painful joints, even if adequate drug treatment were conducted for RA patients. Furthermore, surgery have been also performed to fulfill patient's cosmetic needs, which was rarely operated before, since the control of RA disease activity is currently feasible. I will give an outline of updated role of the surgery in RA treatment.

LS32-2

Treatment strategy for rheumatoid arthritis with IL-6 antagonist in clinical practice

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Conflict of interest: Yes

Tocilizumab (TCZ)—a humanized monoclonal anti-interleukin 6 (IL-6) receptor antibody developed to inhibit the action of IL-6—has been used for treatment of RA in whole world and shown its effectiveness. In our observational study, FRAB registry, showed remission rates at 3 years of 66.7% with the EULAR remission criteria and drug retention rate (68.2%) at 3 years in routine clinical practice. RTCZ retention rates at 36 months were 63.7% for the biologics-naïve group and 70.4% for the anti-TNF-exposed group. The concomitant MTX showed no significant effects on this rate. Among the patients with remission, the majority remained in remission or had low disease activity. A manageable safety profile was noted. We conclude that TCZ represent good therapeutic options for patients with RA refractory to previous TNF therapy as well as those with no previous exposure to biologics.

Evening Seminar

ES1-1

Topics: Psoriatic arthritis and Spondyloarthritis

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Conflict of interest: Yes

Spondyloarthritis (SpA) includes: ankylosing spondylitis, reactive arthritis (formerly Reiter's syndrome), psoriatic arthritis, Juvenile SpA, enteropathic arthritis (spondylitis/arthritis associated with inflammatory bowel disease), and undifferentiated SpA. All display a variety of symptoms and signs, but they also share many features in common, including: inflammation of axial joints (especially the sacroiliac joints), asymmetric oligoarthritis (especially of the lower extremities), dactylitis (sausage digits), and enthesitis (inflammation at sites of ligamentous or tendon attachment to bone). Additional features include genital and skin lesions, eye and bowel inflammation, an association with preceding or ongoing infectious disorders, positive family history, elevated acute phase reactants, and a strong association with the human leukocyte antigen (HLA)-B27. The clinical manifestations, diagnosis, and classification of the SpA family of disorders in adults will be reviewed here. In agreement with the new ASAS classification criteria for axial and peripheral SpA and emerging data on TNF blockade and IL17 blockade, these data emphasize the need for early diagnosis and its differential diagnosis, and optimal treatment of not only AS and PsA but also other SpA sub-forms.

ES1-2

Imaging of spondyloarthritis

Hideharu Sugimoto
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Conflict of interest: None

Spondyloarthritis is a group of chronic inflammatory rheumatic disorders. Assessment of SpondyloArthritis International Society proposed new classification criteria; axial spondyloarthritis with spinal arthritis as its main affected site, and peripheral arthritis with peripheral skeleton as the main affected site. Sacroiliitis is a major finding of axial spondyloarthritis. In MR imaging, besides structural change, inflammatory changes such as bone marrow edema (osteitis) can be depicted. Early X-ray findings of spondyloarthritis are the erosion of the vertebral corners and squaring of the vertebral body by remodeling. In spondyloarthritis, bone marrow of the vertebral corner cause signal change due to active osteitis and fat metaplasia. The signal change is prominent at the ligament attachment site, especially the anterior longitudinal ligament attachment part. Psoriatic arthritis is a representative disorder of peripheral arthritis. The role of MR imaging in psoriatic arthritis is early diagnosis and therapeutic evaluation. MR imaging can depict bone marrow edema, synovitis, erosion, tenosynovitis, edema of extra-articular tissues, and periostitis. With the exception of bonny proliferative changes, MR imaging is superior to plain radiography with respect to the depiction of these findings. MR imaging can detect joint lesions before clinical symptoms become apparent. Bone marrow edema is MR finding preceding erosion. It can predict mutilans deformity and treatment effect. On contrast-enhanced MR imaging, synovial membrane shows marked enhancement. Although it have been pointed out that there are differences in the terms of infiltrating cells and angiogenesis between rheumatoid arthritis and psoriatic arthritis, it is difficult to distinguish them by MR imaging.

ES1-3

Treatment options widening for plaque psoriasis and psoriasis arthritis in Japan

Akimichi Morita
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Conflict of interest: Yes

Psoriasis is a common chronic inflammatory disease that affects ~2%

of the population in the USA. In Japan, the prevalence of psoriasis is lower than that in Western countries. Kubota et al. reported that the national prevalence of psoriasis was 0.34%. The prevalence of psoriatic arthritis (PsA) in Japan approaches 10-20%, similar to that observed in Western countries. It is associated with a significantly impaired quality of life and comorbidities such as cardiovascular disease, metabolic syndrome, and depression. The pathogenesis of psoriasis has become better understood by successful treatment with biologics, including infliximab (IFX), adalimumab (ADA), ustekinumab (UST), secukinumab (SEC), ixekizumab (IXE) and brodalumab which are currently available in Japan. The discovery of the interleukin (IL)-23/helper T cell (Th) 17 axis in the pathophysiology of psoriatic diseases. Based on the Japanese guideline, theses biologics can be used for the treatment of moderate-to-severe plaque psoriasis as a systemic treatment. Phototherapy is an important modality also in Japan. Narrow-band UVB and 308nm Excimer light are commonly available in the whole country. From topical application to systemic treatments, we are now focusing on "3T" including Time-management (early intervention), Tight control (PASI90/100), and Transition. Recent advance in investigation has suggested that IL-17A is also produced by a wide range of cells in psoriatic lesions, including dendritic cells, macrophages, neutrophils, and mast cells. IL-17A is known to be produced by Th17 cells, a class of helper T cells that act outside the established Th1/Th2 paradigm for regulation of innate and adaptive immunity, which are generated with IL-23 presence. A recombinant, high-affinity, fully human immunoglobulin G1κ monoclonal antibody that selectively binds and neutralizes IL-17A, is an efficacious treatment for plaque psoriasis and psoriasis arthritis. The efficacy of these biologics based on our experience in Nagoya City university will be shown in this seminar.

ES2-1

Clinical efficacy and safety of abatacept in rheumatoid arthritis in clinical practice: Results from Tsurumai Bilogics Communication Registry (TBCR)

Nobunori Takahashi
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Conflict of interest: Yes

[Background] Abatacept has been used for rheumatoid arthritis (RA) for 5 years in Japan. Major proportion of patients treated with abatacept used to be with poor characteristics including elderly or ineligible for methotrexate use due to comorbidities because of the emphatic safety profile. Currently, the evaluation of clinical efficacy has been increasing based on the results of the AMPLE, a head-to-head trial of efficacy between abatacept and adalimumab, and the studies in clinical practice patients. [Methods] We demonstrated the clinical efficacy and safety of abatacept using the data from Tsurumai Biologics Communication Registry (TBCR), a multicenter registry system for RA patients treated with biologics. [Results] Discontinuation rate due to adverse events was 2.9% at 24 weeks and 8.2% at 4 years. Clinical efficacy was quite similar in the patients with high disease activity at baseline and those with inadequate response to an anti-TNF monoclonal antibody agent, compared with other classes of biologic agent. Clinical efficacy was significantly increased even after 24 weeks. The achievement of low disease activity at 52 weeks was statistically predictable within 12 weeks, similar to the results of anti-TNF agents and tocilizumab. [Discussions] Safety profile was relatively better based on the lower discontinuation rate due to adverse events. Considering both the results of our clinical practice studies in TBCR and the AMPLE trial, abatacept should have quite comparable efficacy with anti-TNF agents and tocilizumab. Distinctively, we can use abatacept for longer than 24 weeks with expectation of adequate response in the patients without next promising treatment option. On the other hand, we can judge the clinical response of abatacept within 12 weeks in compliance with the modern recommendations or guidelines for rheumatoid arthritis treatment in the patients with next treatment options. Abatacept would be applied for a wider range of patients than ever.

ES2-2

Immunogenetic mechanism of Rheumatoid Arthritis and immunologic effect abatacept

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

Conflict of interest: Yes

It is widely accepted that inflammatory cytokines contribute to the pathogenesis of rheumatoid arthritis (RA). In contrast, the roles of adaptive immunity and T/B lymphocytes have not been elucidated. However, the clinical efficacy of co-stimulation blockade by abatacept strongly suggests the importance of adaptive immunity in RA pathogenesis. The relatively low incidence of infection was observed in several trials using abatacept, and abatacept is recommended to patients with a history of serious infection in ACR2015 recommendation. These facts suggest that immune-regulatory effect induced by abatacept is closely related to the abnormality in RA adaptive immunity. We have recently established a research system combined with immunophenotyping, transcriptome analysis with next generation sequencing, and single-nucleotide polymorphisms (SNPs) to address the immunogenetics of RA. This approach revealed that RA CD4+ T cells shows increased gene expressions of TCR proximal genes which is associated with DAS28, and immune cells in RA have altered gene expressions of cellular metabolism that is related to RA-associated SNPs. Intriguingly, abatacept decreased expressions of TCR-proximal genes to the baseline levels, and altered gene expressions of cellular metabolism have been skewed toward normal expressions. Moreover, in immunophenotyping, abatacept suppressed activation of helper T cells without reduction of the frequency of those cells. These results suggested that abatecept suppresses excessive adaptive immunity without induction of overt immunosuppression in RA. In this seminar, our research and novel reports in the field of rheumatology are collectively considered and discussed in the context of immunogenetic mechanism of RA and immunologic effect of abatacept.

ES3-1

Benefit of multi-target therapy

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Conflict of interest: Yes

The Japan launch of methotrexate (MTX) in 1999 and biologic disease-modifying antirheumatic drugs (bDMARD) in 2001 triggered a paradigm shift which dramatically improved treatment outcomes. It was not only the introductions of molecularly targeted drugs such as biologics that drove this paradigm shift in treatment, but the current practice of early diagnosis and early treatment intervention also played a significant role. In recent years, treating patients with conventional synthetic DMARDs (csDMARD) including MTX from early diagnosis, and the concept of optimizing treatment based on disease activity evaluation, the "Treat to Target (T2T)" strategy has become widely accepted. Treatment outcome has further improved by the introduction of effective RA treatments, bDMARDs and JAK inhibitors, and reaching clinical remission has become an achievable treatment goal for many RA patients. However, the clinical remission rate by currently available bDMARDs remains less than 50%, and there are patients requiring a new treatment option. In addition, recent report showed that even patients who have reached clinical remission experience remaining subjective symptoms. Recently, tofacitinib, a small-molecule targeted drug which acts on JAK tyrosine kinase involved in cytokine signaling pathway was launched. Furthermore, JAK1/JAK2 selective inhibitor, baricitinib, JAK1 selective inhibitors, filgotinib and upadacitinib are in its final development phases. JAK inhibitors are proven to have quicker onset and better clinical efficacy compared to existing bDMARDs in the clinical trials. It is also proven to be effective for suppression of structural damage. However, as JAK inhibitors inhibit the intercellular signaling pathways unlike other therapies that target single signals, building strong clinical evidence on long-term safety is still required. Since JAK inhibitors have proven efficacy for patients with refractory disease from biological drug therapy, the drugs are highly expected to improve patients' subjective symptoms such as pain, fatigue, and stiffness due to its rapid onset of effect and high anti-inflammatory properties, which may bring another paradigm shift in RA treatment. The objective of this seminar is to discuss the treatment outcomes by JAK inhibitors for RA and their differences from biological drugs.

ES3-2

Beyond treat to target - patient satisfaction and QOL

Peter C. Taylor
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Conflict of interest: Yes

Rheumatoid arthritis is a chronic, systemic inflammatory syndrome with its predominant manifestation in synovial joints. Synovitis may be associated with cumulative joint damage resulting in pain, disability, limitation of physical function, and other impairments in aspects of life important to patients. Early intervention gives rise to favorable outcomes and many studies demonstrate that optimum results can be achieved when disease activity is assessed regularly and treatment titrated according to the therapeutic response with the ideal treatment target of remission. Where remission is not achievable, low disease activity is an alternative goal. While such "treat-to-target" management approaches have improved the mean achievable outcomes at a cohort level, in the context of limited time for a patient consultation, there is a danger of treating the disease while inadequately treating the patient who has the disease! In order to identify aspects of life that continue to cause concern to the patient despite optimal suppression of systemic inflammation and disease activity, patient-reported outcome (PRO) assessments may be helpful. PRO measures include health-related quality of life (HRQOL), physical function, disability, fatigue, sleep, mental health status, work productivity and work activity impairment. These are standardized measures for which minimum clinically important differences (MCIDs) have been determined in most cases. Since PRO measures are obtained directly from patients, they may more accurately reflect how the patient feels and functions in relation to RA and to the treatment received. PRO measures also may facilitate doctor-patient communication with a view to shared decision-making to improve the holistic quality of care. Therefore, when used in addition to a treat-to-target approach, PRO assessment may facilitate other management strategies to optimise quality of life at any time and treat the patient who has the disease.

ES4-1

Overarching Principle in the RA treatment

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

Conflict of interest: Yes

Overarching principles influence every part of the recommendations of rheumatoid arthritis treatment. One of the most important overarching principles is shared decision and it is described as the treatment of rheumatoid arthritis must be based on a shared decision between patient and rheumatologist. Sufficient and appropriate convey of medical information to patients is imperative to achieve shared decision, and it is thought to facilitate success of management.

ES4-2

T2T in the clinical practice of RA

Toshihiko Hidaka
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Conflict of interest: Yes

Recent advances in the treatment of rheumatoid arthritis (RA) have enabled RA patients to meet the goal of remission, and live their life as usual. Behind this background, there were the influences from dissemination of the concept of "Treat-to-Target (T2T)". In chapter "Overarching principles" of the EULAR 2014 T2T recommendations, it is described that the treatment of RA must be based on a shared decision between patient and rheumatologist. In chapter "10 recommendations", it is also described the importance of communication between rheumatologist and patient. However, according to the results of the questionnaire survey on the practices of T2T, recommendation no.1 to 9 out of 10 recommendations are easy in practice in almost rheumatologist, to the contrary, recommendation no.10 (;"the rheumatologist should involve the patient in setting the treatment target and the strategy to reach this target") was difficult in practice in about half of rheumatologist. Therefore, recommendation no. 10, especially "communication between rheumatologist and patient" and "patient education", gets in the way of daily clinical practice of T2T. In this seminar, we would like to present details of the T2T practice focusing on these points in daily clinical practice.

ES4-3

Shared Decision Making in the clinical practice of RA

Yuko Kaneko
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Conflict of interest: Yes

The management of rheumatoid arthritis has remarkably advanced over the two decades thanks to the advent of effective drugs. The treatment strategy for rheumatoid arthritis has also changed with recommendations of early intensified treatment induction and periodic treatment adjustment if the previous one is ineffective. On the other hand, the change in drugs can lead to new adverse events and financial problems. The decision is made considering both blessings and risks of the new treatment, in which it is extremely important to share the decision making process between the doctor and the patient. It does not depend on the doctor or the patient, but on discussion involving both. The shared decision making is easy to say but difficult to do in practice. So many variables including scientific point of view, patient's life style, and limited time are concerned. In this seminar, we are talking about the gap between doctors and patients and the skill to share the knowledge and compassion to practice shared decision making.

ES5-1

Differential Diagnosis of Fever of unknown origin

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Conflict of interest: Yes

Proper strategies are necessary to diagnose fever of unknown origin (FUO). Diagnostic interventions lacking a plan and therapeutic interventions based on poor evidence result in wasteful medical expenditure and may even be harmful to patients. On rare occasions, a diagnosis is made in a single attempt; however, diagnosing FUO is not easy. It is necessary to adopt a logical clinical inference by utilizing a wide range of the knowledge and experience of fever-producing illnesses, taking the in-depth history and performing a thorough physical examination, and effectively performing clinically significant and contributory diagnostic tests. Recently, with advances in studies on natural immunity, the pathological condition of autoinflammatory diseases has been identified, which includes familial Mediterranean fever, TNF receptor-associated periodic syndrome, and PAFPA (periodic fever with aphthous pharyngitis and adenitis syndrome) in adults. Patients with these conditions often present to clinicians with FUO. As the concept of autoinflammatory diseases has become widespread, it has become part of the differential diagnosis of unidentified fever. Now, autoinflammatory diseases can be referred to as the fourth cause of FUO in addition to the three major causes of infections, malignant neoplasms, and connective tissue diseases. Today, I will talk about how we can identify autoinflammatory diseases in the process of diagnosing FUO and how we should make a differential diagnosis of it.

ES5-2

Hereditary periodic fever syndrome: pathophysiology and treatments

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Conflict of interest: None

Autoinflammatory syndrome is a hereditary disease with systemic inflammation as a main clinical feature. It has been 15 years since Dr. Daniel L. Kastner from NIH proposed the disease entity, "autoinflammatory

syndrome" as opposed to "autoimmune diseases". Although the word "autoinflammatory syndrome" is getting well-known especially among the rheumatologists in Japan, its clinical features have not been well-recognized yet, probably due to its low prevalence in Japan. Since insufficient treatments would cause the patients to suffer from decreased QOL and preventable late-onset sequelae, early diagnosis as well as early introduction of adequate treatments are critical for the patients care. Since the disease onsets of the autoinflammatory syndrome are usually during childhood, diagnosis of these patients is performed mainly by pediatricians. But the diseases entity is still young, so there have been a lot of case reports in which patients are diagnosed during adulthood with typical clinical features. In addition, the transitional care from pediatric rheumatologists to adult rheumatologists is becoming more important since the current treatments for the autoinflammatory syndrome is not curative due to its genetic nature. Therefore, it is essential for rheumatologists to recognize and understand the autoinflammatory syndrome. In this symposium, I would like to focus on the periodic fever syndromes, namely, familial Mediterranean fever, TNF receptor-associated periodic syndrome, mevalonate kinase deficiency (hyper IgD syndrome), and cryopyrin-associated periodic syndrome among the autoinflammatory syndrome, and will give a talk on their clinical features, pathophysiology, and treatments. I will include the presentation of the typical cases of these diseases since I strongly believe the knowledge of them should help their early diagnosis.

ES6-1

Does ultrasound-based tight control improve the outcome of rheumatoid arthritis?

Kei Ikeda
Department of Allergy and Clinical Immunology, Chiba University Hospital

Conflict of interest: Yes

Musculoskeletal ultrasound directly visualizes synovitis, which is the central pathology of rheumatoid arthritis (RA), and determines the severity of inflammation more accurately than does clinical assessment. Moreover, ultrasound frequently detects synovitis in patients with RA in clinical remission that actually causes joint damage progression. Therefore, the treatment strategy to minimize ultrasound-detected synovitis should be necessary for the complete prevention of structural progression. However, recently published data did not support the benefit of ultrasound-based treat-to-target strategy (ARCTIC trial: Haavardsholm EA, et al. BMJ 2016;354:i4205). The interpretation of and controversy about the ARCTIC trial will be discussed in this session. On the other hand, for the successful withdrawal/ dose reduction of a potent anti-rheumatic drug such as biologics, achieving "deep remission" has been shown to be important. Furthermore, a pilot study indicated that ultrasound predicts relapse after discontinuation of biologics more accurately than does clinical index (Iwamoto T, et al. Arthritis Care Res 2014;66:1576), which is currently under scrutiny in a large-scale multicenter trial. The role of ultrasound in determining "true deep remission", which is necessary to successfully withdraw/ reduce the dose of biologics without worsening the clinical outcome, will also be discussed in this session.

ES6-2

Therapeutic strategies for preventing large joint destruction in rheumatoid arthritis

Isao Matsushita
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Conflict of interest: Yes

In recent year, the treatment for rheumatoid arthritis (RA) has improved drastically. Achieving structural remission is now considered as a realistic goal of RA treatment. Joint damage appears early in the disease course and progresses more rapidly in the earlier phase in RA. Minimizing joint destruction therefore requires early diagnosis, early treatment, and strict control of disease activity. Weight-bearing joints such as the hip and knee joints should not be treated in the same way as small joints. It is difficult to inhibit the progression of hip and knee joint destruction after the appearance of joint damage, even with TNF blocking therapies. Inhibiting progression of hip and knee joint damage requires initiation of effective intervention before Larsen grade II. Small joint destruction can be prevented by TNF-blocking therapies without control of disease activity. However, disease activity is very important in treatment of weight-bearing joints. Destruction of weight-bearing joints can progress even with TNF-blocking therapies, if disease activity is insufficiently controlled. We evaluated 182 joints (96 hips, 86 knees) in 51 cases of RA treated with TNF blockers for 2 years using ARASHI scoring system. Joint destruction progressed within 2 years in all 12 joints having a baseline ARASHI status score of ≥3. Joint space narrowing score was more strongly associated with subsequent progression of joint damage than the erosion score, indicating that halting joint destruction is difficult after the appearance of joint space narrowing. In contrast, only 6.5% of joints with a baseline status score of ≤2 showed progression of destruction. Among cases with a status score of ≤2, disease activity was significantly higher in cases with joint damage progression than in those without progression. In this seminar, we will discuss the characteristics of large joint destruction in RA, and share therapeutic strategies and our experience aimed at preventing joint destruction.

ES7-1

How Imaging can be used for managing clinical remission: The real value of remission for patients

Paul Emery
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Conflict of interest: None

Clinical remission has become the goal of therapy for patients with RA and is increasingly reached by many patients. However there is a realisation that clinical remission alone may not be sufficient. Patients in clinical remission may deteriorate both clinically with flares of disease activity and subsequent loss of function and also radiologically. A better goal for patients to reach is sustained remission. To do this, may require a more profound suppression of disease than is achieved by those in conventional clinical remission. Using the new ACR/EULAR criteria has improved on this situation, by being more stringent, but they still rely on subjective measures. There is now much evidence that patients in clinical remission have sub-clinical disease as measured by sensitive imaging; either MRI or ultrasound. In the original study it was shown that Power Doppler ultrasound was the most predictive of subsequent flare and loss of function. Since that time, there have been various attempts to aim for not only clinical remission but ultrasound remission. Large cross-sectional studies have shown not only prevalent sub-clinical synovitis but frequent abnormalities of T-cell sub-sets. There is now a move to define remission in the three dimensions of clinical, imaging and immunological. When all three dimensions are normalised the state of so called true remission then it is anticipated that patients can start to successfully taper therapy. This is being studied in prospective studies. It is clear that true remission is achieved more frequently if patients are treated optimally from the onset. This is seen most frequently with very aggressive DMARD therapy or by use of biologics from onset. Once stable state is reached, a major question is whether patients can be converted from clinical remission alone to clinical and imaging remission? Should this not be possible, then remission induction by biologics and very aggressive therapy may well become the standard approach for these patients.

ES7-2

Impact of Work Productivity and Activity Impairment from the Viewpoints of Patient-reported Outcomes and Health Economics: Magnitude of the Japan's First Large-scale Evidence (Results from a special drug-use investigation)

Eiichi Tanaka
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Conflict of interest: Yes

Outcome of Rheumatoid arthritis (RA) have been improved a great deal lately, by the development of the disease-modifying antirheumatic drugs and biological DMARDs (bDMARDs). Clinical remission and pre-

vention of joint destruction are realistic treatment goals. bDMARDs, however, are costly and thus their appropriate use is important. In Japan, growing healthcare expenditure including costs of RA treatment has become a major social concern. It is the key agenda for physicians how to maximize the outcomes while minimizing the treatment costs when providing clinical care from a health economic perspective. We, Institute of Rheumatology Tokyo Women's Medical University, have started research on direct treatment costs of RA and work productivity losses in a cohort of RA patients in the Institute of Rheumatology Rheumatoid Arthritis (IORRA) study. This research figured out that the progression of functional impairment and decrease in quality of life (QOL) are associated with higher direct and indirect costs of RA treatment. These findings suggest the importance of early prevention of the structural damage due to RA and long-term maintenance of sustained effectiveness. Though it is widely recognized about the importance of health economic research, available related evidence is insufficient especially in Japan. Given this situation, a large-scale, prospective, observational study of work productivity and activity impairment (WPAI) in Japanese patients with rheumatoid arthritis receiving adalimumab, named the ANOUVEAU study was conducted as a special drug-use investigation of a tumor necrosis factor (TNF) inhibitor adalimumab. The ANOUVEAU study results were reported at the 2016 EULAR Annual Congress by Tsutomu Takeuchi et al. At the 2016 ACR Annual Meeting, Yoshiya Tanaka et al. reported the health economic impact analysis results from the ANOUVEAU study. In this seminar I will present the research in the IORRA cohort and also from the ANOUVEAU study as Japan's first large-scale study of work productivity and economic impact. The seminar will provide a clear insight about a health economic review of patient-reported outcomes of RA treatment with bDMARDs, the importance of establishing evidence to serve as a basis for promoting proper and optimal use of bDMARDs, and what clinicians should know in RA treatment.

ES7-3

Treatment Holiday: Benefit of Early Intervention －Significance of the Accumulated Evidence－

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Conflict of interest: Yes

The clinical landscape of rheumatoid arthritis (RA) in Japan has been experiencing a major shift. To date eight biological DMARDs (bDMARDs; including biosimilar) and a JAK inhibitor are available, with appropriate use of methotrexate producing a synergistic effect for the treatment of RA. This advance in treatment of RA has also shed light to early diagnosis, thereby encouraging diagnostic imaging such as ultrasonography and MRI. Drastic improvement of the treatment outcome of RA is attributable to the rigorous early intervention guided by the "Treat to Target" principles. While bDMARDs have significantly contributed to the advance in the clinical practice of RA, issues concerning medical economy and long-term safety have been raised. "How long will I have to be treated with biologics?" is a question brought up by many RA patients. Rheumatologists need not only to provide remission induction at an early stage, but also to anticipate treatment strategy after patients achieve remission. Thus, "treatment holiday" can be a solution to the concerns voiced by many RA patients. In Japan, studies, such as the BeSt study (infliximab) and the HONOR study (adalimumab), were conducted to explore the feasible drug discontinuation. In 2016, results of the HOPEFUL-2 study were published, thereby adding new evidence of adalimumab in Japanese patients. The HOPEFUL-2 study reexamined the significance of early intervention with adalimumab. The study is particularly interesting given it evaluated not only disease activity after discontinuing adalimumab, but also the extent of structural damage, therefore assessing the feasibility of drug discontinuation while preventing joint destruction. The HOPEFUL-3 study, the successor of the HOPEFUL-2 study, evaluated the feasibility of long-term drug discontinuation over three years and was presented at ACR in 2016. In this seminar, the possibility and significance of biologic treatment holiday from various perspectives based on the accumulated evidence will be reviewed.

ES8-1

2016 Updated EULAR RA Management Recommendations in a Global Perspective

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Conflict of interest: Yes

Rheumatoid arthritis (RA) is a chronic inflammatory disease which causes progressive joint damage and disability. Treatment algorithms involve evaluating signs and symptoms, applying a treat-to-target strategy, and use of conventional synthetic and biological disease-modifying antirheumatic drugs. Since the level of information on the outcomes using these drug is not always equal among rheumatologists, treatment strategies may differ among them. However, the optimization of using these drugs may lead to therapeutic success. Taking into these consideration, the 2016 update of the EULAR RA management recommendations is based on evidence from three systematic literature reviews about the above drugs, treatment strategies and safety issues. The 2016 update was developed by an international task force including experts from all regions of the world. When compared with the 2013 update, the major change involves the stringent recommendation to combine csDMARDs with glucocorticoids (GC); the down-grading of combinations of csDMARDs in the algorithm in favor of MTX monotherapy (with GC); and the inclusion of the possibility to use targeted synthetic DMARDs (Jak-inhibitors>) in phase 2 with a preference of bDMARDs. The total number of recommendations was reduced from 14 to 12, while the overarching principles were increased from 3 to 4. A treat-to-target strategy, introduced into the recommendations already as early as 2010, is continued to be highly recommended with stringent remission or low disease activity as the therapeutic goal. The 2016 update of the EULAR recommendations provides the state of thinking in the field of RA management from a global perspective. However, despite so many advances, some RA patients may still not reach the therapeutic target. New therapies are still needed and are on the horizon. The update on EULAR recommendations was presented in London, at EULAR 2016. In this seminar, I will highlight EULAR recommendations for the treatment of RA from current global perspective.

ES8-2

The perspective of Japanese RA treatment considering 2016 EULAR Updated Recommendation

Tsutomu Takeuchi
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Conflict of interest: Yes

Currently we aim at the remission in RA using DMARDs including biologic agents. At this stage, we need to consider the maximization of RA treatment using approved DMARDs, although much better development for diagnosis tools will be expected, and preventive care, pre-emptive therapy and personalized healthcare will be located as next candidates of future RA strategies. Patients and rheumatologists are overwhelmed by these drugs' information which does not always allow one to decide easily in RA patients. On the other hands, it is essential to lead optimized strategy treated with RA drugs to achieve a remission. Therefore, EULAR draw up treatment recommendations in 2010 toward to overcome these issues. The EULAR recommendations were mainly consisted of several points that when csDMARD is initiated, what kind of csDMARD is prescribed, and so on. This recommendations were amended in 2013, and these placed combination therapy of csDMARDs at the same level as MTX monotherapy as a first line. These amendments also placed non TNF inhibitors at the same level as TNF inhibitors as second line. However, a significant proportion of RA patients still not achieve the desired therapeutic target, and EULAR updated recommendations were revised in 2016. This updates include that the aggressive use of glucocorticoids, the effectiveness of MTX monotherapy, the placing of JAK inhibitors, the advantage of IL-6 and JAK inhibitors as a monotherapy without MTX, and tapering/withdrawal RA drugs after remission. Among these, monotherapy of biologic agent and the next strategy after remission may be so attractive. Treatment strategy using TNF inhibitors

added on MTX was developed for MTX-IR patients. Meanwhile, results of the SURPRISE study suggested that treatment is enhanced by adding on TCZ for MTX-IR patients, and tapering/withdrawal of MTX after the remission will be feasible. Thus, we will discuss the optimization of RA treatment from the latest evidence and updated EULAR recommendations.

ES9-1

The importance of measurement of matrix metalloproteinase 3 (MMP-3) in patients with rheumatoid arthritis (RA) treated with biological disease modifying anti-rheumatic drugs (bDMARDs)

Satoshi Ito
Niigata Rheumatic Center

Conflict of interest: Yes

MMP-3 is a marker for joint destruction but there were few reports in the treatment of RA. We have reported the effectiveness of dose escalation and/or shortening of dosing interval (Intensification) of infliximab (IFX) in JCR 2011. There were 30 responders and 11 non responders. Even though we counted the data at the last observation of non responders, intensification of IFX maintained SJC, TJC, or DAS28. Even more, intensification of IFX significantly reduced the level of rheumatoid factor and MMP-3. By the introduction of golimumab, the level of MMP-3 was significantly reduced along with SJC, TJC, DAS28, CRP or ESR (JCR2016). We reported the spacing of intravenous (IV) administration of tocilizumab (TCZ) in JCR 2016. The number of the patients with normal level of MMP in patients with spacing were 25/45 (55.6%). And it was significantly higher than that of the patients who were not able to do spacing 3 /18 (16.7%, p=0.00567) Since steroids reduce the level of MMP-3, we compared the dose of PSL in patients with spacing and without spacing, but former was higher than that of latter:(PSL)1.9 (0-5.5)vs 1.4 mg/day (0-4), p=0.0072)). Sawano H reported that MMP-3 is useful to predict the effectiveness of TCZ (Jpn J Joint Dis 31:115-119, 2012). It is possible that the reduction in MMP-3 might be a good marker for the spacing of TCZ. We reported that it is desirable to use IV TCZ than subcutaneous (SC) TCZ in heavy, high body mass index patients (Kobayashi D et al, Rheumatology 2017). With this result, we switched SC TCZ to IV TCZ with iguratimod and dosing up of PSL in a patient who had partial response with SC TCZ. The level of MMP-3 transiently rose due to PSL, but it decreased markedly with the improvement of the symptoms and the tapering of PSL. The numbers of white blood cell were decreased probably due to the rise of the blood concentration of TCZ by switching. Measurement of MMP-3 was thought to be important when we use bDMARD, especially TCZ.

ES9-2

The Predictive Factors for Better Outcome of Switching of Biologics for Patients with Rheumatoid Arthritis in Daily Clinical Practice

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Conflict of interest: None

Eight biologics have been approved for rheumatoid arthritis (RA) in Japan. However, little is known regarding what to do when patients have an inadequate response to first biologics in daily clinical practice. This study aimed to evaluate the effectiveness of biologics as 2nd-line use in RA patients in daily clinical practice from our university cohort (FIRST registry). We retrospectively examined more than 2500 patients who were treated with biologics in our institute between July 2003 and December 2015. We compared the effectiveness of TNF-inhibitors (TNFi), TCZ, ABA as 2nd-line use and efficacy of switching from 1st TNFi to 2nd TNFi, TCZ or ABA based on CDAI and biomarkers such as CRP, ESR and MMP3, IL-6 (LOCF). Propensity score (PS) were generated using multinomial logistic regression. In addition, in order to find out the characteristic of 2nd biologics, we conducted comparison between the upper (1yCDAI-H; low response) and lower (1yCDAI-L; good response) quartiles in CDAI at 1 y after switching. CDAI at 1year was comparable among TCZ, 2ndTNFiand ABT after the adjustment by PS. Interestingly, comparison between the upper (1yCDAI-H) and lower (1yCDAI-L) quartiles in CDAI at 1 y after switching revealed that disease activity might improve despite of a high disease activity at switching in the case of TCZ. In addition, higher CRP, MMP-3 at switching were predictive factors for better outcome despite of higher RF factor in the case of switching to TCZ. Titer of Serum IL-6 but not TNF was markedly elevated in patients showed better outcome. In contrast, ABT showed a lower efficacy especially in the patients with RF low, CRP high.

ES10

The Role of Interleukin 6 in the Rheumatoid Arthritis and Collagen Disease

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Conflict of interest: Yes

TNFα is playing an indispensable role in inflammatory progression and leukocyte activation. In the other hand, Interleukin-6 (IL-6) affects broad types of cells including immune system such as Th17 and T-reg and characterized by frequent hormone like action that maintains the body homeostasis. Since IL-6 has context-dependent pro- and anti-inflammatory properties, IL-6 trans-signaling promotes inflammatory responses while the classical IL-6 receptor signaling through the membrane-bound receptor is critical for regenerative and protective function. Therefore, IL-6 is recognized as a remarkable target clinically and various clinical applications are explored. All of these features are hallmarks of rheumatoid arthritis (RA) and some of other autoimmune diseases, and the benefit of IL-6 R monoclonal antibody is confirmed in these diseases. However, potential targets to inhibit IL-6 signaling are not single, but several approaches have been taken to inhibit IL-6 signaling pathways, including IL-6 itself, IL-6 receptor, JAK and GP130. In this lecture these potential benefits and risks of inhibitors on IL-6 signaling pathway will be reviewed and discussed.

ES11-1

Consideration of tapering first line anti-TNF therapy in early rheumatoid arthritis

Paul Emery
Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, UK

Conflict of interest: None

The logic for dose reduction can be seen in terms of cost saving, safety, reduced TNF expression and patient preference. The Data: there are now extensive databases of dose reduction. These are very difficult to make sense of because of heterogeneity of patients and definitions of remission used, etc. At the very minimum data should be separated into dose reduction and stopping and late remission studies should not be mixed with those from early disease. During the talk the key studies will be discussed. Recommendations of learned societies: these now largely recommend dose reduction in stable remission, although specific guidelines are not provided. The recommendations for stopping biologics are also not clear. Finally, there are the practical issues of how a clinician can manage patients. Additional information can be obtained from better understanding the clinical state of remission and with the use of sensitive imaging and the availability of immunological analyses. It is possible with these to make more a more accurate prediction of likely outcome, with direct implications for best practice.

ES11-2

The Future Beyond the Sustained Remission

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Conflict of interest: Yes

Rheumatoid Arthritis (RA) is the joint synovitis and the chronic inflammatory disease causing synovial proliferation, and bones/cartilages

destruction. By reason of joints destruction progresses in the early onset and creates the irreversible physical dysfunction, the appropriate diagnosis and treatment is critical. As it is mentioned in Treat to Target (T2T) concept, the treatment is earlier the better within "Tight Control" and it is believed as the principal of current RA treatment goal. Thanks to MTX and Anti TNF inhibitors, remission rate is higher than past and became capable of preventing the joint destruction and made patients QOL improved more than ever. Literally, we, the Rheumatologist, inevitably should project the patient's sustained remission treatment strategy who's already achieved the remission following the T2T as we reached the phase of standardizing the Deep Remission and Sustained Remission. The high persistent rate of golimumab treatment is reported at the GO-FORTH Study in Japan. To sustain remission and Low Disease Activity condition, the level of immunogenicity of golimumab is noted as it is relative to efficacy and safety in clinical. Thinking of Japan is the only country which 100 mg dosage of golimumab is approved, we are in the ideal situation that can implement the strategy of "control the disease activity with 100 mg at induction phase and sustain remission with 50mg at maintenance phase after". Seeing that Golimumab is always administrated in the medical facility (this is not only advantage but also disadvantage) we can retain the great medication adherence and that is contributing to the high persistent rate. Thus we are likely to achieve the deeper remission. This lecture will strategically consider the best anti TNF inhibitors RA treatment through the study showing golimumab's benefit which possibly enable to achieve "Deep Remission" and "Sustained Remission" through the study results.

ES12-1

Overview of Lupus Nephritis Management Guidelines

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Conflict of interest: Yes

Lupus nephritis (LN) is a common and important manifestation of systemic lupus erythematosus (SLE). Treatment guidelines for LN have recently been issued by American College of Rheumatology and European Renal Association-European Dialysis and Transplant Association. A number of immunosuppressants has been used for the treatment of systemic lupus erythematosus in daily practice, and they contribute to improve the prognosis of the affected patients. In those guidelines, Mycophenolate mofetil (MMF) is recommended for the initial and maintenance treatment. Despite the fact that MMF has not been officially approved for treating LN neither in USA nor in EU, MMF has been used in clinical practice worldwide. In order to clarify the real-world use of MMF as a treatment for LN in Japan, Japan College of Rheumatology surveyed the use of MMF in daily clinical practice. Last year, as a result, MMF was approved for treating LN in Japan, and has been commonly used for the treatment of adult LN patients since then. In this seminar, the better management for LN SLE in Japan, considering Japanese guideline for SLE is currently under construction, will be discussed.

ES12-2

Induction and maintenance therapy for lupus nephritis

Akio Morinobu
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Conflict of interest: Yes

Several guidelines in Lupus nephritis were published in 2012. They recommend MMF or IVCY for induction therapy, and MMF or AZA for maintenance therapy. Those guidelines are essentially similar because they are based on the sameclinical trials. Since those trials include Caucasian, African American, Hispanic, and Asian, but no Japanese, the efficacy and safety on Japanese patients are no clear. Here I talk about our experiences on MMF use, both for induction and maintenance therapies. 25 patients were given MMF for induction therapy, and 74% of them reached complete remission at 6 months, defined by the criteria of EULAR/ERA-EDTA. These results were not inferior to IVCY therapy. Also during maintenance therapy, the clinical manifestation of patients on MMF are similar to those on AZA. MMF is useful for the treatment of lupus nephritis in Japanese.

ES12-3

The clinical strategy for Lupus nephritis

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Conflict of interest: None

Lupus nephritis is common in systemic lupus erythematosus. Steroids are used for treatment, and an immunosuppressant is also frequently required. Mycophenolate mofetil (MMF) is an ester form of mycophenolic acid (MPA), which was extracted from Penicillium in the nineteenth century. Its immunosuppressive effect has been studied since the 1980s, and MMF has been used for the treatment of lupus nephritis since about 1999. In Japan, MMF was approved for patients with lupus nephritis in 2015. According to the American College of Rheumatology (ACR) 2012 guideline for lupus nephritis treatment, steroid pulse therapy followed by 0.5-1 mg/kg of prednisolone with 2-3 g/day of MMF or intravenous cyclophosphamide (IVCY) is recommended for patients with International Society of Nephrology (ISN) class III and IV lupus nephritis. The European League against Rheumatism (EULAR) 2012 guideline also recommends 0.5 mg/kg of prednisolone with 3 g/day of MMF or low-dose IVCY every two weeks, followed by steroid pulse therapy. Guidelines also recommend 0.5 mg/kg of prednisolone with 2-3 g/day of MMF in patients with ISN class V lupus nephritis. Ethnicity has been considered in the evaluation of the effects of MMF. A report from Hong Kong assessed the effect of 2 g/day of MMF, and a Taiwanese study reported the effect of 1 g/day. On the basis of these reports, the ACR guideline adjusted the dose recommendation for Asian patients to 2 g/day of MMF. However, the Aspreva Lupus Management Study, which was conducted as an MMF vs. IVCY group comparison of 370 cases, reported inferior efficacy of MMF in only Asian patients, even though patients with various ethnicities received nearly the same dosage regimen. Therefore, the appropriate dosage of MMF for Asian patients is now controversial. Unfortunately, because MMF was only recently approved in Japan, there are few reports about the effect of MMF in Japanese patients. Herein, we report the results of MMF therapy in 42 Japanese patients with lupus nephritis.

ES13-1

Optimal Initial Treatment for Induction and Maintenance of Remission

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Conflict of interest: None

The primary goal in the treatment of rheumatoid arthritis (RA) is to induce remission. As for drug therapies for achieving the induction of remission, treatment strategies using various drugs, including csDMARDs, tsDMARDs, boDMARDs, and bsDMARDs, have become possible. Especially, bDMARDs have been widely recognized as life-changing drugs for the physicians specialized in rheumatism as well as to the patients with RA. As for the treatment goal, not only inducing but also maintaining remission and low disease activity are considered important. In the European League Against Rheumatism Recommendation in 2016, the recommendation 2 states that "Treatment should be aimed at reaching a target of sustained remission or low disease activity in each patient," which was a revision of the previous recommendation (2013) that stated, "Treatment should be aimed at reaching a target of remission or low disease activity in every patient." At present, treatment strategies after achievement of sustained remission includes discontinuation and tapering (spacing) of TNF inhibitors. To achieve this goal, the maximum dose of methotrexate (MTX) was increased to 16 mg/week since February 2011. In case the effect of MTX is insufficient based on the treat-to-target strategy, introduction of bDMARDs is considered. However, even with bDMARDs, not all patients with RA achieve and sustain remission. The causes are presumed to be primary or secondary inefficacy of bDMARDs or partial treatment response. Moreover, the timing of introduction of the

biological agents becomes an important issue. By understanding or resolving these issues, remission can be achieved and sustained in patients with RA, which will lead to further treatment strategies. This seminar aims at improving the conditions of patients with RA by considering the optimal initial treatment strategies.

ES13-2

Optimal Treatment Strategy during Remission Maintenance Period

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Insutitution of Rheumatology, Zenjinkai Shimin-no-Mori Hospital

Conflict of interest: Yes

In the treatment of rheumatoid arthritis (RA), recent advances in diagnostic technology and use of biological disease-modifying antirheumatic drugs (bDMARDs) have enabled early diagnosis and appropriate treatment, with the goal of remission. If remission is achieved, maintenance is considered essential. After remission is maintained for a prolonged period, considering their safety and cost, dose of drug (steroids, conventional synthesized DMARDs (csDMARDs) such as methotrexate (MTX), and bDMARD etc.) may be reduced or discontinued. In 2013, the European League Against Rheumatism recommendation stated that if a patient remains in remission, after the steroid dose is tapered, especially with combined use of csDMARDs, tapering of bDMARD dose can be considered. Thus, in case that the remission condition can be maintained, first, dose reduction or discontinuation of steroids is taken into consideration. Subsequently, the choice of drug that is reduced or discontinued will be determined according to age, complications, economic status, and immunogenicity of preparations. In this seminar, we will consider appropriate treatment strategies following maintenance of remission.

ES13-3

New Surgical Approaches Improving the Quality of Life in Patients with Rheumatoid Arthritis in the Era of Biological DMARDs

Hisaaki Miyahara
Rheumatology Center, National Health Organization Kyushu Medical Center

Conflict of interest: None

Recent improvements in medical treatment including biological DMARDs in patients with rheumatoid arthritis (RA) have caused suppression of synovial proliferation, prevention of joint destruction, and the change from polyarticular and inflammatory nature to oligoarticular and osteoarthritic nature. It is suggested that these improvements have contributed to the decrease in numbers of RA-associated surgeries. On the other hand, with the trend toward milder disease because of improved medical treatment, RA patients want and need better function for the activities of daily living. For this purpose, new surgical approaches and implants such as TSA, reverse TSA, TEA, RA hand surgery, advanced type of THA, TKA, TAA, and metatarsophalangeal joint-preserving surgery were expected to apply to RA patients.

ES13-4

Safety Management in treatment of articular rheumatism

Tsukasa Matsubara
Department of Rheumatology, Matsubara Mayflower Hospital

Conflict of interest: Yes

Certolizumab pegol (CZP), TNF-αinhibitor, was released in Japan in 2013. CZP is a preparation having unique structure that polyethylene glycol is combined with Fab domain in which Fc domain is removed from IgG1 antibody, being the same as TNF-α inhibitor. The administration method is so characteristic that the double dose of the maintaining dose is administered at the initial time, two weeks and four weeks later. Consequently, after the administration in patients with articular rheumatism, the clinical effects appear promptly. As for its safety, clinical studies in Japan (J-RAPID, HIKARI) demonstrated similar safety profile to conventional TNF-α inhibitors. However, because these studies were conducted in limited patients, actually clinical safety profile is unknown. Based on intermediate reports on post-marketing surveillance of CZP for three years, its appropriate use is considered in this lecture.

ES14-1

Early Diagnosis and Treatment of Psoriatic arthritis in daily practice ～"New Kid" Ustekinumab～

Mitsumasa Kishimoto
Immuno-Rheumatology Center, St. Luke's International Hospital

Conflict of interest: Yes

Psoriatic arthritis (PsA) is a chronic inflammatory seronegative spondyloarthritis associated with psoriasis. The prevalence of PsA among Japanese psoriasis patients is thought to be less than that of Westerners. However, in keeping with our clinical experience that the prevalence of PsA among Japanese patients may actually be higher, we reported prevalence rates of up to 20.4% among Japanese psoriasis patients (1). Further improvements in awareness of this disease entity is necessary to allow patients to receive early and appropriate care. In the first half of this session, I will review the distinguishing clinical features of PsA, which will allow us to improve both under-diagnosis and misdiagnosis of the increasingly treatable disease, and emphasize the need for early diagnosis and appropriate differential diagnosis. TNF-α inhibitors have revolutionized the treatment of rheumatic diseases, including PsA, however, not all patients respond to these agents. Thus, there is a need for additional treatment modalities with a novel mechanism of action. In the past few years, the IL-23/Th17 axis has emerged as an important mechanism in the pathogenesis of PsA. Ustekinumab, a fully human IgG1κ monoclonal antibody that targets the common subunit p40 of IL-12 and IL-23, has been shown in clinical trials, to be well-tolerated and effective in patients with active PsA. with a safety profile consistent with the one observed in patients with psoriasis. Moreover, it was to be effective in anti-TNF-α experienced patients, definitely fulfilling an unmet need in the management of PsA.

ES14-2

Update of treatment for psoriasis

Kenji Kabashima
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Conflict of interest: None

Psoriasis is a common disease especially among Caucasian people. Although the pathogenesis of psoriasis has been rigorously revealed these days, the role of obesity and keratinocytes remains unclear. In this talk, I would like to update the pathogenesis of psoriasis.

ES15-1

The role of csDMARDs in the era of biologics and iguratimod, a new Japanese csDMARD

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

Conflict of interest: Yes

The role of csDMARDs in the treatment of rheumatoid arthritis has been receiving more attractions in the recent years. With the advance of laboratory serological tests and wider use of imaging studies such as joint ultrasound which can detect early synovial inflammation, the early diagnosis of rheumatoid arthritis leads to early interventions, eventually results in better response to csDMARDs. Personalized medicine based on each patient's profile including age, gender, occupation, family planning, comorbidity, socioeconomic status etc. The goal of pharmacological treatment of rheumatoid arthritis is achievement of clinical remission of disease activity, structural remission without progression of joint damage and functional intactness in daily life of each patients no matter what kind of initial regimen is chosen by shared decision of rheumatologists and patients. Monotherapy of csDMARD, not only methotrexate but also other options, is often effective enough to achieve remission in certain patients, but it is important to modify the treatment plan without delay as

needed. Familiarity to variety of DMARDs and its combination in conjunction with appropriate use of NSAIDs and glucocorticoids is helpful to practice personalized medicine. The efficacy of combination of csDMARDs has been reported to be comparable to biologics. In addition, cost-effectiveness and safety of csDMARDs can be preferred. Iguratimod is a newly introduced csDMARD in Japan. The pharmacological effects include modification of pro-inflammatory cytokine secretions and regulation of immunoglobulin production including autoantibodies. Post-marketing surveillance of iguratimod will be reviewed and its safety and the potential role in the biologic era will be discussed.

ES15-2

For More Effective Use of Oral-Dose DMARDs –Focusing on Iguratimod

Kensuke Oryoji
The Centre for Rheumatic Diseases, Matsuyama Red Cross Hospital

Conflict of interest: Yes

Iguratimod (IGU) is an oral-dose antirheumatic drug not inferior to salazosulfapyridine (SASP). This drug has been shown to be clinically useful in reducing the level of rheumatoid factors (RF) of each class such as IgM when used with or without concomitant MTX treatment. To identify groups of patients responding better to IGU, our department carried out the logistic regression analysis on presence/absence of EULAR good response achievement using the data of 98 patients with rheumatoid arthritis treated for 12 weeks (4 weeks with IGU 25 mg and 8 weeks with IGU 50 mg), with the following parameters serving as independent variables: sex, age, duration of illness, CRP, SDAI, levels of RF, ACPA, MTX dose and PSL dose, as well as history of bio use. In this analysis, the RF level only was identified as a significant factor ($p=0.015$). Thus, the cut-off RF level was determined from the ROC curve, and the subjects were divided into two groups by the cut-off level (93 IU/mL) for comparison of IGU's efficacy. When the magnitude of change in SDAI from the baseline to Week 12 was compared between the RF≥93 IU/mL group (n=53) and the RF<93 IU/mL group (n=45), the improvement in SDAI was more markedly significant in the former (higher RF) (-10.1±0.8) than the latter (-2.6±0.9) ($p<0.0001$). Furthermore, in the logistic regression analysis using the above-mentioned independent variables, the odds ratio for achievement of EULAR good response in patients with RF≥93 IU/mL was 10.0 (95% confidence interval: 3.4-35, $p<0.0001$), suggesting that IGU was more effective in high RF groups. To examine whether or not similar results could be obtained at facilities other than our hospital, multivariate analysis by the propensity score matching method was carried out, adding the data of 97 iguratimod-treated patients at Mima Hospital Yoshinogawa Rheumatism Center. Also in these patients, the odds ratio for achieving EULAR good response in the RF≥93 group was 4.5 (95% confidence interval 1.5-16, $p=0.008$). When comparison was made between patient groups with identical background variables other than RF value (n=64/64), the reduction in DAS28-CRP· CRP (mg/dl) was also greater in the RF≥93 group than in the RF<93 group, and the EULAR good response achievement rate was significantly higher in the RF≥93 group. These results suggest that IGU is particularly effective in patients with relatively high RF values. Based on the findings recently accumulated about the mechanism for induction of inflammation by RF, this paper outlines the clinical significance of RF in rheumatoid arthritis.

ES16-1

The current actuality of hand surgical therapy for rheumatoid arthritis

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Department of Orthopedic Surgery, National Hospital Organization Osaka Minami Medical Center

Conflict of interest: None

This study group, which has been held once a year since 1999, will be the 19th meeting. Compared with about 20 years ago, methotrexate and biologics are used from an earlier stage and control of the disease activity of rheumatoid arthritis (RA) is becoming more feasible. For this reason, RA patients have become more interested in the function and appearance of the hands, and the problem of RA patients' hands and the treatments are also changing. Therefore, this meeting will focus on actual clinical practice of operative treatment of the hands in RA and will consist of a floor-participation case study examination using an answer pad, and special lecture. In the case study, we would like to ask the presenters to present the problems of actual cases of thumb, fingers, and wrist joints in RA and ask the floor participants to discuss the treatments. We will also invite Dr. Minami to give a lecture on the surgical indications and tips of the surgical techniques of total wrist arthroplasy that were developed and are used in Japan, with the aim of contributing to the knowledge of the participants concerning the total wrist arthroplasy. Finally, Dr. Minamikawa will speak on the history of this study group and future efforts for the 20th meeting. We would like to make this meeting useful for all participants and to make it possible to contribute to realization of higher treatment goals of RA patients.

ES16-2

Total Wrist Arthroplasty using Newly Designed Artificial Wrist Joint for Rheumatoid Wrist

Akio Minami
Hokkaido Spinal Cord Injury Center

Conflict of interest: None

Wrist joint plays an important role as a key stone in the upper extremity and is commonly affected in patients with rheumatoid arthritis (RA). There have been various operative options for RA wrist. Total wrist arthoplasty (TWA) is indicated for RA wrist (Larsen stage IV and V). In the American and European countries, many artificial joints were used for the rheumatoid and osteoarthritic wrists. Even mid-term postoperative results showed unsatisfactory clinical and roentgenographic results. These artificial wrist joints can not be used legally in Japan. Therefore, we have no artificial wrist joints actually. We developed newly semi-linked artificial wrist joint. New artificial wrist joint was designated to simulate darts throw motion, which motion was biomechanically physiological. New wrist joint is composed of three components; radial, metacarpal and carpal parts. As a clinical trial we performed TWA for 20 patients with rheumatoid arthritis (Larsen Grade IV and V) in two institutions. All patients were followed at least one and a half year. At follow-up there was no revision case. Clinical efficacy rate was 85%. However, roentgenographically, radiolucent line around the carpal component appeared in 4 wrists (20%). The PMDA organization approved to make new artificial wrist joint in September, 2016. In this lecture, we want to report development concept of the newly artificial wrist joint, operative indications, meticulous operative techniques, clinical and roentgenographical postoperative results and problems.

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