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ABSTRACTS

Presidential Lecture

PL

"Quest with an Open Mind" in the rheumatic surgery

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Conflict of interest: None

[Background] In the treatment of rheumatoid arthritis (RA), old style diagnostic procedures and treatments have been replaced with new diagnostic procedure, therapy, and various guidelines in late years. The diagnosis and treatment systems were globally standardized, then the remission became realistic treatment goal that all clinician should proceed. Whereas surgeries for rheumatoid arthritis also have been changed from the surgical therapy for recovering joint function to achieving much higher level of joint functions. In this presidential lecture, I'll review the history of surgery for RA and also describe the transitional changes of the surgical procedures in our university and associated hospitals. Also, I'll describe the changes of characteristic of rheumatoid joint destruction in recent surgical cases after the introduction of methotrexate and various biologics, in order to prospect and to predict future orthopedic surgery in RA. [History of joint surgeries in RA] Upper extremities: The number of surgery in upper extremities was used be less than lower limbs surgeries, but it now showing continual increase in late years. In particular, surgeries for wrist and the finger joints that have direct affection with activities of daily living shows obvious increases. In this part, although surgical method does not have major change, I'll discuss about surgical techniques to aim higher level of ADL. Lower extremities: The number of surgeries for large joint such as hip and knee have been dominant in late years, but those cases are showing continual decrease, on the other hand, toe surgery became more often. In this part, the history of toes surgery will be described, then problems of the current techniques in toes surgery will be discussed. [Recent surgical outcomes, the change of the joint distractions, and the characteristics of the joint destruction and its prediction] Elbow joint: Our data suggested that wide synovectomy of the elbow joint showed stable long-term clinical results. The joint preservation surgery such as wide synovectomy for elbow joints will be good surgical indication for the cases with lower disease activity. Finger joints: Although there is no dramatic change of surgery, the finger surgeries have been shown established and stable results. In the future, surgeries for ideal functional motions and movements will be desired. Hip and knee joints: Osteoarthritic changes of hip and knee joints became more distinct from our data of evaluation in radiographic change of surgical cases. Also our data suggested that the joint destruction is found to progress in 0.4 Larsen score / year. [Prospects of the orthopedic surgery for future RA] The improvement of disease activity and joint destruction will advance in the near future in inflammatory arthritis. Not only the control of disease activity, but also the management of osteoporosis and the correspondence for the osteoarthritic changes of RA joint should be required.

Representative Session

RS

Hematopoietic stem cells and their niches

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Conflict of interest: None

In 1961, stem cells were defined by Till and McCulloch using a spleen colony forming assay (CFU-S). Transplantation of bone marrow cells to irradiated mice resulted in the formation of CFU-S-derived colonies in the spleen which identifies the self-renewal capacity of stem cells. The function of hematopoietic stem cells (HSCs) can also be assayed through their bone marrow reconstitution activity upon bone marrow transplantation to irradiate mice. The advances in research on HSCs has helped establish the fundamentals of stem cell biology which maybe broadly applied to other tissue stem cells. In contrast to HSCs which loosely reside in the bone marrow, studies of the stem cell microenvironment (niche) for tissue stem cells, such as epithelial stem cells, neuronal stem cells and germ stem cells, have shown great advance owing to the more solid tissue structure in which these stem cells reside in. In this lecture, we would like to show how HSCs maintain homeostasis and how they respond during stress hematopoiesis. Both processes are regulated by intrinsic cell autonomous programs and extrinsic niche factors. We will discuss our studies regarding the interaction between the bone marrow niche and HSCs, especially focusing on our recent studies on the HSC and osteoclast metabolism.

Symposium

S1-1

Treatment of rheumatoid arthritis – Update

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Conflict of interest: Yes

Despite all supposed pathogenetic insights and therapeutic advances, rheumatoid arthritis (RA) continues to be a chronic disease that cannot be cured. However, the probability to reach a cure-like state on therapy, i. e. remission (REM), has never been higher than today. This can be seen from a follow-up of patients in our clinic over the past 20 years – never before have so many patient attained REM. This success is owing to the development of and adherence to novel treatment strategies, such as the treat-to-target (T2T) approach, and the availability of an increasing array new therapies. Historically, the first therapeutic break-through came from learning how to use methotrexate (MTX) optimally, both in terms of dosage (in Europe up to 25-30mg weekly, in Japan now up to 16mg weekly) and prevention of adverse events via the use of folate substitution. Additional conventional synthetic (cs) disease modifying antirheumatic drugs (DMARDs), are sulfasalazine, leflunomide and, for very mild cases, hydroxychloroquine. The second therapeutic break-through came from the study and approval of tumor necrosis factor (TNF) inhibitors. These first biologic (b) DMARDs were followed by others, such as tocilizumab (anti-IL-6 receptor [R] antibody), rituximab (anti-B-cell antibody) and abatacept (T-cell co-stimulation inhibitor). Today, in Europe, we have 5 types of TNF-blockers, 2 types of anti-IL-6R molecules and 1 each of anti-CD20 antibody and costimulation inhibitor. While these drugs had significant costs in earlier days, with the advent of biosimilars in Europe (infliximab, etanercept, rituximab and soon adalimumab), also costs for bDMARDs have come down. While the bDMARDs have to be applied parenterally, either i.v. or s.c., a novel class of synthetic DMARDs, the targeted synthetic (ts) DMARDs, the Janus kinase (Jak) inhibitors have recently been licensed as small molecules that can be taken orally and appear to have at least similar efficacy as the bDMARDs by targeting signal transduction pathways of various cytokines, foremost IL-6. This can be considered yeat another therapeutic breakthrough. Thus, today we have at least 5 treatment principles and almost 20 agents available to treat RA. Importantly, even when a particular drug within a drug class, such as a TNF-inhibitor, is insufficiently efficacious, another drug of the same class appears to convey similar efficacy as switching to another mode of action. However, we usually do not use more than two agents from the same class before switching to another mode of action. Of note, a variety of agents predicted to be efficacious by virtue of pre-clinical and ex-vivo analyses failed in clinical trials. Among this agents are IL-12/23, IL-23 and IL-17 blockers. Also, in contrast to TNF- and IL-6 pathway inhibitors, IL-1 inhibition is only weakly efficacious. Thus, by these failures we also learn about pathogenesis. However, these agents are meanwhile effectively used for other rheumatic diseases, such as juvenile idiopathic arthritis, axial spondyloarthritis and psoriatic arthritis, finally expanding the armament there which until recently had consisted only of TNF-blockade. Targeting remission (for patients with early RA) or at the least low disease activity (for patients with established RA) is todays paradigm for RA. Importantly, once patients have reached such good outcomes, one can reduce the dose of or increase the interval between medication applications without jeopardizing this good state. Stopping drugs, however, is afflicted with a much higher risk of flares and loss of the good outcome. Other important advances relate to strategies. The first breakthrough in this respect was the development of response criteria and continuous scores. The second breakthrough was the recognition that RA had to be referred to and treated with DMARDs as early in its course as possible. And the third paradigm change relates to the development and practice of the T2T strategy, rather than waiting to see a response for many months or even years. In summary, the evolution of RA treatment has been remarkable and one of the major successes of the 21st century. Alas, almost 30% of the patients continue to have significant disease activity. For these patients we need new therapies.

S1-2

Current and future perspective of DMARD treatment in RA

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S1-3

Treatment of rheumatoid arthritis from Japanese perspective

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Conflict of interest: None

Rheumatoid arthritis (RA) is characterized by persistent synovitis with immunological dysregulation, resulting, without proper treatment, in irreversible joint destruction and functional impairment. Recent advance in treatment and management of RA has remarkably improved multifarious outcomes. In this symposium, I would like to focus on biological DMARDs (bDMARDs) and review the recent evidences showing the effectiveness and safety of individual bDMARDs and strategic analysis for bDMARDs. Although all patients should achieve the goal of remission or alternatively low disease activity by these treatments, it has yet to be attained by existing treatment and strategy. Early and personalized medical care for individuals are being tried, but not completed. Strategies for ageing patients with RA are another problem in practice. Difference in gene and environment between Japanese and western people makes it difficult to extrapolate and interpret study results conducted in Western countries. Finally, I would like to discuss current issues and advances in the management of RA with bDMARDs with Japanese experiences.

S1-4

Perspectives of targeted synthetic DMARDs for rheumatoid arthritis

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Conflict of interest: Yes

The combined use of methotrexate and biological DMARDs has revolutionized treatment of RA, and 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. Janus kinase (JAK) inhibitors have been developed as a new class of targeted synthetic DMARD that inhibits the non-receptor tyrosine kinase family JAK involved in intracellular signaling of various cytokines and growth factors. Orally available JAK inhibitors have been developed as new therapies for patients with RA. Tofacitinib, a JAK inhibitor, was approved in 2013 and baricitinib, a JAK1/2 inhibitor, was approve in 2017 in Japan. Both tofacitinib and baricitinib are effective in patients who showed inadequate response to biological DMARDs as well as synthetic conventional DMARD such as methotrexate. In addition, clinical phase III trials using filgotinib and upadacitinib, JAK1 inhibitors, and peficitinib and decernotinib, JAK3 inhibitors, are currently underway. Because JAK inhibitors inhibit multiple cytokines and signaling pathways, further studies are needed to determine their risk-benefit balance 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 or post-marketing surveillance.

S1-5

Management of rheumatoid arthritis in the eye of pharmacovigilance

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Conflict of interest: Yes

Disease modifying antirheumatic drugs (DMARDs) are classified into conventional synthetic DMARD (csDMARD), targeted synthetic DMARD (tsDMARD), and biological DMARD (bDMARD). Rapid progress in the development and approval of various classes of DMARDs has provided significant improvement in disease activity, and lent increased importance of clinical management with special consideration of safety. There are two types of adverse drug reactions (ADR); those common to various kinds of DMARDs and specific to an individual DMARD or a class of DMARD. Important ADRs of the former include infection and renal, hepatic, hematological, pulmonary, and cutaneous disorders. Proper screening, selection of patients, and monitoring after starting treatments form the center of clinical management of rheumatoid arthritis (RA). Regarding infection, especially severe/serious one, a spate of high-quality evidence has been reported, and assimilated in clinical settings. Incidence of severe or hospitalized infection of patients with RA are twice as high as those of non-RA. Data from clinical trials and observational studies has shown that use of bDMARDs and tsDMARDs increase the risk of serious infection 1.5 to two folds. Drug-induced pulmonary injury has been reported for all classes of DMARDs, and comorbid interstitial pneumonia is a significant risk factor of the ADR. Diagnosis of drug-induced pulmonary injury is a challenge to rheumatologists and requires radiological examination at baseline and during treatment at a regular interval. ADRs specific to an individual DMARD or a class of DMARD include positive conversion of anti-nuclear antibody and lupus-like symptoms during treatment with TNF inhibitors, intestinal perforation with IL-6 inhibitors, herpes zoster with JAK inhibitors, and lymphoma/lymphoproliferative disorders with MTX. In this symposium, clinical management of RA in the current treatment milieu will be discussed based on the recent available evidence.

S2-1

Trends in Orthopedics : Why do my RA Patients Still Need Surgery?

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Conflict of interest: None

Background: While rates of arthroplasty in the general population are skyrocketing, the rates of large joint arthroplasty for patients with RA have remained stable, and the rates for small joint surgery and soft tissue procedures for patients with RA have decreased. The widespread use of potent disease modifying drugs and biologics has been temporally associated with these trends, but the relationship is not straightforward. If inception cohorts of RA patients recruited between 1986-2011 are studied and analyzed by recruitment period, rates of small joint procedures are lower in the more recent cohorts, while major surgery rates including arthroplasty have remained stable. The elbow has been considered an “RA specific” arthroplasty; up to 80% of total elbow arthroplasty (TEA) are performed on patients with RA in some series. In the US, where differences in biologic use between races are reported, there has been a persistent racial disparity in elbow replacement, while in New Zealand, where biologics are limited to those with erosive disease, TEA rates have decreased. In Britain, after tumor necrosis factor inhibitors (TNFi) were approved in 2002, the rate of total knee arthroplasty decreased, while the rate of hip arthroplasty did not. Methotrexate use has been consistently associated with decreases in arthroplasty, even in studies of MTX with TNFi; concomitant MTX with TNFi decreased the rate of arthroplasty over TNFi alone. In patients with early RA, use of methotrexate and other DMARDs in the first year after diagnosis decreased arthroplasty by 2-3% per month of MTX use, for a maximal decrease in arthroplasty of 36% for a full year of methotrexate use. Rates of arthroplasty and small joint procedures may become an outcome measure for successful therapy in RA, but recognition of the contextual factors that influence the rates is required before the significance of the changes can be understood.

S2-2

Rheumatoid arthritis surgery: were do we stand where do we go?

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Conflict of interest: None

In terms of surgical indications, advances in the use of new medication therapies currently challenge the surgeon. Careful planning is required for the discontinuation of immunosuppressive therapy, especially for TNFα inhibitors with long administration intervals. We discontinue the biological therapy in our institution only for more complex hand surgical interventions like extensive bone and joint procedures. There is a clear shift in the type of interventions applied to treat RA patients. Procedures known from treating degenerative or posttraumatic osteoarthritis, which were rarely performed in RA patients 20 years ago, are now considered standard for this specific patient group. The interventions include: four-corner fusions, PIP arthroplasty and a revival of wrist arthroplasty including more complex devices. In addition partial wrist fusion is applied even in suboptimal residual joint conditions. Patients always prefer a residual wrist mobility. Observations in our patients suggest that patients with low disease activity and stable inflammation status are primarily concerned about the appearance of their hand and hope to achieve a better quality of life through a more normal looking hand. Therefore indications for surgical interventions especially in good visible finger deformities are often driven by aesthetical motivation. It is important to communicate with the patient possible functional loss versus gain in the aesthetical appearance of the hand. Methods for measuring outcome after hand surgery continue to evolve. Rheumatoid arthritis with its physical and emotional manifestations that extend beyond the upper extremity poses a special challenge. An ideal set of healthcare questionnaires for the assessment of outcome after RA surgery includes beside patient’s demographics a generic health status, an upper extremity score and an intervention specific outcome measure. We are still at the search for ideal a core set of outcome instruments for RA interventions.

S2-3

Further “wellness” is provided by orthopedic surgical intervention in the patients with rheumatoid arthrtis

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Conflict of interest: None

Introduction: The treatment aim of rheumatoid arthritis (RA) is achieving and maintaining clinical remission (REM) or a low disease activity (LDA) via tight medical control. Recent remarkable advances in pharmacotherapy for RA have resulted in good control of previously uncontrollable synovitis. However, if adequate medication is not administered in the very early stage of the disease, progressive deterioration and deformity of the affected joint can occur. Recently, patients have expressed a desire to achieve a higher quality of life (QOL) with functional REM and mental well-being. **Objectives:** To investigate the effectiveness of orthopedic surgical intervention in patients with rheumatoid arthritis (RA) by assessing the serial patient-reported outcomes (PROs), clinical data and disease activity. **Methods:** A prospective observational cohort study was performed in 294 sites of primary elective surgery in 276 patients with functional loss due to RA. The average age was 64 (19-89) years old, and the average disease duration was 16 (1-60) years. There were 99 sites in 96 patients who were in REM or had LDA before surgery. Assessments were done at the baseline and 6 and 12 months after surgery. **Results:** In total, the physical function, QOL and depression improved and the disease activity significantly decreased at 6 and 12 months after surgery ($p<0.01$), despite some differences in the outcomes by surgical site. In the REM/LDA group, an improvement was noted in the physical function and QOL. **Discussions:** In Japan, the meaning of surgical intervention have changed from “maintaining the ADL” to “improving the QOL and mental health as well as the physical function”. Intensive combination therapy with medication and orthopedic surgical intervention is effective for ameliorating the disease activity. **Conclusions:** Further “wellness” was obtained by orthopedic surgical intervention even in the patients who had reached the treatment goal of pharmacotherapy.

S2-4

Patient satisfaction after total knee arthroplasty in rheumatoid arthritis patients

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Conflict of interest: None

Introduction: Poor patient satisfaction for TKA gains attention and remains common problem in RA and OA. The focus is increasingly on patient-reported outcome measures (PROMs). This study aimed to examine pain catastrophizing scale (PCS), pain DETECT score (PDS) and New Knee Society Score (KSS) 2011, all of which are robustly related to patient satisfaction. Methods: The study enrolled 505 knees of 452 patients undergoing primary TKA with a minimum follow-up of two years. The 505 TKAs were divided into three groups based on a primary diagnosis, including 57 RA-TKAs, 430 OA-TKAs, and 18 osteonecrosis (ON)-TKAs. At a mean of 41.2 months postoperatively, New KSS 2011, PCS, and PDS were assessed and compared between the three groups. Multiple regression analysis with patient satisfaction score considered as dependent variable was carried out to identify postoperative variables affecting patient satisfaction after TKA. Results: Preoperatively, PCS was relatively low in patients with RA. Assessment with PROM after TKA indicated that scores for walk and standing activities, advanced activities, and total activities were significantly worse in RA-TKA than in OA- or ON-TKA, however range of motion was significantly better in RA-TKA. Multiple regression analysis revealed that diagnosis of RA itself positively affected patient satisfaction ($p = 0.002$). The scores of symptom, basic activities and expectation further improved patient satisfaction ($p < 0.001$). Discussion: Recent meta-analysis revealed that RA-TKA carried a risk of higher deep infection than OA-TKA, and the rate of revision within postoperative 5 years was higher in RA-TKA than in OA-TKA. In contrast to such negative aspects of RA-TKA, patient satisfaction after TKA tended to be higher potentially because nociceptive pain accounted for most of knee pain with few proportion of pain sensitization. To improve functional outcome as well as patient satisfaction is probably challenges for the future.

S2-5

What elbow surgeries can bring in for elbow impairments in RA patients?

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Conflict of interest: None

It is well-known that the elbow joint is frequently impaired in patients with rheumatoid arthritis (RA). Several etiological studies indicate that the involvement of the elbow greatly affects quality of life of patients with RA. Swelling and pain of the joint can be treated by conservative treatment such as steroid injection, but it is effective only without joint destruction. As such, elbow surgeries sometimes are the only possible option for the destructed joints. Synovectomy has been historically a valuable surgical option for persistent joint swelling and pain, but is currently indicated for resultant symptoms only after potent medical treatment such as biological and targeted synthetic disease-modifying anti-rheumatic drugs. On the other hand, total elbow arthroplasty (TEA) has been shown a strong surgical treatment for most of elbow impairment even with a periarticular fracture. Recently-developed implants and refined surgical techniques has, furthermore, bestowed more reliable, better outcomes. However, several large studies reported higher complication rates of TEA than total knee and hip arthroplasties. Surgeons and rheumatologists should pay careful attention to such complications along with adequate medical treatment in a perioperative period.

S2-6

Latest trend of rheumatoid surgery in foot and ankle

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Conflict of interest: None

There had been several procedures of metatarsopharangeal (MTP) joint preservation surgeries. Every method was recommended for forefoot deformity in well-controlled rheumatoid arthritis (RA), encouraging us to do forefoot surgery. In such situation, we had been performed modified Scarf osteotomy (horizontal osteotomy + medial capsular interposition) for hallux valgus (HV), and modified metatarsal shortening offset osteotomy for lesser toes MTP joint destruction/subluxation. These procedures also induced good clinical outcomes even in severe deformity/destruction cases. However, recurrence cases were also recognized. Resubluxation of MTP joint in lesser toes was seen in 30% of cases, especially in varus hindfoot. On the other hand, recurrence of HV deformity was seen in poor controlled valgus hindfoot. Taken together, correction of not only forefoot, but also hindfoot deformity is important. Furthermore, midfoot corrective osteotomy [V shape osteotomy, rotational osteotomy (Japas et al. JBJS Am. 1968, HG Jung et al. JOS 2017)], Cotton osteotomy also should be utilized to obtain adequate plantigrade position for varus/inversion cases. To treat severe valgus hindfoot, creative and unique correction procedure was reported (Matsumoto et al. Mod Rheumatol 2017). Total ankle arthroplasty (TAA) is also one of the weapons against destructive ankle. Although subsidence of talar component (16%) should be surely resolved, we confirmed good outcomes, and more increased social activity in biologics treatment group. A challenging procedure of TAA against ankylosing rheumatoid ankle is also established (RC Emilie et al. Foot Ankle Surg. 2016). On the other hand, ankle joint restoration using distraction arthroplasty technique is also challenged (Nakasa et al. J Foot Ankle Surg. 2015). Such challenging, creative, and unique techniques are desired to be keeping established and developed to rheumatoid foot disorders to obtain more wonderful activity of RA patients.

S2-7

Latest trend of forefoot surgery in rheumatoid arthritis

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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. A variety of surgical procedures have been performed for forefoot deformities in patients with RA. Some of these procedures, such as arthrodesis or resection arthroplasty, require that the function of the MTP joint be sacrificed. Recently, the paradigm shift of RA treatment led us to reconsider the benefits of joint preservation. In 2010, we developed rotational closing-wedge osteotomy of the first metatarsal, which corrects varus and rotational deformities of the first metatarsal. We previously reported the positive results of this procedure in 2013. We have been performed a modified oblique shortening osteotomy for lesser toe deformities. The amount of shortening of the lesser metatarsals is selected by considering the degree of the dislocations and contractures of the metatarsophalangeal joints. The modified oblique shortening osteotomy procedure for lesser toe deformities often causes non-unions at the sites of osteotomy, but we have successfully reduced the rates of the nonunion significantly through several efforts during surgery. The first aim of this presentation is to describe the surgical procedure in detail and to assess the short-term subjective, functional, and radiographic results of this joint-preserving procedure for patients with RA. The second aim is to consider the cause of and preventative methods for the unique complications of forefoot surgery in RA patients. The third aim is to present the latest findings and problems of joint-preserving surgery for rheumatoid forefoot deformities by summarizing previous reports.

S3-1

Clarification of pathophysiology in Takayasu arteritis through genetic and epidemiological analyses

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Conflict of interest: None

Takayasu arteritis (TAK) is an immune-mediated vasculitis affecting large arteries first reported from Japan. We have collected DNA samples from patients with TAK from Akebono-kai, a TAK patients' group, and more than dozen research institutions all over Japan to analyze pathophysiology of TAK. Our group conducted HLA-B genotyping using 173 patients of TAK and 2000 controls and showed HLA-B*67:01 as a susceptibility HLA-B allele in addition to HLA-B*52:01, an established susceptibility allele. We also demonstrated that amino acid positions 171 and 67 are important for TAK. We performed genome-wide association study (GWAS) of TAK for the first time in the world and identified IL12B as a susceptibility locus to TAK. The susceptibility allele of IL12B to TAK had a high effect size (rs6871626 in IL12B: odds ratio = 1.75 (95% confidence interval: 1.42-2.16)) and was associated with high complication rate and severity of aortic regurgitation, one of the most severe complications in TAK. These indicate a central role of IL12/23p40 encoded by IL12B on TAK. Thus, IL12/23p40 is a promising treatment target in TAK. Ustekinumab, a monoclonal antibody against IL12/23p40, is widely used for patients with inflammatory bowel diseases (IBD), and psoriasis and displayed favorable outcomes. We also showed that ulcerative colitis, one of IBD, is frequently found in patients with TAK. Common genetic background was shown in both diseases beyond GWAS significant loci, suggesting common molecular pathways underlying TAK and IBD. Based on these findings, we performed a pilot clinical trial using ustekinumab to patients with refractory TAK for whom conventional treatment was not effective. All of the three patients showed good response to ustekinumab. We conducted the 2nd GWAS of TAK for further clarification of pathophysiology in TAK and identified six novel loci. Enrichment analysis showed natural killer cell as a promising therapeutic cell target which plays critical role on TAK.

S3-2

Understanding the etiology and discovering drug targets of autoimmune diseases based on genetic analysis

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Conflict of interest: None

One of the ultimate goals of the study of autoimmune diseases is to elucidate the detailed etiology at the molecular level, and search for drug targets based on it. To comprehensively evaluate the causal mechanisms of autoimmune diseases, genetic analysis such as genome wide association study (GWAS) is a useful technique. In addition, because it is often experienced that the causal gene identified by GWAS (or its related molecule) is consistent with targets of approved drugs, searching for novel drug targets based on genetic analysis is a promising approach. Genetic understanding of autoimmune diseases has greatly advanced due to accumulation of various data and progress of analytical techniques. In this presentation, I focus on expression quantitative trait loci (eQTL) analysis and polygenic analysis. eQTL analysis is a method that comprehensively evaluates how each genetic polymorphism regulates gene expression. Many genetic polymorphisms identified by GWAS of autoimmune disease are accumulated in immune cell-specific regulatory regions. Therefore, dysregulation of gene expression in immune cells should be a causal mechanism of autoimmune diseases. Based on this background, several eQTL analyses using immune cells have been conducted, and they have identified causal genes and pathways. Recently, the understanding of the pathogenesis of autoimmune diseases is progressing by a technique called polygenic analysis. The accumulated impact of genetic polymorphisms with small effect sizes, which are difficult to be identified by GWAS, occupies the majority of the genetic background of autoimmune diseases. Polygenic analysis enables us to evaluate the biological significance of such genetic polymorphisms, and to identify causal cell types and transcription factors. In this presentation, I will explain the progress of genetic understanding of autoimmune diseases, and introduce current attempts to search for drug targets.

S3-3

Trans-layer multi omics analysis elucidates disease biology and drug discovery

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Conflict of interest: None

Statistical genetics is a research field that evaluates causality of human genetic variations on diseases, using statistical and bioinformatics approaches. Recent developments of sequencing technologies have provided human disease genome data of hundreds of thousands of the subjects, and successfully identified comprehensive catalogues of genetic susceptible loci. However, little is known regarding how to develop methodology to integrate large-scale human genome data with diverse biological resources, to which statistical genetics should contribute. We have developed such methods, which is named mutli-layer trans omics analysis, and applied to a pioneering example of large-scale genetic association studies on a variety of human complex traits, including immune-related diseases. We demonstrated that the disease risk genes were significantly enriched in overlap with the target genes of the drugs currently used for treatment of the diseases, and that network analysis between the disease risk genes and the drug target genes could identify candidates of drug repositioning. These results should empirically show the value of statistical genetics to dissect disease biology and novel drug discovery.

S3-4

Personalized medicine for pediatric autoinflammatory syndromes - current status of diagnosis and treatment

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Conflict of interest: Yes

The term "autoinflammatory syndromes" was proposed by Dr. Kastner, NIH, in 1999. The autoinflammatory syndromes are mainly monogenic diseases that cause systemic inflammation and lack autoantibodies as well as self-reactive T cells. Their clinical features consist of fever of unknown origin, periodic fever, rash, arthritis, and gastrointestinal symptoms, which resemble those of rheumatic diseases. Although the onsets of autoinflammatory syndromes are usually early childhood, it seems obvious that many undiagnosed adult patients should exist since the history of autoinflammatory syndromes is still young. These evidences indicate that adult rheumatologist as well as pediatric rheumatologists should pay attention to the autoinflammatory syndromes for early diagnosis and treatment. In addition, understanding of their disease mechanism brought some important inflammatory mechanisms in non-genetic inflammatory diseases such as inflammasome in gout and abnormalities of nucleic acid sensing systems in autoimmune diseases like SLE. Recently, the discoveries of responsible genes for autoinflammatory syndromes have been accelerated by completion of the human genome project and advancement of DNA analysis technology. Of note are haploinsufficiency of A20 clinically similar to Bechet disease, ADA2 deficiency resembling to polyarteritis nodosa, and type I interferonopathy showing autoimmune phenotype. In the advancement of their treatments, canakinumab has been approved for TRAPS, Hyper IgD syndrome and colchicine-resistant FMF in Japan. In this review talk, I will show the spectrum of the current autoinflammatory syndromes and focus on the current treatments which could lead to personalized medicine. I will also mention the Minds-based guideline for the autoinflammatory syndromes and a newly-established genetic diagnosis platform in Japan that has been introduced after the approval of genetic tests for some autoinflammatory syndromes.

S3-5

Genetic classification of auto-inflammatory diseases in adults and establishment of optimized medicine - Precision medicine for familial Mediterranean fever

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Conflict of interest: None

Autoinflammatory diseases are a group of diseases that sustain or repeat systemic inflammation due to dysfunction of the innate immune system. A typical disease of adults with autoinflammatory diseases includes familial Mediterranean fever (FMF), which is classified as hereditary periodic fever syndrome. This disease is characterized by periodic fever, arthritis, serositis, and that mutations in *MEFV* gene encoding pyrin contribute to the pathological condition of FMF, but the mechanism of the development or progression of FMF is not clear. Approximately 10-20% of FMF patients are ineffective or intolerant to colchicine, which is the first-line drug for FMF. The use of IL-1β inhibitors has been recently approved for such cases but there is no established therapeutic agent in colchicine-resistant FMF patients. Although FMF is an autoinflammatory disease with genetic factors deeply involved, it is suggested that genomic abnormality of FMF in Japan is different from that of in the classical Mediterranean region. It is thus important to elucidate that difference for the development of a novel molecular target drug for FMF. Our research team has been developing a consortium of FMF and building an FMF registry. We are conducting association analysis of FMF genomic abnormality and severity based on clinical information, genomic DNA and serum in FMF patients and searching for molecular targeted drugs controlling FMF inflammasome. Regarding the association analysis of FMF genomic abnormality and severity, the severity of FMF is 1. mild (colchicine or NSAIDs), 2. moderate (steroid), 3. severe (biologic agents or amyloidosis). We are trying to identify genes that contribute to severity by classifying them. In this presentation, I would like to introduce the genetic classification of adult autoinflammatory diseases and new findings of precision medicine based on the results on FMF obtained by our consortium and personalized medicine of autoinflammatory diseases in recent years.

S3-6

Development of precision medicine of Behcet's disease using genetic data

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Conflict of interest: None

Behcet's disease is an autoinflammatory disease, causing periodic inflammation of the eyes, skin, and mucosa. In addition to previously known HLA-B*51, recent genome-wide association studies identified multiple loci associated with the disease. However, clinical application of these genetic data to individual patients is still unknown. A preliminary clustering analysis of Behcet's patients using clinical phenotypic data suggest that the patients could be divided into several independent groups. One of the group consists of intestinal Behcet's disease, whose HLA-B*51 positivity is significantly lower than patients with uveitis, implicating that these intestinal patients might have distinct disease prognosis compared with the other groups. Moreover, whole exome sequencing of familial Behcet's disease identified mutations within the genes such as *TNFAIP3*, a direct target for developing disease-specific treatment. Categorization of Behcet's disease patients into subgroups based on clinical and genetic data is essential to develop precision medicine for the disease. In the current presentation, I will describe recent genetic data and efforts to develop precision medicine for Behcet's disease.

S4-1

Recent advances in spondyloarthritides and sapho syndrome

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Conflict of interest: Yes

The gut plays a vital role in shaping our immune system and maintaining tolerance. About 50% of patients suffering from spondyloarthritides have signs of microscopic gut inflammation, regardless of gastrointestinal symptoms. This inflammation is linked to disease severity and extent. Here we will provide a recent update on how the gut mucosal immune system is dysregulated in spondyloarthritis by focusing on microbe-host interactions and its impact on mucosal immunity. It will be discussed how this may alter the course of arthritic disease.

S4-2

Pathogenesis and the development of novel targeted immune therapies in psoriasis

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Conflict of interest: None

Psoriasis is induced by a complex interplay among the immune system, susceptibility gene loci, possible autoantigens, and environmental factors. Recently, research has clearly demonstrated that psoriasis represents a T cell-mediated disease driven by pathogenic T cells that produce IL-17 (which are called Th17 cells). Th17 cell are induced by cytokines, including IL-23 that is produced by dendritic cells. The discovery of the central role for the IL-23/Th17-cell axis in the development of psoriasis has led to a major paradigm shift in the pathogenesis. IL-17 drives the development of mature psoriatic plaques by inducing epidermal hyperplasia, epidermal cell proliferation, and recruitment of leukocyte subsets into the skin. mAbs against TNF-alpha, IL-17 signaling and IL-23p19 underline the central role of these cytokines as predominant drivers of psoriatic disease. We have recently discovered that obesity aggravates psoriasis by inducing IL-17 production by gamma delta T cells in mice. In this symposium, I will introduce the recent pathomechanism of psoriasis and review the novel therapeutic approaches to psoriasis.

S4-3

Management of ankylosing spondylitis: up-to-date

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Conflict of interest: Yes

Early diagnosis, patient education, and physical therapy are fundamental for the successful management of AS. Non-steroidal anti-inflammatory drugs (NSAIDs) are essential treatment of AS. Continuous NSAIDs use may revert the effects of inflammation on radiographic progression. Selective COX-2 inhibitors are preferred than traditional NSAIDs due to better safety. Anti-depressants, acetaminophen or tramadol might help patients with central pain. Corticosteroid local injections directed to enthesitis or peripheral arthritis may be considered. Long-term systemic steroid was not suported by evidence. Sulfasalazine is preferred disease-modifying anti-rheumatic drug (DMARD) for AS patients with peripheral involvement, uveitis, psoriasis and inflammatory bowel diseases. Thalidomide and Pamidronate might be considered in refractory

AS. TNF blockers are very effective in symptom relief and controlling inflammation, and seems to have the true disease modification effect. Monoclonal antibodies such as are better than receptor antagonists extra-articular manifestations, eg. psoriasis, uveitis, and inflammatory bowel diseases. IL-17A monoclonal antibody, secukinumab was approved for AS and PsA. However, anti-IL17 might harm the gut of SpA. IL23 MoAb was not effective in a phase II trial. Tofacitinib showed promising results in a phase II trial. Unfortunately, tocilizumab, rituximab, apremilast all showed negative results in their pilot studies in AS. For all patients under biological therapy, a risk management plan to monitor safety, such as tuberculosis and hepatitis was necessary, esp. in the endemic area.

S4-4

Diagnosis and Treatment of SAPHO (synovitis, acne, pustulosis, hyperostosis, and osteitis) Syndrome

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Conflict of interest: None

SAPHO syndrome represents a rare heterogeneous disease involving skin, most commonly palmoplantar psoriasis, severe acne or hidradenitis suppurativa, and the skeleton, mainly the anterior chest wall, in particular the sternoclavicular junction, followed by the spine and sacroiliac joints (sacroiliitis). Non-infectious sterile osteitis with subsequent hyperostotsis resulting in osteolytic and osteosclerotic bone lesions represent a distinct pathological and radiographic feature of SAPHO. Etiopathogenesis of SAPHO seems to be multifactorial. One possibility is related to low virulent pathogens, such as P. acnes, triggering an exaggerated inflammatory response of the bone marrow in genetically susceptible individuals, leading to a form of "reactive osteitis". The true incidence and prevalence of SAPHO is unknown since the syndrome is commonly misdiagnosed or under recognized. SAPHO mainly affects children and young adults, negatively influencing the quality of patients' life. Diagnostic criteria by Chamot (1988) and Kahn (1994) are the most frequently applied in the clinical practice. However, both criteria are preliminary and lack validation. They rely on the clinical grounds only. To date, no formal guideline outlining diagnostic approach to SAPHO exists. In view of advances in imaging techniques, application of an appropriate imaging modality for diagnosis and disease activity follow up is highly needed as well as avoidance of unnecessary tests. No evidence-based treatment algorithms exist in SAPHO. Treatment choice is based on retrospective reports. A wide spectrum of medications has been used to treat SAPHO. To date, there is no data on long-term efficacy, adverse events, and outcome of different treatments. We have conducted an international survey among the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) members (n=77). SAPHO was considered a subtype of SpA by 48%, a subtype of PsA by 19.5%, and a separate entity by 26%. The majority (84%) agreed upon the need for modification of the present diagnostic criteria, the application of MRI (41%) during the diagnostic stage, and treatment with NSAIDs, conventional DMARDs, and anti-TNF biologics as the preferable options. Recognizing an unmet need for long-term observational data, our group has proposed to set an international multi-center registry for SAPHO.

S4-5

Present issues in Japanese patients with SpA and SAPHO syndrome

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Conflict of interest: Yes

HLA B-27 positivity has been reported less than 1% among Japanese population, and typical axial SpA (ankylosing spondylitis: AS) has been rare disease in Japan. After ASAS classification criteria for Axial SpA was published, confusion in clinical real world has been a big issue. The main problem has been this classification criteria are widely used for diagnosis without rule out of other diseases. Second issue is too much confidence on MRI findings. There are so many diseases to show bone edema or inflammatory signals at SI joint, however, Positive findings in MRI are directly thought to axial SpA. The third issue is the natural course of non-radiographic axial SpA has not been fully elucidated. Even between Europa and North America, the progression rate to radiographic axial SpA from non-radiographic condition is widely separated. At present, three clinical trials for "non radiographic axial SpA" have been performed in Japan, however, entry failure rate are around 50 %. From the administrative point of view, in Japan only AS is listed as Japan intractable disease, we have to rule out AS from the other axial SpA. Recently psoriatic arthritis (PsA) has been interested due to approval of several drugs, however, MTX is not approved in PsA not yet in Japan. SAPHO syndrome is also umbrella disease not a single disease and at least several conditions are included. Pathogenesis of SAPHO syndrome has not been fully elucidataed. Treatment recommendation is not systemically organized yet. I will introduce a recent actual treatment for pustulotic arthro-osteitis (PAO) reported by rheumatologists in Japan.

S5-1

Overview of spondyloarthritis

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Conflict of interest: Yes

Recently, it becomes well known that spondyloarthritis (SpA) is a kind of umbrella inflammatory disease concept including ankylosing spondylitis (AS) or psoriatic arthritis (PsA). SpA exhibits not only arthritis or spondylitis but enthesitis. It also includes inflammatory bowel disease (IBD), such as Crohn disease, related arthritis, reactive arthritis after chlamydia infection, some part of juvenile idiopathic arthritis, and so on. It is required to collaborate with several departments beyond the border because SpA shows various extra-articular symptoms, such as uveitis, psoriasis, IBD, or comorbidities. In this symposium, several experts would present the concept, diagnosis and treatment of SpA in each viewpoint.

S5-2

Peripheral involvements of Spondyloarthritis (peripheral SpA)

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Conflict of interest: Yes

Considering predominance of axial or peripheral involvement and manifestation, spondyloarthritis (SpA) could be currently classified as axial SpA (axSpA) including non-radiographic axial SpA (nr-axSpA) as early or mild axSpA and peripheral SpA (pSpA) due to ASAS classification criteria. On the other hand, according to disease unit, SpA group is composed of ankylosing spondylitis (AS), reactive arthritis (ReA), psoriatic arthritis (PsA), Juvenile SpA (jSpA), IBD-related SpA (IBD-SpA), and undifferentiated SpA (uSpA). The disorders classified as pSpA include mainly PsA, ReA, IBD-SpA and uSpA. 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 skin lesions including psoriasis, 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. On therapeutic strategy for pSpA, especially for PsA, TNF inhibitors, IL-12/23 inhibitor and IL-17 inhibitor are approved in Japan. Moreover, clinical trials of CTLA4-Ig and JAK inhibitor for PsA are in progress. In this session, we will examine ASAS classification criteria with understanding the difference between classification criteria and diagnostic criteria, especially the concept of pSpA. Furthermore, the clinical diagnosis and treatment of pSpA will be reviewed here with a focus on physical and imaging findings of peripheral involvements of SpA,

which are so important findings on diagnosis.

S5-3

Axial involvements of Spondyloarthritis (axial SpA)

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Conflict of interest: None

Spondyloarthritis (SpA) has been proposed to classify into Axial SpA (axSpA), Peripheral SpA (pSpA) according to the ASAS classification standard, and the concept of non-radiographic axial SpA (nr-axSpA) as an early phase of axSpA has been proposed. On the other hand, from the concept of disease / diagnosis, the prototypes are ankylosing spondylitis (AS), reactive arthritis (ReA), psoriatic arthritis (PsA), juvenile SpA, inflammatory bowel disease spondyloarthritis (IBD-SpA) undifferentiated SpA (uSpA), AS is representative as a disease classified as axSpA, and nr-axSpA is attracting attention as an early phase of AS. For ankylosing spondylitis (AS) in Japan, anti-TNF inhibitor is applied for insurance. In addition, JAK inhibitors and IL-17i against axSpA and nr-axSpA are under clinical trials and can be expected for future treatment. However, the diagnosis of axSpA and nr-axSpA is often very confusing. The ASAS classification standard is a tool created to early screening and cannot diagnose the disease itself. Therefore, "overdiagnosis" occurs structurally. For example, it should be avoided that biologics are administered to osteoarthritis of sacroiliac joint in elderly people. To that end, it is important to firmly confirm the symptoms of "inflammatory back pain" which is a major premise, and we want to refrain from easily diagnosing with images only. In this session, we reconsidered the SpA classification criteria by ASAS, fully understand the differences between classification standards and diagnostic criteria, especially on the spinal symptoms and lesions of SpA, an important finding in the diagnosis of ax-SpA, nr-axSpA, I would like to explain it based on findings and image findings.

S5-4

Juvenile Spondyloarthritis (JSpA)

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Conflict of interest: None

There are some clinical challenges in Juvenile Spondyloarthritis (JSpA). 1) There is no validated criteria for JSpA: In the ILAR classification criteria which is widely used for diagnosis of juvenile idiopathic arthritis (JIA), JSpA cases are included in enthesitis-related arthritis (ERA), psoriatic arthritis (PsA) and unclassifiable arthritis (U). Inflammatory bowel disease related arthritis and reactive arthritis are excluded from JIA. 2) Many cases of JSpA don't develp axial involvement at diagnosis. 3) The Japanese people have a low frequency of the heuman leukocyte antigen-B27 (HLA-B 27) in general population. 4) Skin symptoms are poor in Juvenile PsA (JPsA): About half of cases of JPsA develop joint symptoms prior to skin symptoms. 5) JSpA cases develop chronic pain symptom frequently. 6) Many cases of JSpA may not diagnosed over a long period: The frequency of JSpA in JIA was as low as 2% according to the Japanese nationwide survey in 2007. JIA patients in my clinic were classified in Systemic JIA 10%, Oligoarthritis 15%, Rheumatoid factor (RF) negative polyarthritis 17%, RF positive polyarthritis 17%, PsA 13%, ERA 15%, U 12% by the ILAR criteria. There were many cases with chronic pain syndrome in PsA subtype (77%) and ERA subtype (36%). JSpA cases tended to require a long period of time until diagnosis than other subtypes of JIA.

S5-5

Diagnosis and treatment of psoriatic arthritis

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Conflict of interest: Yes

Psoriatic arthritis is not rare and reported to be found in about 15% of psoriasis patients in Japan. Psoriasis patients could accompany comorbidities such as metabolic syndrome or uveitis. Those who have widespread psoriasis lesions, scalp lesions, nail dystrophy and intergluteal/perianal lesions are at higher risk of accompanying psoriatic arthritis. For diagnosis, CASPAR criteria is frequently used. Bone X ray showing mixture of bone erosion and juxta-articular new bone formation is characteristic, and for early diagnosis, magnetic resonance imaging is useful. As for treatment, there are NSAIDs, DMARDs, and biologics, however, only biologics shows the evidence of suppressing progressing bone destruction due to arthritis. For better prognosis, the importance of early diagnosis and tight control is emphasized. The diagnosis and treatment of psoriatic arhthritis from the point of view of dermatologists is discussed.

S5-6

Ocular manifestations in spondyloarthopathies -Focusing on uveitis-

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Conflict of interest: Yes

In spondyloarthropathy (SpA), uveitis occurs in 9 to 40% of cases and the frequency varies depending on the causative disease. Ankylosing spondylitis is the most likely to complicate (34%) with uveitis, and the rate is low (9%) in psoriatic arthritis. The cause diseases of uveitis are sarcoidosis (about 10%), Vogt-Koyanagi-Harada disease (about 7%), Behcet's disease (about 5%), and uveitis due to SpA is as small as 1%. However, in recent years, many evidence has been reported that uveitis is an important risk factor for SpA and uveitis is an important finding for the early diagnosis of SpA. In Japan, there are few cases of uveitis due to SpA, and there are few reports about the clinical features. Of the approximately 2,800 patients with uveitis who initially visited Tokyo University Hospital in 1998-2015, uveitis cases associated with SpA was 0.7%. Ankylosing spondylitis was the most common, including psoriatic arthritis, Reiter syndrome. Majority of the cases were acute anterior uveitis type, but the cases with pan-uveitis were also seen. Systemic treatments (immunosuppressants, biologics, etc.) were often used for systemic diseases, and local treatments (topical corticosteroid, local injection) were performed for uveitis. Short term use of systemic corticosteroid was administrated in severe uveitis cases. Regarding the onset of uveitis and SpA, skin symptoms preceded uveitis in psoriatic uveitis, whereas back pain or arthralgia preceded uveitis in ankylosing spondylitis and the diagnosis of ankylosing spondylitis happened layer than the onset of uveitis. The DUET study in Ireland shows that there is a very high chance of SpA (96%) if there is back pain for more than 3 months in HLA-B27 positive acute anterior uveitis cases. Whereas there are fewer HLA-B 27 positive population in Japan than in Europe, SpA might have been overlooked in acute anterior uveitis cases in Japan. Further collaboration between ophthalmologists and rheumatologists might be necessary.

S6-1

Recent trends of radiological findings and patients' background of rheumatoid knees

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Conflict of interest: Yes

INTRODUCTION: Our first aim of this study was to investigate changes of patient's background and the radiological characteristics in cases of rheumatoid arthritis (RA). Secondly, we analyze how to predict

the joint destruction in cases of total knee arthroplasty (TKA). **METHODS:** Between 2000 and 2015, 239 TKA cases were performed for primary TKA in regional center for RA. The changes of peri-surgical laboratory data, such as white-cell count and the C-reactive protein (CRP) were analyzed from 1 year before surgery to 4 weeks after surgery. We also investigated the yearly changes of an averaged dose of methotrexate (MTX) and prednisolone (PSL). In radiological analyses, presence of spur formation was evaluated. The averaged Larsen score was analyzed from 10 years before surgery to preoperative in available cases. **RESULTS:** The average age at surgery showed continual increase. There were no changes in pre-operative CRP values and WBC during the observation period. The averaged MTX doses were increased, on the other hand, the averaged PSL doses showed continual decrease. In radiological analyses, the continual increase of cases with the spur formation was observed. Sixty-five percent of the cases showed radiological proceeding of joint destruction. Those cases showed significantly higher CRP at 6 months before surgery. Although the averaged Larsen scores from 10 to 5 years before surgery did not show any changes, the linear increase with the ratio of 0.4 Larsen score / year from 5 years to surgery was observed. **DISCUSSION:** This results of preoperative CRP may be one of predict value of near future joint destruction. The averaged Larsen scores showed linear increase from 5 years to surgery. This results may suggest if joint destruction begins, the advance of joint destruction is irreversible. In conclusions, cases with relatively high CRP and progressive joint destruction, even if Larsen grade was low, clinician thought to consider early arthroplasty.

S6-2

The advancement and recent development of total knee arthroplasty for patients with rheumatoid arthritis in Nagoya Medical Center

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Conflict of interest: None

The amount 3000 total knee arthroplasties in Nagoya Medical Center were performed since 1972 for patients with rheumatoid arthritis at once but osteoarthritis recently. Our principle of major TKA was performed by cement fixation, Tricompartment arthroplasty, patellar resurfacing, CR type in 1972-1999, PS type in 2000-2017. The parapatellar approach with lateral retinacular release had been performed until 1990s, however, the midvastus approach was performed since 2000. In revision surgery, some cases were required because of metal back patellar failure, the wear and the breakage of tibial UHMWPE (PCA, MG1, AMK). But since 1980s by Total Condylar Knee, the long-term result is successful in metal implants with cement fixation and the remarkable advancement of implant design, less invasive surgery. The recent development in RA-TKA in Japan, the number of TKA has been decreased, it doesn't changed the major surgery in patients with RA. In current RA-TKA, I think two major type of the breakdown of rheumatoid knee. One is the mild breakdown that was performed the good timing operation and easy. This rheumatoid knee is shown less invasive synovitis by tight control of biological DMARDs, and secondary osteoarthritis. Another type is the severe breakdown with the destruction of cartilage and subchondral bone by rheumatoid synovitis because of the delay of diagnosis and the medical treatment. It is more difficult operation by bone loss, severe instability, flexor contracture, severe varus or vulgus deformity, severe osteoporosis and so on. Especially, it may be needed the release of the severe contracted soft tissue.

S6-3

Total Knee Arthroplasty for Rheumatic Diseases

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Conflict of interest: Yes

Total knee arthroplasty is one of the established orthopaedic procedures for advanced knee osteoarthritis, rheumatoid arthritis, etc. Pain relief and longevity of the implant has been improved by progress of surgical technique, biomaterial, and design of the implant. Many studies, however, have reported that patient satisfaction after total knee arthroplasty is lower than total hip arthroplasty. Many factors are related to patient satisfaction after total knee arthroplasty. Increasing range of motion and achieving near-normal knee kinematics would possibly improve patient satisfaction. We still need further improvement because not all the patients are satisfied with the results of knee arthroplasty. Probably we need more detailed surgical indications for TKA, and we do not know yet the adequate surgical technique and design for improvement of ROM and satisfaction. We should continue conducting clinical, biomechanical, and biomaterial studies to improve clinical results of TKA.

S6-4

The role of TKA for severe fragility, destruction and deformity in patients with rheumatoid arthritis

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Conflict of interest: None

Improvements in total knee arthroplasty (TKA) have made it the best surgical treatment of choice for most patients with rheumatoid arthritis (RA) involving the knees. Difficulties may be more frequent for TKA in patients with RA than in patients with osteoarthritis because of severe flexion contracture, severe joint laxity, severe osteopenia, and severe bone deficit. For these knees, we used constrained condylar knee systems and recently rotating hinged knee systems. The use of constrained condylar knee systems were achieved to successful mid-term clinical result and no revision of constrained condylar knee systems has undergone.

S6-5

Role of total knee arthroplasty in treatment of RA of the knee

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Conflict of interest: None

The treatment approaches for rheumatoid arthritis (RA) have changed markedly through the clinical application of biological products. However, surgical treatment is necessary when the disease is resistant to drug therapy and severe pain and functional disorder are observed. In the lower limbs, the knee joint is more readily impaired compared with the hip and ankle joints, and when deformity is severe, gait is disturbed. It is important to plan surgery at an appropriate time, corresponding to a reduction of activities of daily living (ADL), such as movement at home and from bed. The main surgical treatment for the knee with rheumatoid arthritis includes synovectomy and total knee arthroplasty (TKA). Previously, synovectomy has frequently been performed to alleviate swelling and pain of the wrist, elbow, and knee joints prior to these advances in drug therapy, and it was a representative surgical procedure for RA. With advances in drug therapy, alleviation of inflammatory synovitis has been achieved, and the indications for synovectomy have become limited. On the other hand, TKA is indicated when arthropathic changes progress and pain, instability, and range of motion restriction are observed. The indication is Larsen grade IV or more severe deformity, but it is also indicated for cases with severe pain and instability, even when the Larsen grade is III. The number of TKA-treated cases has decreased with the appearance of biological products. However, TKA may be an essential treatment approach for drug therapy-resistant patients and for the progression of arthropathic changes among aging RA patients, with respect to improving the ADL. In this study, we investigated the mid-to-long term outcome of RA patients treated with TKA at our department and discuss its positioning as a treatment option to increase QOL. In addition, in order to improve the outcome of TKA, the basic surgical procedure corresponding to deformity of the RA knee will be discussed.

S6-6

In vivo kinematic analysis of TKA for patients with rheumatoid arthritis

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Conflict of interest: Yes

One of the most important goals of TKA for the patients with rheumatoid arthritis (RA) is pain relief. Biological DMARDs (bDMARDs) have been used more than ten years in Japan, and in the clinical real world, the RA knees with osteoarthritis changes have increased. The performances of patients with RA after TKA have been improving. Recently at the time of operation, in vivo kinematics affect on the surgical technique or selection of implants design gradually. This time, we report the results of in vivo kinematic analysis of RA TKAs with deep knee bending performance. Before bDMARDs era, CR TKA with mobile bearing (LCS meniscal bearing) was performed in our hospital. There was no persistent kinematics during deep knee bending and kinematics was different due to the patients. PCL was preserved during the operation, however, the bicondylar rollback during deep knee bending was not recognized. After 2005, single radius PS TKA was performed. The kinematics of external rotation of femoral component relative to tibial component due to medial pivot and bicondylar rollback was persistent and there was no difference in terms of kinematics between RA and OA knees. Valgus deformity knees are not rare in RA knees, and we invested the kinematics of TKA with valgus deformity using single radius PS TKA. There was no difference between varus and valgus deformity knees in kinematics after TKA. At present, under the tight control of RA disease activity, for smaller joints, joint-preserving surgery have been shown good clinical results. In the field of TKA, one of the solutions to improve the patients' satisfaction may be preserving ACL TKA. It is still unclear the effect of inflammation of RA to ligaments in knee joint even under the era of bDMARDs. We will show the preliminary results of ACL preserving TKA kinematics.

S6-7

The role of total knee arthroplaty on rheumatoid arthritis

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Conflict of interest: None

Methotrexate and various biological DMARDs can be used against rheumatoid arthritis (RA), and disease control has become possible. However, surgical therapy is a useful treatment for patients with drug therapy unresponded or patients with joint destruction already advanced. The knee joint has the largest capsule and synovial tissue and is a good site of synovitis. Surgical treatments for knee joints include synovectomy and total knee arthroplasty (TKA). Synovectomy is a surgical method that reduces synovial inflammation by direct targeting of the synovial membrane of RA, but it can not suppress X-ray change, and synovitis returns when activity turns worse, so it has been almost abandoned at the present. Especially when the destruction progresses to the knee joint, TKA is the most necessary operation because it causes a big hindrance to walking, and TKA has become the center of the surgical treatment for RA especially by the progress of the artificial knee joint. Recently, due to the development of drug therapy, the number of operations of TKA is decreasing. But once the destruction progress to load joints, joint repair can not be expected even with biological DMARDs. We have undergone TKA for 478 RA knees from June 1993 to September 2017. Initially we used Kinemax type TKA, and in a study of 123 knees (all cases using cement, patella replacement) and an average follow-up period of 15 years, there were complications of 1 infection and 2 femoral condylar fracture. There were no revisions due to loosening of prosthesis, but 2 revisions in 17 years after operation due to instability of joint relaxation. The disease actiity of RA was high and there were many cases where the stete of bone and soft tissue was bad. But in both cases, the pain relieving effect and the gait improving effect were maintained, and TKA can expect good long-term results for RA.

S7-1

Effects of surgical intervention on body image as a patient reported outcome relevant to the preoperative disease activity

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Conflict of interest: None

As the result of improvement of disease control by advancement of DMARDs and treatment strategy, the number of surgery for rheumatoid arthritis (RA) has been decreasing. In Japan, the rate of hand and foot surgeries have been increasing, and we can expect favorable long-term results of joint-preserving surgeries. The disease control of patients undergoing orthopaedic surgery has been improving, and over 50% of patients are in remission or low disease activity, which is a primary goal of T2T. Under these situations, our focus has moved to the Patient Reported Outcome (PRO), which often includes patients' expectation or satisfaction to the surgery. Body Image (BI) is one of the PRO and can be evaluated by body image assessment tool (BIAT). It has been revealed that BIAT shows high correlation with Beck Depression Inventory (BDI)-II, pain VAS and Health Assessment Questionnaire disability Index (HAQ-DI) are significantly higher and BIAT is significantly lower in patients undergoing surgery than patients who do not require surgery. Furthermore, orthopaedic surgery can significantly improve the patients' BI at 6 months as well as one year after the surgery. We have analyzed the data of 102 RA patients (100 women and 2 men, aged average 64 years-old) after the surgery relevant to the preoperative disease activity. The results showed all four categories of BIAT were significantly improved in patients in remission. As it is difficult to improve patients' BI only by the surgery, but combination with achievement of remission by medical therapy might be an important strategy for the achievement of social and psychological remission in RA patients.

S7-2

Patient's voice in remission maintenance phase of rheumatoid arthritis - Searching for life truth, disease activity evaluation by PRO -

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Conflict of interest: Yes

In the treatment of rheumatoid arthritis, based on the Treat to Target (T2T) strategy, there is a philosophy that patients get involved and obtain a good outcome by tightly controlling with a goal. However, since this T2T strategy is a philosophy, the goal is entrusted individually and the degree of tight control varies depending on the attending physician. Our facility has set higher targets and tighter controls by discussing with patients well. This practice has achieved high remission rates as well as many other institutions, but by realizing optimization of tight control during maintenance period, in particular, it achieves high remission maintenance rate, bio free achievement rate, it is also preventing the appearance of treatment refugees that need 'BIO shopping'. In the maintenance phase, in the situation where remission was maintained the serum CRP value became negative, joint swelling had also disappeared, so the only information on tight control at this time is information from patients, that is, Patients reported outcome (PRO). On the other hand, the index of PRO such as HAQ is an indicator optimized during the remission induction phase, and in the maintenance period, influence of mental and already destroyed joint become large, so it is used as an evaluation of survival function in the research. In recent, it became more important to focus on PRO, and it was shown in the RA-BEAM exam that importance as indicator of disease activity of individual components of PRO, such as stiffness. Here, I would like to propose PRO as a disease activity evaluation in the maintenance period of remission, examine the PRO properly

in the orthopedic mind, and practice the tight control with the internal medicine mind to suggest a way of advanced rheumatic therapy.

S7-3

Combined therapy of drugs and surgery aimed at improving QOL in patients with rheumatoid arthritis ~Centering on upper limb surjery~

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Conflict of interest: None

(Introduction) The treatment of rheumatoid arthritis has remarkably progressed. We have faced the new era of treatment to target (T2T). It is important to diagnose RA early with accuracy and to begin treatment of RA at the right point for T2T, for achievement of remission or low disease activity. Tight control of RA disease activity makes it possible to inhibit the progression of the joint destruction. (Surgical treatment of RA patients) Surgical treatment of RA has been changed under tight control for the possibility of repairing joint destruction. Although RA load joint arthroplasty decreasing, still some RA patients need to undergo load joint replacement. In the new era of RA tight control, there are some patterns of RA 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. Moreover, for prevention of joint destruction, joint-preserving RA surgery has been more indicated recently. For advanced functional reconstruction and appearance improvement, there are also surgeries aimed at higher quality of life. (Combined therapy) In these days, medical combined therapy 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 surgery, especially RA hand surgery is thought to be important under tight control with medical therapy. The close cooperation between drug treatment and surgery is expected to be more indispensable.

S7-4

Drug therapy and surgical treatment in patients with rheumatoid arthritis to improve the quality of life

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Conflict of interest: None

Treatment for rheumatoid arthritis (RA) has made remarkable progress in recent years. Advances in drug therapy including methotrexate and biologic agents have greatly contributed to this progress. Therefore, many RA patients have been able to achieve remission or low disease activity. However, progressive joint destruction continued in some patients, who will require orthopedic surgery during their disease course. In addition, the number of surgeries in cases with mild deformity or slightly pain of the elbow, fingers, and forefeet has been tended to increase. In these cases, quite a few patients request surgeries for beauty and re-conditioning. This means that there are more surgeries aimed at improving the quality of life (QOL) of patients compared to before. Underlying this tendency, there has been progress in drug therapy. Thus, it is no longer necessary to worry about relapses of synovitis owing to joint-preservation surgery. If a patient has relatively mild joint damage, they can expect to recover normal joint function again after joint-preservation surgery. Furthermore, joint damage cannot be completely suppressed during remission for all patients, which is the current treatment goal; thus, in some cases, damage to small joints cannot be stopped. Therefore, we believe the combination therapies for both drug therapy and surgical treatment will be more important in the future for RA treatment, as it can improve patient's QOL. We have been performed hand and foot surgery to improve the joint function and patient's QOL. Recently, we tried to perform more less invasive surgeries such as the DLMO method for hallux valgus deformities and arthroscopic surgery for osteoarthritis of the carpometacarpal joint to achieve higher patient satisfaction. We consider combination therapies for both drug therapy and surgical treatment in patients with RA.

S7-5

Tight collaboration between internal medicine and orthopedic in our facility for the improvement of QOL in rheumatoid arthritis patients

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Conflict of interest: None

Collaboration between internists and orthopedicians is imperative to improve QOL of rheumatoid arthritis patients. In Yokohama City University Hospital, so-called "joined rheumatology" outpatient clinic, in which internists, orthopedicians, rehabilitation physicians, and pediatricians are attending, has been implemented for nearly ten years. Many successful examples of treatment through this joined clinic suggest a rationale for physicians and co-medicals to work as a team for the care of rheumatic disease patients. Favorable responses are heard from patients. In the current session, I will discuss on our efforts to tighten collaboration between internal medicine and orthopedic in our facility.

S7-6

Progress in surgical technique, treatment strategy and system required for best medical care of patients with rheumatoid arthritis in era of advanced pharmacotherapy

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Conflict of interest: None

Rapidly advanced pharmacotherapy and rapid improvement of longevity in the elderly including aged patients with rheumatoid arthritis (RA) inevitably affects the goal and concept of RA treatment. We must aim not only for the improvement of recent activity of daily living but also for long-term normal living activity of over thirty or forty years. In the case of disabled patients, we must return them to a lifestyle with less disability. That is because we can only do it to promise them the independence in at least basic activity of daily living such as getting out of bed and going to the toilet, self-feeding, dressing and grooming of over thirty or forty years. This kind of long-term and broad-ranging perspective could suggest that the progress in at least three fields including surgical technique, treatment strategy and system is required for best medical care of patients with RA. One of progress in surgical technique is a trend toward joint-preserving arthroplasty instead of conventional resection-replacement arthroplasty of forefoot deformities. The progress in treatment strategy is change in providing information for patients. There is a trend toward predictive information of disability not only from rheumatoid arthritis but also aging, instead of conventional information only for the moment. These predictive information over 30 years and more give patients treatments options and life-planning without a risk that they would lose the chance to recover the physical function with properly indicated surgery. Another progress in treatment strategy is improved expertise due to accumulated experiences of rheumatologist in the treatment of RA patients with many comobidities. The progress in system, that should be promoted now, is creating highly specialized comprehensive care center and well-organized cooperation of center and clinic. It is inevitable to use efficiently the limited resources. It could provide not only severely disabled patients with high quality result but also medical staffs of next gen-

eration with high quality education. In this respect, the field of arthritis may be two or three decades behind the field of cancer or cardiovascular disease.

S8-1

The management of juvenile idiopathic arthritis patients in childhood and adolescence

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Conflict of interest: None

Juvenile idiopathic arthritis is defined as the chronic arthritis that developed with under 16 years old. The typical onset age varies according to a type, but most patients develop before puberty. It is 4-5 years old for systemic arthritis and oligoarthritis, and 7-9 years old for polyarthritis. The family members are key persons for the management in the pre-puberty period and the concordance with them is important. We are engaged in managing the anxiety of the family concerning on the side effect of the therapeutic drug, the disease activity control, organ damage and the outcome. What you should pay attention is a phenomenon called the periods of growth. You must minimize complications becoming irreversible if they become adult. Glucocorticoid is a chief drug for systemic arthritis and that may leads the short statue and the osteoporosis. Peak of the secondary sex character is around 14 years old for boys and around 12 years old for girls. You should aim at decreasing it as much as possible before that. It is recommended to decrease by 10% of former dose every 2 weeks in the JCR guidance of JIA, because disease activity itself becomes the risk and too early decrease may lead flair and GC re-increase. The failure of growth cartilage that causes micrognathia, difference of lower limb length and the acetabular aplasia should be noticed. Psychosocial aspects are big problems in puberty. Asocial actions are often seen such as neglect of medicine, the prohibition behabiors, conversation refusals and sexual dissoluteness. When children have chronic diseases, they show delay of the identity establishment by the dependence and parents give overprotection and excessive interference from a sense of guilty. They are easy to become codependency. The maintenance of this period is important for the acquirement of a necessary skill to grow up as a well-developed, independent and self-managed adult patient.

S8-2

Transition of juvenile idiopathic arthritis

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Conflict of interest: None

Juvenile idiopathic arthritis (JIA) is comprised of a heterogeneous group of several disease subtypes that are characterized by the onset of arthritis before the age of 16 years and has symptoms lasting at least 6 weeks. In Japan, tocilizumab was approved for systemic and articular JIA in 2008 following etanercept and adalimumab for articular JIA in 2009 and 2011, respectively. Analysis of database of specific pediatric chronic disease records of pediatric patients who have received financial support for medical costs from a government-funded revealed that 33.2% of JIA patients registered in 2012 applied to biological DMARDs and their clinical manifestations and laboratory data showed improvement compared to patients registered in 2008, pre-biological DMARDs era. However, patients of 19 years of age used biological DMARDs in over 40 % of them and had complications at the higher rate than younger patients. It suggested that JIA patients who transferred to adult healthcare could be severe with complications. In addition to systemic JIA, articular JIA has been approved as an intractable disease by Japanese government. This would support seamless transition from pediatric to adult healthcare systems.

S8-3

The rheumatologist perspective on treatment of rheumatoid arthritis at childbearing age

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Conflict of interest: None

The peak age at rheumatoid arthritis (RA) onset was from the 30s to 50s and female-to-male ratio was around 4. Contrastingly, the average age of first-time mothers of Japan in 2015 was 30.7. Considering that the average age in 2005 was 29.1 and in 1990 was 26.4, the average age of first-time mother was getting older. On the birth rate of age group, the elevation of 35-39 years old age group was remarkable, followed by 30-34 and 40-49 years old age groups. Taking account of that the number of live births did not change, the age of women with a desire for childbearing was advancing. The change of demographics affected RA treatment in a meaningful way. Previously, having children ended before the onset of RA. Recently, we often take into consideration of patients' desire for childbearing when we treat RA. According to 'Treat to target' policy, the primary goal of treating RA patients is to maximize long-term health-related quality of life through control of symptoms, prevention of structural damage, normalization of function and participation in social-related activities. However, not only mentioned above but also bearing their own child was one of the main concerns of females in their life. Although 'Hits early, hits hard' was the concept of recent RA treatment strategy, it was not the unique option in RA patients who had a desire for childbearing. For example, Methotrexate, anchor drug of RA treatment, could not be used in these patients. Prioritizing RA treatment over childbearing until attaining remission was not the best solution because aging increased the likelihood of infertility. Moreover, some patients gave up getting pregnant without consulting their doctor for the sake of the successful RA treatment. Therefore, rheumatologists should give careful attention to childbearing age patients. In this session, rheumatologists' concern about pregnancy and delivery, and results of questionnaires about making treatment decision on some model cases will be presented.

S8-4

Medication for young women with rheumatoid arthritis and juvenile idiopathic arthritis during pregnancy and lactation

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Conflict of interest: None

Rheumatoid arthritis (RA) and juvenile idiopathic arthritis (JIA) are not rare among young women who wants to bear children. However, it is difficult for many rheumatologists how to use anti-rheumatic disease drugs (DMARDs) effectively and safety for during pregnancy and lactation, because many DMARDs have not been established for safety profiles in patients during pregnancy and lactation. Furthermore, an appropriate counselling is needed for women who take any medication during pregnancy and postpartum because she often sensitive to adverse effect on fetus and newborn babies. When considering the influence of mother's medications on children, it is necessary to consider maternal pharmacokinetics, placental permeability, drug exposure time, drug milk transfer rate and absorption rate in neonatal digestive tract. Teratogenicity is the congenital anomaly caused by exposure of the drugs to embryo. The natural incidence of congenital anomalies in humans is estimated about 2-3%. Fetal toxicity is the harmful effect on the fetus after the organogenesis stage caused by the drug. Early preoperative closure of the fetal arterial duct by nonsteroidal anti-inflammatory drugs in the late pregnancy is important. Recently, some biologics DMATRDs and conventional synthetic DMARDs except for methotrexate and leflunomide are considered to be acceptable during pregnancy and lactation. However, there is not enough data on other biologic DMARDs and targeted synthetic DMARDs. It is necessary to accumulate data in the future.

S9-1

Periodontopathic bacteria, *Porphyromonas gingivalis*, infection and Rheumatoid Arthritis

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Conflict of interest: None

Chronic periodontitis, a type of periodontal diseases, is chronic infection by periodontopathic bacteria and results in periodontal tissue destruction, mainly alveolar bone resorption. Recently, it has been emphasized the close relationship between periodontitis and many systemic diseases such as diabetes mellitus, chronic kidney disease, vascular disorder, preterm birth/low weight birth, non-alcoholic steatohepatitis, rheumatoid arthritis (RA) and Alzheimer's disease. The aspects of chronic infection and chronic inflammation are important to understand the relations between periodontitis and systemic diseases because the disease duration of periodontitis is generally long. Almost of periodontopathic bacteria is Gram negative and strict anaerobic. *Porphyromonas gingivalis* (Pg), a member of "Red Complex"group in periodontopathic bacteria, has many pathologic components such as LPS, gingipain and fimbrie, and most strongly relates to periodontitis. Since only Pg possess peptidylarginine deiminase, Pg infection has been implicated as a risk factor of RA. We have studied the relation between Pg infection and RA with SKG mice model. Additional oral application of Pg to SKG RA model mice induced laminarin application exacerbated RA with early and severe arthritis, bone resorption on talus and elevated levels of anti-citrullinated peptide antibody (ACPA), matrix metalloprotease-3 and interleukine-6 in their serums. The high level C5a detected in serum and ankle joints is suggesting that C5a is related early-onset of RA. Furthermore, it was recently reported that the oral Pg administration induced dysbiosis of gut microflora. Dysbiosis of gut microflora was also detected in our laminarin/Pg administration group in RA model and the transplantation of feces from this group could induce early-onset of RA in mice model without direct Pg-administration. Pg can be classified by genotype of fimbrie, *fimA* type, and PG with *fimA* type II or IV is known to closely relate to periodontitis. In RA patient serum, we found that there was significant relation between IgG level against *fimA* typeIV Pg and ACPA level. I would like to discuss about relationship between Pg infection and RA from clinical aspect.

S9-2

Risk of herpes zoster in rheumatic diseases and expectation for new vaccines

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Conflict of interest: Yes

Herpes zoster (HZ) is a common disease caused by varicella-zoster virus (VZV), which is characterized by unilateral eruption along the distribution of sensory nerves, accompanied by neuralgia-like pain. The frequency of HZ occurrence in Japan is about 5 per 1000 people a year, and it tends to increase with age. In HZ, cellular immunity plays a central role in prevention of its onset, severity, and post herpetic neuralgia (PHN). In patients with decreased cellular immunity, it is known that the incidence of HZ is high and the risk of severity also increases. Recently, various biological products have been developed against immune diseases such as collagen disease and rheumatoid arthritis, and surprising therapeutic effects have been obtained. However, the incidence of HZ is increasing as a result of the immunosuppressive condition caused by these new drug administrations. HZ patients under immunosuppression present severe skin symptoms than usual, and sometimes rapidly become severe. Furthermore, in these patients, the decrease in quality of life due to PHN and serious complications are not uncommon, so the countermeasure is an important subject. Regarding the treatment of HZ, treatment results have dramatically improved since antiherpesvirus drugs appeared in the 1980's. However, even now, quite a few patients are suffering from long-term problems due to PHN and complications. Therefore, prevention with vaccines is considered to be important. In March 2016, varicella vaccine has finally become available for prevention of HZ in Japan. Furthermore, the development of subunit vaccines is also progressing now. In this presentation, I will explain the clinical features of HZ in immunocompromised patients and the relationship between immunity and HZ as the basis for considering prevention, and also describe usefulness and precautions on use of HZ preventive vaccine.

S9-3

Hematological management of lymphoproliferative disorders in patients with rheumatoid arthritis; diagnosis, watching, chemotherapy and prognosis

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Conflict of interest: None

Growing number of lymphoproliferative disorders (LPD) has been diagnosed in RA patients mostly in the use of methotrexate (MTX). This entity may include diverse pathological subtypes of lymphoma, so that the patients could not be dealt with merely under one word, 'lymphoma.' It may varies not only in pathological subtypes but also in clinical features or prognosis. Although most cases show regression without chemotherapy after stopping MTX, substantial number of the patients don't show regression. Moreover, patients with a certain pathological subtype, including Hodgkin lymphoma, or patients with strong B symptoms, remarkable CRP or LDH elevation, have been reported to have poorer prognosis. We hematologists will provide rheumatologists with some feedback about situation after referral of LPD.

S9-4

A Clinicopathological Study of Methotrexate-Associated Lymphoproliferative Disorders in Rheumatoid Arthritis Patients: Histological Classification and Predictive Factors for Disease Progression

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Conflict of interest: None

Rheumatoid arthritis (RA) patients treated with methotrexate (MTX) may develop lymphoproliferative disorders (LPD), which are recognized as iatrogenic immunodeficiency-associated LPDs. We analyzed clinicopathological features of MTX-LPD. Between 2004 and 2015, 193 patients were diagnosed with MTX-LPD at Kurume University. Lesions were classified into the 4 diagnostic categories: (1) reactive hyperplasia (RH) (n=28); (2) polymorphic LPD (Poly-LPD) (n=33); (3) diffuse, large B-cell lymphoma (DLBCL) (n=107); (4) classic Hodgkin lymphoma (CHL) (n=25). Low grade B-cell lymphoma and peripheral T-cell lymphoma were excluded. The clinical features are followed 1) median age, 62 (range, 26-81 years), 68 (42-83 years), 69 (39-88 years), and 66 (46-85 years); 2) extra-nodal involvement, 11% (3/28), 36% (12/33), 70% (73/105), and 16% (4/25); 3) multiple involved sites, 46% (12/26), 48% (16/33), 62% (64/104), and 48% (12/25). Of the patients who discontinued MTX, 100% (14/14), 73% (22/30), 49% (34/70), and 11% (2/19) of patients had spontaneous regression. Among those who received chemotherapy, 78% (7/9), 72% (48/67), and 70% (14/20) had complete remission. One, 17, and 2 patients with Poly-LPD, DLBCL-type, and CHL-type lesions had disease- or treatment-related death. Epstein-Barr virus-encoded RNA (EBER)-positive lymphocytes/neoplastic cells were observed in 64% (18/28), 75% (24/32), 54% (56/104), and 84% (21/25). Among patients who discontinued MTX without concurrent chemotherapy at diagnosis, RH and Poly-LPD patients had significant favorable chemotherapy-free survival (CFS) ($p<0.0001$, $p=0.0120$), while CHL patients had unfavorable CFS ($p=0.0344$) compared to DLBCL patients. Moreover, EBER-positive DLBCL patients had significantly favorable CFS compared to negative DLBCL patients ($p=0.0046$), although there were no significant differences in other categorized groups.

S9-5

Respiratory infection (including immune reconstitution syndrome) in rheumatic diseases and their countermeasures

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Conflict of interest: None

Rheumatic diseases are well-known to cause interstitial pneumonia, pulmonary nodular lesions, pleurisy, or small airway lesions. Pulmonary lesions associated with rheumatic diseases, however, are caused by various pathological conditions and accurate differential diagnoses are required. Additionally, since biological products, steroids, or immunosuppressants are widely used in the treatment of rheumatic diseases, attention must be paid to opportunistic infections (e.g., mycobacterial infection) and adverse effects such as interstitial pneumonia. In these instances, modification or discontinuation of the drug regimen is required. When diagnosising interstitial pneumonia in rheumatic disease, physicians frequently refer to the classifications of idiopathic interstital pneumonia. However, these classifications typically overlook causes such as rheumatic diseases, infectious diseases, or drug-induced lung injury. Idiopathic interstitial pneumonia can also be classified based on the degree of alveolar epithelial cell injury. For lung lesions in rheumatic diseases, it is necessary to distinguish vascular endothelial cell dysfunction from alveolar epithelial cell injury. However, due to the close proximity of epithelial and endothelial cells in the lung, almost all lung lesions are regarded as both epithelial cell and endothelial cell damages. Discovered by a Japanese researcher, the markers of epithelial cell injury, KL-6, SP-A, and SP-D, can denote the degree of epithelial cell damage and incrementaly increases in relation to the severity of disease. Where, IPF demonstrates a mild increase in the concentration of these markers, COP, NSIP, and AIP have exponentially increasing values, respectively. Furthermore, by combining the characteristics length of ongoing disease, degree of epithelial cell injury, and chest CT findings, it is possible to predict the tissue injury pattern of lung lesions without invasive biopsy. In addition, these markers could be used to determine the severity and potentially distiguish between the pulmonary lesions of interstitial pneumonia cases complicated with rheumatic disease or opportunistic infections and interstitial pneumonia due to an adverse reaction to medications. In addition, despite the appropriate use of biological products, steroids, or immunosuppressants, it is important to consider the potential complication as the immune reconstitution syndrome, similarly found in HIV patients.

S10-1

Upper limb care and rehabilitation for RA patients

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Conflict of interest: None

Rehabilitation of upper limbs of RA patients has been changing due to the spread of biologics and early rehabilitation. Patients are divided into 4 main groups. (1) Patients that are treated early, and are almost the same as healthy subjects, (2) Patients who have stabilized after minimal joint destruction, (3) Patients who have stabilized after suffering long-term and severe joint destruction, (4) Patients with disabilities progressing at the same speed as with the previous therapy. For category (1), rehabilitation for upper limbs is carried out for the purpose of preventing advancement of disorder and preventing excessive use. For category (2), rehabilitation that prevents destruction caused by excessive use of affected joint is added to (1). For category (3) patients, the symptoms are remarkably reduced compared to the past, and functional destruction may progress from excessive use of affected joint. Therefore, more thorough guidance for joint function preservation, deformation prevention, etc. is required than category (2). For category (4) the goal should be not to maintain the current function but to rehabilitate according to the advancement of disorder. The important thing is that the patients do not know how to use their deformed joints, causing misuse and excessive use. For this reason, the guidance must be given emphasis. Improvement of internal medicine and pathology by drugs such as MTX and biologics, results in clinical remission that improves inflammation and symptoms. Furthermore, structural remission of stopping of joint destruction can be obtained with rehabilitation of upper limb usage as well as drugs. Functional remission that maintains the physical and living functions after that cannot be done without rehabilitation. From the above, rehabilitation is indispensable for complete remission that integrated clinical remission, structural remission, and functional remission.

S10-2

Surgical treatment of RA shoulders

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Conflict of interest: None

Even if clinical remission of RA, there are cases with shoulder dysfunction of pain, ROM limited and joint destruction. Arthroscopic shoulder synovectomy with capsular release was reported as efficacy method in even in Larsen grade IV of RA with severe dysfunction (Kanbe K, et al. Eur J Orthop Surg Traumatol 25:451-5, 2015). Shoulder joint is special joint with sphere joint with full ROM of non weight bearing joints. Therefore improvement of ROM with Arthroscopic shoulder synovectomy induces the environment of more efficacy of medical treatment with MTX or biologics. Joint repair were recognized several cases after arthroscopic shoulder synovectomy. However over 70 years with high joint destruction with more than 10 years disease duration, reverse shoulder arthroplasty (RSA) is selected to improve pain, ROM immediately compared with TSA. The true remission should be discussed for improvements of each joint dysfunction including shoulder joints with RA.

S10-3

Impact of total elbow arthroplasty for social and psychological remission of patients with rheumatoid arthritis

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Conflict of interest: None

The modifications and improvements of elbow prostheses during the ensuing three decades have made total elbow arthroplasty (TEA) a reliable option for reconstruction of a damaged rheumatoid arthritis (RA) elbow. A average 7.7 (2-16) years follow-up data of J-alumina ceramic elbow (JACE) TEA from 130 elbows of 113 patients with RA showed the likelihood of survival of TEA was 99.2% up to 15 years with revision as the end point. The average MEPI improved from 42.5 preoperatively to 95.1 points postoperatively. Recent advancement of pharmacological therapy for RA made comprehensive disease control (CDC) composed of clinical remission, functional remission and structural remission a realistic goal. On the other hand, there is a growing interest in patient-reported outcomes (PROs) in rheumatology. To investigate the impact of TEA on social and psychological remission, we examined the PREE-J and Body image (BI) in RA patients who underwent TEA. The results of average 19.8 months follow-up study of 26 elbows showed disease activity evaluated by DAS28-CRP significantly improved by TEA. PREE-J was also significantly improved with high correlation with DASH and Hand20 scores, but not improved in the items for shoulder and hand function. A high patients' satisfaction was obtained postoperatively but it was lower in patients with over 35 degrees of flexion contracture. The results of the analysis of BI by body image assessment tool (BIAT) showed none of the four categories improved at 6 months after surgery, but body-cathexis and low body-control were significantly improved one year after surgery. The body-depersonalization was not disturbed, and it was difficult to improve body-esteem by TEA. Our results indicated TEA combined with effective medical therapy can improve subjective rating scores as well as PROs, and there are several items which can not improved in RA pa-

tients.

S10-4

Surgical treatment for finger deformities in rheumatoid arthritis

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Conflict of interest: None

Finger joints are frequently affected in patients with rheumatoid arthritis from the early onset of the disease. As the disease progress, the destruction of the finger joints results in characteristic finger deformities such as ulnar deviation, swan neck deformity and boutonniere deformity. The recent progression of medical therapy has led to decrease in joint destruction, however, finger deformities remain problem since the imbalance of the soft tissues due to synovitis, which is a trigger of the deformities, occurs in extremely early phase of the disease. In addition, once the finger deformities occur, they are difficult to treat with medical therapy and surgical intervention is required. The problems of the finger deformities are usually functional difficulties and cosmetic appearance without pain. Thus the finger deformities show little influence on disease activities. However, we think it is important to treat finger deformities in order to achieve the true structual remission. The type of the deformity, the degree of joint destruction and contracture should be taken into consideration for the treatment of finger deformities. The common principles for the treatment of finger deformities including ulnar deviation, swan neck deformity and boutonniere deformity are as follows: 1. The reconstruction of soft tissue balance is necessary for the treatment. For this purpose, we should totally know the mechanisms of the progression of finger deformities. 2. The reconstruction of the joint using implant arthroplasty is considered if the joint is severely damaged. In some situations, arthrodesis is more reliable than arthroplasty. 3. The cooperation with hand therapist is also necessary to gain the good outcomes and to prevent the recurrence of deformities.

S10-5

Rehabilitation of Upper Limb in Rheumatoid Arthritis ~Aiming for true remission

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Conflict of interest: None

In recent years, I feel that motivation is high for dealing with deformation of fingers and pain, because the number of patients and families with high information gathering ability that make good use of IT are increasing. Self-help tools and other welfare equipment became available at general shops due to the influence of universal design. In the last fifteen years, it seems that the obstacle image concerning the upper limb function of rheumatoid arthritis patients had changed. From the literature point of view, the disturbance of reaching function of the upper limb decreased, but the grasping function impairment did not change much, and the difficulty regarding the grasp remained in ADL. Although the rehabilitation approach has not changed from long ago, functional exercises of upper limbs such as joint motion range training, muscular strength training, reaching, grasping, and dexterous behavior, ADL training and guidance considering joint protection, splinting therapy, and hyperthermia, physiotherapy such as low frequency and so on. The above-mentioned rehabilitation approach should not only be used, but also it is necessary to listen to the patient's living situation, to adapt various therapies to the patient, and to combine well. And the most important thing is that patients understand and execute ADL method to prevent hand deformation, that is, patient education is important.

S10-6

Rehabilitation and surgical treatment for rheumatoid hand disorders

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Conflict of interest: None

In the era of biological therapy, the number of surgical treatments that we perform for rheumatoid hand is increasing in our institution. Recently, "Hand rehabilitation (Hand Reha)" based on Strengthening and Stretching for Rheumatoid Arthritis of the Hand (SARAH) trial by Lamb was introduced and carried out with conventional therapy. **Hand Reha:** Subjective assessments of the upper-extremity function, including the level of independence and satisfaction were carried out for the patients who felt that their hands were in trouble. The patients were instructed to perform an exercise program with joint protection regularly. A subjective assessment revealed a favorable outcome after 6 months of the program. However, some patients complained of hand pain after exercise; thus, it was necessary to pay attention not to overload the affected joint. **Hand Splint:** The wrist is a key-stone for the hand function. Patients with wrist pain experience an overall loss of their hand function. A wrist supporter is effective for distal radioulnar joint disorder. By wearing it, pain is relieved and the grip power is increased. For flexible swan-neck deformity of the fingers and unstable IP joint of the thumb, a 3-point-supporting splint or a splint with a strap is applied. For ulnar drift of the fingers, a soft splint is applied for work or a static splint is applied when the patient is at rest to prevent progression. **Postoperative Therapy:** Before surgery, the treatment goal and the postoperative program are determined based on the residual hand function. After surgery, the program might change depending on the intraoperative and postoperative condition of the surgical site; thus, the patient receives tailor-made therapy. Some patients needs require time to reacquire muscle power, dexterity and durability of the hand; thus, concrete work is started early to reduce their uneasiness. In conclusion, hand therapy is a complementary measure that can help a patient achieve true remission.

S11-1

Respiratory manifestation of collagen vascular diseases - from the view point of morphology

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Conflict of interest: None

Collagen disease (collagen vascular disease) is a concept of disease proposed by a pathologist Paul Klemperer from the patho-anatomical precise observation of many strange disease of unknown cause. It is the most innovative point of this concept that it forms some unique lesions on various organs but does not indicate diseases of a specific organ but a disease which can spread to general diseases or involve multiple organs. Progress in immunology will lead to deepening of understanding of collagen diseases as diseases of immune abnormality, so that the significance of morphology seems to be decreased. However, morphology can play one of the two wheels with immunology. In rheumatic diseases or collagen diseases, various lesions are frequently found in the lung. Those are understood as interstitial pneumonia (LIP, NSIP, UIP) associated with collagen disease, collagen disease related bronchial and/or bronchiolar lesions, and pulmonary lesion preceding collagen disease. Is it so? Interstitial pneumonia associated with Sjögren syndrome has been understood as a complicated LIP. In fact, it should be considered that the essential lesion of Sjögren syndrome was formed in the "interstitium" of the lung. It is not an associated pulmonary diseases but "lung lesions of Sjögren syndrome". Even if the main disease is in the lungs, is it not possible to clarify the true nature of lesions if we are only looking at the lungs? It is similar to looking at a man with sickness, not disease.

S11-2

How to understand the pathology of rheumatic diseases based on the skin histology

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Conflict of interest: None

Rheumatic disorders show a variety of skin symptoms characteristic of each disease. Since skin biopsy is less invasive than biopsy of internal organs, the analysis of skin histology is a useful strategy to obtain some clue to better understand the disease-specific pathogenesis. In the histology of skin lesions associated with rheumatic diseases, the characteristic changes of the epidermis, dermis, vessels, and inflammatory cells are generally seen, which help us speculate the systemic pathological processes when taken together with clinical features of the skin and internal organs. For instance, recent advance in the field of dermatomyositis-associated autoantibodies has established a new framework of disease classification, and the histological analysis of its skin lesions seems to be insightful to unravel the difference in disease-driving mechanisms among disease subsets. With respect to systemic sclerosis, altered phenotypes of epidermal keratinocytes and dermal blood vessels and the progression process of dermal fibrosis have suggested various hypotheses explaining the complicated disease pathology, shedding new light on previously unrecognized disease-driving cells through animal model studies. In my talk, I would like to introduce potential disease mechanisms arising from the histological analysis of skin lesions, especially focusing on dermatomyositis and systemic sclerosis.

S11-3

Pathological aspects of vascular involvement in rheumatic diseases

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Conflict of interest: None

The vasculature is not rarely involved in rheumatic diseases. The histological features of affected vessels include granulomatous inflammation, fibrinoid necrosis, and thrombosis. Primary granulomatous inflammation of blood vessels is characteristic of Takayasu arteritis and giant cell arteritis, while secondary one is evident in sarcoid vasculitis. Although Th1 cytokines could be implicated in the pathogenesis of granulomatous inflammation, the precise mechanisms remain unknown. Fibrinoid necrosis in vascular wall occurs primarily in polyarteritis nodosa, anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis, anti-glomerular basement membrane (GBM) disease, IgA vasculitis, and cutaneous arteritis, and secondarily in lupus and rheumatoid vasculitis. The etiologies of fibrinoid necrosis include immune complexes and ANCA. Immune complex-mediated diseases are classified into 2 subtypes, in situ immune complex diseases, such as anti-GBM disease, and circulating immune complex diseases, including IgA vasculitis and lupus vasculitis. In both cases, complement-mediated tissue injury is critically involved in the development of fibrinoid necrosis. Regarding the pathogenicity of ANCA, the ANCA-cytokine sequence is well-known. Recent studies have revealed that ANCA-induced neutrophil extracellular traps (NETs) also play roles in the formation of fibrinoid necrosis. NETs are actually present in the affected vessels in ANCA-associated vasculitis. Idiopathic thrombosis occurs in Buerger's disease, whereas secondary or antibody-mediated thrombosis occurs in cryoglobulinemic vasculitis or anti-phospholipid syndrome. In scleroderma and mixed connective tissue disease, onion skin-like thickness of vascular wall is sometimes observed. These histological characteristics are considered to reflect the pathogenesis of diseases. Thus, an exact recognition of pathological findings of affected vessels is important for understanding the pathophysiology of rheumatic diseases.

S11-4

Renal Pathology in Rheumatic Disease

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Conflict of interest: None

In rheumatic diseases (RD), auto-immune abnormalities provoke variety of systemic organ damage. Kidney is one of the frequent targets of RD and renal pathology reflects background immune abnormalities. Renal tissue damage is categorized by three compartments; glomeruli, tubulointerstitium and vasculatures. Glomerular lesions in RD are deposition, hypercellularity in mesangium, endocapillary and extra-capillaries portions. Particularly wire-loop is seen in acute onset or aggravation of lupus nephritis by excessive auto antibody production. Proliferative lesions are caused by immune-complex-mediated type III reaction. Particular patterns are mesangial hypercellularity/sclerosis, endocapillary hypercellularity having inflammatory cells and crescents and they are occasionally mixed. Tubulointerstitial injury is particularly seen in Sjögren's syndrome. Cell mediated immunity may be involved in this lesion. Because such lesions is seen in secondary events associated with glomerular damage, pathologist needs to awaire detailed clinical information for diagnosis. Vascular lesions includes vasculitis (immune complex-mediated vasculitis), intimal fibrous thickening (onion skinning) in scleroderma and vascular necrosis by immune deposition (lupus vasculopathy). Intimal hyperplasia is another important lesion suggesting APS. Histological patterns of different kidney compartment may represent background RD or immune abnormalities. In addition, recent therapeutic options for RD may change kidney histology. Therefore, not just classify the histologic pattern of each kidney compartment, but integrate these lesions comprehensively according to clinical information. Pathologic diagnosis should be done to interpret pathophysiology with intimate discussion between clinician and pathologists.

S11-5

Innate immune perspective of rheumatic diseases

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Conflict of interest: Yes

Rheumatic diseases are the consequence of a dysregulated immune system. The immune system consists of two arms, innate and adaptive immunity. Autoinflammatory diseases (e.g. FMF, CAPS, TRAPS) are caused by single mutation of genes of innate immunity that leads to activation of inflammasome - IL-1 pathway or TNF receptor signaling. Behçet's disease (BD) is a systemic condition characterized by oral aphthae and genital ulcers, as well as ocular and skin manifestations. Although the mechanism of the disease is not fully understood, BD is thought to consist of a combination of autoinflammatory and autoimmune dysfunctions, inclining more towards the autoinflammatory spectrum of disorders. Neutrophils, Th17 cells, γδT cells, NK cells, monocytes, and macrophages have a role in various processes in BD. Activation of innate sensors leads in turn to the activation of inflammasomes, which serve as a platform for IL-1β processing and release. In this respect BD is very similar to another autoinflammatory disease, Familial Mediterranean Fever, as seen in the activation of the inflammasome by molecular mechanisms and its inhibition by colchicine. The production of neutrophil extracellular traps (NETs) is a process that enables neutrophils to help catch and kill bacteria. Recently, increasing evidence suggests that this process might also occur in various rheumatic diseases including SLE and ANCA associated vasculitis. Recent advances in our understanding of the cellular and molecular pathogenesis of rheumatic diseases as well as in their treatments, are reviewed here from the perspective of innate immunity.

S11-6

Role of Histopathological Analysis in Rheumatic Disease

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Conflict of interest: None

Rheumatoid arthritis is the most common rheumatic disease in bones and joints in rheumatic disease. For a long time people has been have

suffered from pain, and destruction and deformity of joints resulting in inconvenience of in daily life for a long time. Although recent developments in biotechnology the have produced biological drugs which produced by recent developed biotechnology that alleviate the disease, all the mechanisms of the illness, including the its genesis, were not clearly elucidated. Until now various histological findings associated with the clinical symptoms of RA were have been reported, especially after the development of optical microscopy. For example, histological change in very early stages begins with the inflammatory infiltration in bare area. The main factors such as CD4 and CD20 lymphocytes in RA were defined by immunohistochemically. Many kinds of lymphocytic cells, and the distribution pattern and numbers of each kind of cell were revealed by histopathology. Furthermore, two kinds of synovial cells, **A and B cells**, were proposed by an electron microscopic study. They produce many kinds of cytokines, growth factors and various proteolytic enzymes in patient's tissues as well as HLA/DR antigens. All these findings were visually revealed by histopathological methods including immunohistochemistry, *in situ* hybridization and other methods. However, many problems were still remained concerning RA. For example, MP-3 evaluated as the most important marker of joint destruction were not detected in the lesions of bone destruction called pannus. Furthermore, some of the important problems are: what What is an **A cell**? What is a **B cell**? Where do they come from? How does the mechanism for continuing the long term inflammation work? In this session we will focus on the **Nursing Phenomenon** of synovial tissues in RA, which is specifically observed between FLS and lymphocytes. We show an important role of histopathological study in rheumatology.

S12-1

Perioperative management of anti-rheumatic medication in patients undergoing orthopaedic surgeries

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Conflict of interest: None

Total hip (THA and total knee arthroplasty (TKA) are frequently performed successful procedures, but patients with rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and spondyloarthritis (SPA), including ankylosing spondylitis (AS) and psoriatic arthritis (PSA), are at higher risk for adverse events after surgery. Patients with SLE, RA, and SpA have an increased risk of infections that may be mitigated by careful perioperative management of the immunosuppressant medications and glucocorticoids used to treat these diseases. While there is little direct information addressing the risk of post-operative infection attributable to anti rheumatic medications, clinical trial data and observational studies demonstrate an increase in infection seen with TNF inhibitors and other biologics. There is surgical data pertaining to infection risk of synthetic DMARDs like methotrexate indicating these agents appear safe to continue through surgery. Multiple studies indicate that glucocorticoids increase the risk of infection, yet common practice is to administer supraphysiologic doses of glucocorticoids ("stress dose steroids") on the day of surgery for those who have received glucocorticoid therapy, although studies demonstrate that this may not be necessary to maintain hemodynamic stability. Based on mostly indirect evidence, the American College of Rheumatology and American Association of Hip and Knee Surgeons have recommended that all biologics be withheld a prior to surgery, synthetic DMARDs be continued, and the usual daily dose of glucocorticoids rather than supraphysiologic doses be given on the day of surgery for most patients undergoing elective THA or TKA. Patients with rheumatic diseases have an increased risk of perioperative cardiac events and thromboembolism. Although control of inflammation has been associated with a decrease in long term cardiovascular risk there is no known role for perioperative risk mitigation through anti-rheumatic medications. Careful planning by experienced clinicians can do much to improve arthroplasty outcomes for patients with rheumatic diseases.

S12-2

Pearls and pitfalls in rheumatoid hand surgery

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Conflict of interest: None

Perals and pitfalls in classical RA hand surghery interventions: Total wrist fusion Trend: More plate fusion Pearls and pitfalls 1. Endomedullary rod technique in severe destruction 2. Use of non CMC bridging plates 3. Fusion angle according to the needs of the patient Partial wirst fusion Trend: Replaced wrist arthroplasty Pearls and pitfalls 1. Generous indication instead of total wrist fusion 2. Stable fixation for early mobilisation 3. Reposition of the wrist Caput ulnae treatment Trebd: Sauvée-Kapandji procedure Pearls and pitfalls 1. More aesthetic results with Sauvée-Kapandji procedure instead of ulnar head resection 2. Easiest technique with canulated screw 3. More distal, 10 mm resection; no graft interposition MCP joint arhroplasty Trend: Much less interventions overall Pearls and pitfalls 1. Still Silicone implants preferable prebend shape; Role of the flexor tendons 2. Little evidence for effectivness of intrinsic transferin ulnar deviation 3. Tell the patients ulnar drift of fingers returns MCP joint fusion thumb Trend: A winner: The earlier the better Pearls and pitfalls: 1. Early intervention avoids secondary IP joint deformity 2. Rather fusion early than soft tissue procedures first 3. Avoid double fusion MP/ IP; consider IP joint arthroplasty PIP arthroplasty Trend: More generous indication in RA Pearls and pitfalls 1. The earlier the better the results 2. Silicone implants still golden standard 3. Two component implants in radial digits for stability Stop the biologicals Trend: Individual handling 1. Smaller interventions: leave biologicals 2. Bundle interventions 3. MTX/steroids as a temporary substitute.

S12-3

Perioperative trouble shooting in hip and knee surgeries for rheumatic diseases

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Conflict of interest: None

Rheumatoid arthritis (RA) is one of the major indications of total joint arthroplasty (TJA). Total hip (THA) or knee (TKA) arthroplasty improve functional ability of the patients by reconstructing a deteriorated joint. However, patients with RA may be more susceptible to complications following TJA such as surgical infections. Several meta-analyses showed significantly higher risk of complications relative to those with osteoarthritis. In the series of RA patients with TJA in Kyushu University and Kyushu medical center, the followings were major complications after THA and TKA. 1. Periprosthertic infection was not frequent, but deep infection occurred in several cases. 2. Periprosthertic fracture usually occurred intraoperatively but occasionally after weight bearing. 3. Dislocation following THA decreased with the large head diameter. Modern implant technology and surgical skill may reduce the complication rate these days, however, the importance of postoperative care of patients should be emphasized involving prophylactic antibiotic usage, coordinating care with the orthopedic surgeon and physical therapist, and to ensure the recommended rehabilitation program, and observation for any complications.

S12-4

Foot and ankle surgeries for the patients with rheumatoid arthritis in BIO-era

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Conflict of interest: None

Object: Biologic agents (BIO) drastically changed not only drug therapy but also the surgery for rheumatoid arthritis (RA) from starting to use biologics at 2003 in Japan. Previously, gold standard of the surgery for RA foot and ankle deformity was resection arthroplasty and ankle arthrodesis. Nowadays, joint preserving surgeries of MTP joint and total ankle arthroplasty (TAA) have spread for RA forefoot and ankle deformi-

ty instead of resection arthroplasty or arthrodesis of MTP joint and ankle joint. The aim of study is to investigate the rate and trend of forefoot surgeries including joint-preserving procedures and TAA for RA forefoot and ankle deformity in RA patients for fourteen years, as called BIO-era. Methods: We surveyed the number and rate of orthopaedic surgeries including forefoot and ankle surgeries in RA treatment with BIO or Non-BIO in the fourteen years in our institutes. Results: We had 29,175 cases of orthopaedic surgeries, including 717 rheumatoid surgeries from 2003 to 2016. They contained 487 cases of total joint arthroplasties (TJA, 70%), including 320 TKA,113 THA, 23 TEA, 20 TAA, and 106 upper limb surgeries (15%), 42 forefoot and ankle surgeries (6%), 30 spine surgeries (4%). The numbers of rheumatoid surgeries were decreased compared to all orthopaedics surgeries in this fourteen years ($p<0.05$). The numbers of TAA, upper limb surgeries, forefoot and ankle surgeries, and spine surgeries for RA patients in 2010-2016 increased 2.0, 1.4, 1.3 and 1.3 times compared to them in 2003-2009, but TKA and THA was not changed. We had 386 RA patients treated by biologics agents and 109 rheumatoid surgeries in them from 2003, including 60 TJA (55%), 16 upper limb surgeries (17%), 16 forefoot and ankle surgeries (17%). In addition, the joint preserving surgeries for RA forefoot deformity and TAA trended to increase annually. Conclusion: The numbers of rheumatoid surgeries decreased year by year compared to all orthopaedic surgeries in our institutes. However rheumatoid surgeries for upper joint, and forefoot and ankle joint increase more in the RA patients of this BIO-era. They may regain the function of joints and improve the quality of life although we have many unmet needs yet such as optimal indications, preventing peri-operative complications and long-term results of them.

S12-5

Collaboration of multi-disciplinary team for the perioperative management in rheuma-orthopaedics

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Conflict of interest: None

The Rheumatism Foundation Hospital in Heinola, Finland, was from the early 1950's an important place for the development of rheuma-orthopaedics. The chief orthopaedist, late professor Vainio, had very good connections with Japanese colleagues. He believed in multi-disciplinary team work, which is still needed in perioperative management of patients with rheumatic diseases (RDs). In the old days in-patient times were long, which made multi-disciplinary collaboration easier. Today the treatment is organized so effectively that it may be challenging to implement the necessary team-work. However, we have to ensure that the operation will be safe for the patient and that it will give optimal benefit. The disease-modifying anti-rheumatic drugs (DMARDs) are so effective today, that early cases with RDs seldom need orthopaedic operations. Thus most of the operated patients are older than earlier and have a chronic disease with permanent changes in the joints and often also in other tissues. Several specialists co-work to evaluate the condition of the patient to ensure the safety of the operation. For example, patients with chronic RDs may have critical instability in the cervical spine, which has to be noticed before the operation, especially if intubation may be needed. Plain lateral view radiography during full flexion position is the most sensitive diagnostic method. MRI taken in supine position may miss the instability or it's severity. Multi-disciplinary collaboration aims to best possible outcome of the operation. The DMARD-treatment should be optimized before surgery, since active systemic inflammation may impair the result. Health professionals (nurses, physiotherapists etc) also inform the patient of the operation and how to prepare for it. Anesthesia team takes care of the safe pain management and homeostasis during and after surgery. Careful postoperative rehabilitation which sometimes includes occupational therapy ensures the optimal result of the operation.

S13-1

The value of RA Ultrasound algorithms in clinical decision making

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Conflict of interest: None

The validation and subsequent use of sensitive imaging modalities has been one of the most significant advances for rheumatology in the last few years. Ultrasound like MRI, can help in diagnosis, document damage, measure inflammation and also document extra-articular disease. Unlike MRI it is readily available and multiple joints can be scanned on multiple occasions, particularly convenient for the patient if done at a clinic visit. Algorithms have been developed to guide clinicians in management. Five algorithms have been described along the patient pathways[1], these are as follows: 1. Diagnosis of patients at risk of/ suspected RA 2. Confirmation of the diagnosis of ACR/EULAR positive patients 3. Assessment of a patients initial response to a DMARD 4. Assessment of a patients loss of response to a DMARD 5. Assessment of stable state/remission. It needs to be clarified that it is not necessary to perform ultrasound at all these time points for every individual. However, each time point can be important under specific circumstances. The indications for when ultrasound becomes more important are: 1. When synovitis is equivocal. 2. When assessment of response is equivocal. 3. Arguably, in all patients when a stable state is reached, (particularly the value of ultrasound finding and predicting response when therapy is reduced). **Reference:** D'Agostino MA, Terslev L, Wakefield R, Østergaard M, Balint P, Naredo E, Iagnocco A, Backhaus M, Grassi W, Emery P. Novel algorithms for the pragmatic use of ultrasound in the management of patients with rheumatoid arthritis: from diagnosis to remission. Ann Rheum Dis. 2016; 75:1902-1908.

S13-2

Usefulness of ultrasonography in differential diagnosis of rheumatoid arthritis

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Conflict of interest: None

The 2010 ACR/EULAR classification criteria for rheumatoid arthritis (RA) is often referred in clinical practice for the purpose of early diagnosis. Although it is helpful to predict chronic erosive inflammatory disease to be treated with methotrexate, physicians need to go through the lists of other forms of arthritis and conditions for confirming diagnosis. Ultrasonography (US) has been recognized to be able to detect synovitis more sensitively than clinical examination. It further enables to detect inflammation around the joints, disease-specific or characteristic findings, and subradiological bone change/structural damage, which is helpful for detecting early inflammatory arthritis and differential diagnosis. The use of US has now been spreading to other forms of arthritis such as spondyloarthritis including psoriatic arthritis, crystal-related arthropathy and osteoarthritis. US is non-invasive, easy to repeat evaluation even in multiple joints, and cost-effective and can provide additional information in proportion to the level of equipment and scanning technique complementary to conventional imaging modalities. The practical application of US, pitfalls and limitations to be determined in the presentation.

S13-3

Quantitative assessment for synovitis using joint ultrasonography in patients with rheumatoid arthritis

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Conflict of interest: None

In the rheumatoid arthritis (RA), rapid induction and maintenance of clinical remission are important. In recent, more efficient induction and more cost-benefit maintenance method for clinical remission are focussed on. For these purposes, many clinical studies are ongoing in diagnosis, therapeutic and assessment field of rheumatology. Joint ultrasonography has been shown to have clinical utility in diagnosis and assessment of RA. Joint ultrasonography could visualize active synovitis by detecting synovial hypertrophy and/or vascularization. Semi-quantitative 4 grade scoring is used for estimate the level of synovial hypertrophy and vascularization. This scoring is universal use and have high reliability, however

is a rough measure to detect sequential change in single joint. We established quantitative measurement for synovial vascularization in finger joint and studied pathophysiology of synovitis. To make better methodology for induction of clinical remission in RA, diagnosis and therapeutic monitoring play important role. We reported that undiagnosed patient with high level of synovial vascularization in finger joints finally lead to diagnosis of RA. This revealed that joint ultrasonography could have high usability for early diagnosis or confirmation of RA. In the aspect of therapeutic monitoring, we reported that changement in synovial vascularization in each finger joint correlated with structural deterioration. Quantitative measurement of synovial vascularization played major role in these studies. Detailed observation of synovitis revealed that synovial vascularization still showed positive in some joints in patients with RA who achieved and was maintaining clinical remission. Such joint with persistant of synovial vascularization despite the clinical remission is called as residual synovitis. Residual synovitis were not dependent on therapeutic regimen and had risk of structural deterioration. We also reported that joints with active synovitis lead to residual in the presence of osteitis. Some studies reported that patients with residual synovitis may have risk of easy relapse. Although further studies need to confirm the results, residual synovitis may be important factor and key in maintenance of clinical remission of RA. Quantitative measurement for synovitis using joint ultrasonography revealed pathophysiology of rheumatoid arthritis.

S13-4

The value of MRI in early detection and prognostication of rheumatoid arthritis

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Conflict of interest: None

Detection of joint inflammation and damage MRI allows assessment of all the structures involved in rheumatoid arthritis (RA), i.e. synovial membrane, intra- and extraarticular fluid collections, cartilage, bone, ligaments, tendons and tendon sheaths. MRI, histopathological and mini-arthroscopical signs of synovial inflammation are closely correlated. MRI bone marrow edema represents inflammatory infiltrates in the bone marrow, i.e osteitis, as demonstrated by comparison with histological samples obtained at surgery in RA patients. A high level of agreement for detection of bone erosions in RA wrists and MCP-joints between MRI and CT, the gold standard reference for detection of bone destruction, documents that MRI erosions represent true bone damage. Diagnosis of RA Follow-up studies of undifferentiated arthritis have documented an independent predictive value of MRI, in particular presence of bone marrow edema, in the diagnosis of RA. In the ACR/EULAR 2010 criteria for RA, classification as definite RA is based on presence of definite clinical synovitis in at least 1 joint, and achievement of a total score at least 6 from the individual scores in 4 domains. In the joint involvement domain, presence of MRI synovitis count, and this domain can provide up to 5 points of the 6 needed. Prognostication Several studies have demonstrated a predictive value of MRI pathology in wrist and/or MCP joints to radiographic progression. In particular bone marrow edema is established as a strong independent predictor of subsequent radiographic progression in early RA. Clinical trial data has confirmed this predictive value, and that early treatment-induced changes in bone marrow edema and synovitis also predict the rate of future radiographic progression. MRI findings, and changes therein, are related to key patient reported outcomes, such as HAQ, VAS pain and VAS patient global. In patients in clinical remission, MRI synovitis is found frequently in patients in clinical, and several studies have reported that baseline MRI is significantly related to subsequent progressive structural damage. These studies encourage further exploration of MRI for predicting the disease course and for evaluating disease status, including defining remission.

S13-5

Early diagnosis and therapeutic evaluation by MRI and US in RA

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Conflict of interest: None

We have previously reported clinical usefulness of MRI and US in RA. In this symposium, we will discuss the necessity of MRI and US in evaluation of early diagnosis and therapeutic response based on our research results. First, we have shown the usefulness of Gd-enhanced MRI of bilateral hands in early diagnosis. If patients have two or more of (1) MRI symmetric synovitis, (2) MRI bone marrow edema (osteitis) or bone erosion, and (3) positive of autoantibody (RF, ACPA), they highly likely progress to RA (Nagasaki-MRI criteria). Second, we have shown synovitis with power Doppler (PD) grade ≧2 by US is important for early diagnosis. Furthermore, diagnostic accuracy was improved by (1) PD grade ≧2 synovitis, or (2) combination of PD grade ≧1 synovitis and RF/ACPA positive (Nagasaki-US criteria). Thirdly, we have reported a good correlation between severity of MRI bone marrow edema and that of PDUS synovitis. In evaluation of therapeutic response, we have been promoting the US prospective cohort study for patients introduced biologic or targeted synthesis DMARDs in multiple rheumatic centers in Kyushu region. In this study, short disease duration, no previous biologic DMARDs and low PD activity at baseline were factors predicting PD remission at 6 months after introduction of treatment. In patients switched from first TNF inhibitors, US outcome was better in patients treated by non-TNF inhibitors than in patients treated by alternate TNF inhibitors. In our early arthritis cohort study, MRI bone marrow edema was associated with progression of joint destruction after treatment. In evaluation of remission, US and MRI are also useful for detection of subclinical inflammation, and subclinical inflammation is a risk factor for progression of joint destruction. In addition, we have reported that the presence of bone erosion by US was a factor predicting relapse after discontinuation of biologic DMARDs.

S14-1

Medical insurance system in private clinic especially in judged position

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Conflict of interest: None

(Object) In rheumatic clinics using biological products inevitably the average recipe score has to be high. In this lecture I will present about the counterplans against individual instruction. (Individual instruction) In each prefecture in the case of recipe score exceed in average score, the top 8% were instructed as group individual instruction and top 4% instructed as individual instruction. (Individual instruction in my clinic) 1. Special medical treatment guidance management fee. In private clinic, in the case of treat to chronic gastritis, hypertension and diabetes mellitus so on, the clinic can get the instruction fee from the patients. Although when the clinic get the fee, the clinic must list the contents that instructed in the chart. If the clinic not list the instructed evidence in the chart, such clinic must return the money to government. 2. Facility criterion and chemotherapy fee. In the case of chemotherapy in private clinic, the clinic can get chemotherapy fee from the patients (30% from patients and 70% from government) when fulfilled the term. 11 years ago, my clinic submission the official paper to government. Although government once agreed this official paper, the government pointed out the papers deficiency passed after 11 years. I returned the chemotherapy sum for 5 years to the government. (Counterplans against individual instruction.) Once the clinic has instructed by government, the clinic must decreased the average recipe score compared with followed year by decrease the examination and expensive drugs. (Conclusions) In private clinic, truly honest examination and treatment are the best way to avoid individual instruction.

S14-2

Insurance treatment of RA treatment which is often assessed recently

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Conflict of interest: None

In Fiscal Year (FY) 2017, general account expenditures and tax revenues in Japan are estimated to be 97.8 and 57.3 trillion yen, respectively; the public debt and government bonds make up for this difference. On the other hand, social security benefits (pension, medical care, welfare, and others) are estimated to be 120.4 trillion yen, accounting for almost 30% of the national income of 404.2 trillion yen. As per the Basic Policy on Economic and Fiscal Management and Reform (2015), the government aims to improve social security benefits by FY 2020, given that the growth in social security expenditures equals the increasing expenditures related to population aging in Japan. Preventing increase in social security benefits including pension and nursing care is difficult; thus, social security benefits in medical care are expected to greatly decrease. Concerning gains from social security benefits, the medical insurance claims (receipts) are expected to be examined and assessed more carefully by social and national health insurance providers. In clinical practice, physicians usually treat rheumatoid arthritis (RA) with monitoring their treatment response and adverse drug reactions to improve patients' quality of life. Relatively expensive drugs and various examinations are used to treat RA compared to other orthopedic diseases and general internal medical conditions. Thus, medical insurance claims for RA treatment tend to stand out and are assessed frequently by insurers due to their lack of specialized knowledge for RA, even if the claims are validated by review committees. I will mention precautions and future measures against the issues specified above through specific cases recently assessed by insurers, mainly of medical management fee, home healthcare (self-injection), examination, diagnostic imaging, and rehabilitation field. Standards of insurance reviews differ according to area and type of insurance (social or national insurance) and trends in RA treatment in each medical institution, although the government aims to reduce these differences.

S14-3

Management of rheumatoid arthritis without biologics

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Conflict of interest: Yes

The progress in the management of rheumatoid arthritis has been remarkable in the past 20 years in developed countries. The factors which contributed to the improvement are including advancement of diagnostic laboratory tests such as anti-cyclic citrullinated peptide antibodies, introductions of new imaging modalities such as musculoskeltal ultrasound, and articular MRI, successful advocation of Treat-to-Target concept, and as a matter of course the development of new therapeutic medication such as biologics and JAK inhibitors. Nevertheless, the most important factor is believed to be emerge of biologics but fair control of rheumatoid arthitis is achievable even without usage of biologics if the appropriate early diagnosis and the proper initiation of conventional anti-rheumatic drugs are instituted.

S14-4

Multicenter clinical study on a longer interval treatment of rheumatoid arthritis with biological disease-modifying anti-rheumatic drugs

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Conflict of interest: None

(Objective) Biological disease-modifying anti-rheumatic drugs (bDMARDs) have improved the outcome from therapy for patients with rheumatoid arthritis (RA). A multicenter clinical study on a longer interval treatment with three bDMARDs, Golimumab (GOL), which is one of TNF inhibitors, and two of non-TNF inhibitor, Tocilizumab (TCZ) and Abatacept (ABT) was investigated. **(Methods)** Patients, who were maintained at low disease activity by DAS28 score for more than 3 months treated with GLM, TCZ, ABT, were enrolled. These selected patients were treated with these drugs with 1.5 fold longer interval of standard schedule for 60 weeks, and the rate of patients, who preserved low disease activity were determined. The patients who were not tolerated these drugs because of the side effects or adverse events, were withdrawn from this study. **(Results)** One hundred thirty-one patients treated with GLM, 149 with ABT (S.C. 61, I.V. 88) and 299 with TCZ (S.C. 87, I.V. 212) were enrolled. Among these, 57 patients treated with GLM (43%), 40 with ABT (26%, S.C 18, I.V 22), 93 with TCZ (31%, S.C 21, I.V 72) were successfully maintained at low disease activity with this 1.5 folds longer interval treatment, respectively. The age of patients in ABT group was 73.5±10.6, and significantly higher than those in TCZ (58.8±13.9) and GOL (58.1±14.7) groups. At 60 weeks, DAS28 in ABT group was 3.1±0.5, and significantly higher than those in TCZ (2.6±0.7) and GLM (2.6±0.7) groups. On the other hand, CDAI in GOL was 6.6±3.4, and was significantly higher than those in TCZ (4.4±2.6) or ABT (4.6±2.3) groups. Accordingly, successive rate at 60th week in ABT group was 52% and lower than those in TCZ (69%) or in GOL (73%) groups. **(Discussion)** This study clarified that TCZ and GLM had higher successive rate than ABT for maintaining low disease activity for 60 weeks by longer interval treatment. This effectiveness might relate to the high therapeutic efficacy of TCZ and low antigenicity of GOL.

S14-5

The landscape of biosimilar DMARDs for Japanese patients with rheumatoid arthritis

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Conflict of interest: None

In the "Basic Policy on Economic and Fiscal Management and Reform (Stoutly-Built Policy) 2017" and "Future Investment Strategy 2017," Prime Minister Abe administration expressed the intention to reform social security. They stated that measures for promoting generic drug use would be devised to elevate the share of generic drugs to 80% by September 2020, by making use of the planned simultaneous amendment of prices of healthcare and daily life care services in fiscal year 2018. Concerning high-priced biological DMARDs products, the policy extended support for the research and development of biosimilar DMARDs to double the number of biosimilars available. When dealing with issues of high medical care expenses and large amount of billing under the health insurance system related to RA management, it is desirable not to attempt to resolve medico-economic issues related to biological DMARDs through achieving bio-free status. Instead, we should create an atmosphere where biological DMARDs with reduced prices can be used easily and administered in a stable and continuous manner at sufficient dose levels. To materialize this plan, the major step will be to reduce the price of forerunner biological DMARD products or promote the use of biosimilar DMARD whose price is 70% of forerunner products. Unlike the situation in the United States, in Japan, although price reduction of forerunner products has already been partially implemented in a stepwise manner, it has not yet produced sufficient effects that we can perceive in clinical practice. Biosimilar DMARD to infliximab are the only type of biosimilar products available for use in Japan, and their extent of spread is still insufficient. Only 44 cases have been treated with biosimilar DMARD compared to 362 cases treated with the original infliximab according to the latest cross-sectional survey conducted within the framework of multicenter database study program on RA management in Japan called "NinJa 2016," of which I am a contributing member. It is incorrect to say that the future of biosimilar DMARD in Japan is not bright. Besides biosimilar infliximab in the form of preparations for drip infusion in medical facilities, global development of biosimilar DMARD to etanercept and adalimumab is underway, and such biosimilar DMARD have already been approved in some countries. These biosimilar DMARD take the form of preparations for subcutaneous injection, allowing self-injection by patients. Moreover, these biosimilar DMARD can be supplied through pharmacies outside hospitals, thereby facilitating their widespread use.

S15-1

Treatment for rheumatoid arthritis and osteoporosis in aging population: problems those are unsolvable by biologics or MTX

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Conflict of interest: None

Treat to target is currently recommended for RA treatment, and it is standardized to target remission or low disease activity by active use of MTX and biologics. However, elderly people often have decreased physical function or complications, and treatment is not always possible as recommended. None have shown clear guidelines for elderly patients in the EULAR recommendation etc., although it is proposed to choose treatment according to complications and the condition of individual patients. In the elderly, there are many cases where joint destruction has already progressed due to long-term morbidity, and there is concern that the ADL and QOL will decline. The risk of fracture also increases in elderly RA patients, which is a problem affecting the decline of ADL and QOL, and the life prognosis. Indeed, it is reported that the incidence of fractures has not decreased, even if the disease activity of RA improves. Recent reports suggested that biological products could not significantly inhibit fracture and sufficient osteoporosis treatment is not performed in RA patients. Therefore, there is a problem that can not be solved by biologics or MTX for elderly RA patients, and it is necessary to respond separately. Orthopedic surgery is useful for reconstruction of destroyed joints, and there are cases who improve disease activity after surgery. In addition to RA treatment, aggressive intervention for osteoporosis is necessary for fracture prevention. In this symposium, we discuss problems and solutions that can not be solved by biologics and MTX for elderly RA patients.

S15-2

Treat-to-target strategy for elderly rheumatoid arthritis and impact of osteoporosis on treatment outcomes: a prospective cohort study (CRANE)

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Conflict of interest: None

The prevalence rate of elderly RA increases in line with the increasing life expectancy. The age of onset also shifted to elderly side. Management of elderly RA is a common and important point in clinical practice for rheumatologists. The aims of treatment for RA are clarified in principles of treat-to target strategy, however treatment goals may be verify among elderly patients, because it can be changed with physical function, mental status, and social status. Working ability is one of most important goals for elderly RA and also non-frail status should be goal of elderly RA, since it is associated with health expectancy. Established RA is quite different from early RA in terms of clinical features, treatment response, and comorbidities. This is same as elderly RA. Decision of goals and treatment strategy is corporate with such a patient status. Comorbidities of long-standing elderly RA are complex in various factors including disease activity, drug use, and ageing (arteriosclerosis, sarcopenia, osteoporosis, dementia, physiological dysfunction, and immunosenescence) and make it difficult to treat elderly RA. Our previous prospective study (CRANE) showed that achieving low disease activity (LDA) and structural and functional remission were realistic goals for patients with elderly-onset RA. In this study, the treatment was scheduled in advance to achieve LDA, and 32% of the patients were receiving biological DMARDs at week 52. Biological DMARDs may have a major role in the treat-to-target strategy of elderly-onset RA, because a high dose of MTX was intolerable, and corticosteroid use was associated with serious infection. On the other hands, clinically relevant radiographic progression (CRRP) was observed at 40 % of the patients, and anti-CCP antibody positive, high disease activity, presence of bone erosion are associated with CRRP. Interestingly, no response by EULAR response criteria and non-achievement of LDA at week 24 were both strongly associated with CRRP. Rapid improvement of disease activity may be prioritized in the treatment strategy of elderly-onset RA. In this symposium, I will also present 3 yeas outcomes of the treatment targeting LDA in CRANE, associated adverse events, and impact of adverse events including osteoporosis on treatment outcomes.

S15-3

Treatment for elderly patients with rheumatoid arthritis

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Conflict of interest: Yes

Recently, there are many elderly RA patients that rheumatologists have to manage. National Database of Rheumatic Disease in Japan (NinJa) showed rates of patients with 75 years old or older were 10.9%,15.8% and 20.6% in 2005, 2010 and 2015, respectively. We have to perform T2T practice for elderly patients with RA as same as non-elderly patients. However, there are many problems and difficulties of management for elderly patients. Renal dysfunction is considered as the one of most important problems. The renal function gradually deteriorates with aging. It was reported that RA patients were ease to have chronic kidney disease than non-RA patients. It is difficult to use MTX and to perform appropriate T2T practice for RA patients with renal dysfunction. Many data showed an advanced age was a risk factor of infection during biological DMARDs (bDMARDs) therapies. In addition, the elderly patients often has respiratory complications. So we have to take care of treatment with bDMARDs for elderly patients. NinJa indicated that the rates of achievement to remission decreased with age. However, there was no difference of swelling joint count between elderly and non-elderly patients. VAS tends to be higher in elderly patients than non-elderly patients, so the disease activity may be evaluated more badly. We must assess each component of composite measure to practice appropriate treatment for elderly RA patients. Osteoporosis is serious complication. It was reported that the RA patient with the past of the vertebral fracture showed significantly higher HAQ-DI than the patient without the past history. Rheumatologists have to practice dual T2T aiming at suppression of disease activity and inhibition of bone density loss in order to maintain ADL of elderly RA patients. It is necessary to make up treatment target and a treatment strategy for elderly patients with RA.

S15-4

Comprehensive bone care in rheumatoid arthritis patients

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Conflict of interest: Yes

Treatment of rheumatoid arthritis (RA) has been dramatically changed by biological agents and methotrexate (MTX). It became a realistic goal to achieve remission and prevent joint destruction. According to the NinJa database, the number of patients who achieved remission or low disease activity has increased year by year. However, the rate of hospitalization due to the osteoporotic issue has not changed. It seemed that we could only focus on the disease activity, but not on bone. This casts a light on that we should care about bone since stronger bone leads to less joint destruction. In elder RA patients, we tend to avoid to use biologics and MTX because of chronic kidney disease or other comorbidities. We struggle to control them, and sometimes use glucocorticoid instead of biologics or MTX. RA itself and glucocorticoid are known as risk factors for osteoporosis. Now we know that vitamin D deficiency is common in RA patients. We also know that RA patients may not load on their bone because of pain. We should consider all kind of issue about bone in RA patients and provide the comprehensive bone care.

S15-5

Osteoporosis in elderly Japanese patients with rheumatoid arthritis; results from the IORRA cohort study

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Conflict of interest: None

Utilizing data from our Institute of Rheumatology Rheumatoid Arthritis (IORRA) cohort study, we reported osteoporosis in Japanese patients with rheumatoid arthritis (RA). Despite improvements in disease activity and functional disability, the non-vertebral fracture incidence exhibited no apparent change in our patients with RA. The incidence of non-vertebral fractures increased in women aged >40 years, whereas similar change was not observed in men. Thus, osteoporosis treatment and non-vertebral fracture prevention remain important regardless of the disease control in patients with RA. Rates of clinical vertebral and hip fractures increased, while those of rib and foot fractures decreased with increasing age. Incidence of falls, as causes of non-vertebral fractures, also increased in older age groups. Falls were the primary cause of upper extremity and lower extremity fractures. Older age was one of the significant risk factors of vertebral, hip, distal radius, and upper humerus fractures. Older age was significantly associated history of fall. The prevalence of vitamin D deficiency were 70% in women and 50% in men among the patients >70 years old. The serum vitamin D levels were not significantly associated with history of falls. Among the patients >70 years old, 50% and 10% reported having had dental treatments and tooth extractions within the past 6 months, respectively. The prevalence of osteonecrosis of the jaw (ONJ) was 0.26% among female RA patients >65 years of age. Among the RA patients, 20% and 30% were diagnosed with periodontitis by dentists during the previous 6 months and past (submitted).

S15-6

Pathophysiology and therapy of osteoporosis and rheumatic diseases in aged patients

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Conflict of interest: None

As Japanese population has been aging, patients with rheumatic disease are also rapidly aging, that is an urgent problem. The common age of rheumatic diseases was from thirties to forties so far. However, the number of elderly patients with rheumatoid arthritis (RA) was increased and the duration of therapy was prolonged as the prognosis was improved by introducing newly developed drugs. Besides, the onset age of RA is becoming slightly older than the age reported previously. The rheumatoid arthritis of which onset is over 60 years old is called elderly-onset rheumatoid arthritis (EORA). The percentage of steroid use is higher in EORA than in a conventional type of RA, as EORA needs to be medicated more carefully On the other hand, osteoporosis is a common disease in the aged society. Usage of corticosteroid, a therapeutic medication for RA, increases the risk of osteoporosis. Osteoporosis and RA correlate with each other through the medium of osteoclast that is a main character in both of osteoporosis and RA. Patients with RA or osteoporosis, which directly influence bone in aged people, will be more and more increased from now on. Different way of therapeutic approaches is necessary between younger patients and elderly patients, because the elder patitens are at high risk for fall and whose disease activity is not under the control. Denosumab, approved recently, is expected to effective to both RA and osteoporosis. The high-resolution peripheral quantitative CT (HR-pQCT) is a new modality that was developed to analyze peripheral bone structure. HR-pQCT has been revealing changes in microstructure of cortical and trabecular bone due to aging and bone diseases. In this lecture pathophysiology in elderly people will be also discussed from the view point of bone microstructure.

S16-1

Dynamic analysis of bone destruction using intravital imaging techniques

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Conflict of interest: Yes

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by synovial joint inflammation and progressive bone destruction. Arthritic bone destruction is considered to be mediated mainly by enhanced activation of osteoclasts at inflammatory sites. To prevent RA-associated bone destruction, it is important to understand the cellular dynamics in inflammatory bone destruction *in vivo*. Biologic DMARDs, such as monoclonal antibodies against the anti-IL-6 receptor and anti-TNFα, and CTLA4-Ig, have recently been developed to treat RA. Despite differences in the molecular targets of these drugs, they strongly inhibit bone erosion and synovitis even in patients with high-level clinical disease. Recent basic studies have revealed that these biologics exert direct effects on osteoclast differentiation and function, although little is known about the differences in mode of action. We originally established an advanced imaging system to visualize living bone tissues using intravital imaging techniques. By means of this system, we revealed the *in vivo* behavior of bone-resorbing osteoclasts and their precursors. We found that the migration of osteoclast precursors was controlled by the blood-enriched lipid mediator sphingosine-1-phosphate. We also could grasp the real time-course of osteoclastic bone resorption which was finely regulated by cell-cell contact with bone-forming osteoblasts. Furthermore, intravital imaging revealed that various biologic DMARDs acted at specific therapeutic points during bone destruction, with different efficacies. In this symposium, we show the latest data, and also discuss the further application of intravital bone and joint imaging.

S16-2

Development of Diagnostic Techniques for Early Rheumatoid Arthritis Using Positron Emission Tomography

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Conflict of interest: None

Joint destruction in rheumatoid arthritis (RA) induces not only a pain but has a major influence on the functional prognosis. Furthermore, its social influence is large in terms of medical economics. In RA treatment, administration of a nonsteroidal anti-inflammatory drug that controls pain and inflammation was reported to introduce pain relief in patients, but progress of joint destruction cannot be suppressed. On the other hand, various anti-rheumatic drugs to prevent the progress of joint destruction have been developed and contribute greatly to improve the functional prognosis of patients. Dramatic advances in RA research have revealed that joint destruction in RA rapidly progresses in two or three years after onset. As a result, world's rheumatology-related associations (ACR, EULAR, and JCR) have revised treatment guidelines and recommended early diagnosis and treatment intervention. So, how should we diagnose early stage of RA? It has long been used for plain X-rays (XP) for diagnose of RA. There is no doubt that XP is still important for the evaluation of progress of bone destruction and joint space narrowing. However, it has the disadvantage that XP has low detection sensitivity of bone erosion and inflammatory lesions in early RA cannot be evaluated. On the other hand, ultrasonic and MRI may be suitable for evaluation of joints which are difficult to judge by palpation and evaluation of subclinical synovitis of patients in clinical remission. However, the symptoms of RA involve various biochemical changes such as infiltration of inflammatory cells into synovium prior to morphological change. Positron Emission Tomog-

raphy (PET) is the unique imaging device capable of detecting in biochemical changes with high sensitivity. Therefore, several researchers reported that PET is useful for early diagnosis of RA. In this symposium, we will report the current status of imaging researches in the RA field and our PET imaging research on RA.

S16-3

The association of recent imaging modalities and molecular pathogenesis of rheumatoid arthritis

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Conflict of interest: None

MRI and ultrasonography (US) in RA are useful modalities that can directly visualize joint inflammation and they have been shown to improve discriminative sensitivity over that of traditional X-ray regarding structural damage. The usefulness of MRI and US were well validated, and it is promising to be valuable in many clinical studies. On another front, cytokines, including TNF-α, IL-1 and IL-6, play an important role in the pathogenesis of RA. However, the relationship between active inflammation and structural damage which detected recent imaging modalities and cytokines is still unclear. We assessed structural damage progression detected by MRI associated with pre-treatment plasma cytokines in newly diagnosed RA. Progression of bone erosion were observed more frequently in MRI than in X-rays (erosion, 52% *vs* 26%, $P < 0.001$). Baseline IL-6 levels and seropositivity were independent factors for MRI erosion progression. Baseline IL-6 level of 7.6 pg/ml for predicting erosion progression during 1 year, with an area under the curve of 0.82; higher IL-6 levels resulted in more erosion progression. Baseline low IL-6 was also an independent predictor for MRI erosion repair. Next, we studied to determine whether US inflammatory findings including synovial hypertrophy, vascularity, and echogenicity reflect local joint pathophysiology. Synovial echogenicity was significantly higher in treated RA patients. Quantitative vascular (power Doppler) area and echogenicity were significantly associated with synovial fluid (SF) IL-6 and VEGF ($p < 0.05$), although synovial tissue (grey scale) area did not correlate with any SF cytokines in the treated RA group. Histopathological analysis also revealed that treated hypoechoic RA synovium represented marked infiltration of lymphocytes and hypervascularity. Our studies demonstrated that MRI and US not only visualize the joint inflammation and destruction but also reveal the pathogenesis of RA via local and systemic cytokine levels.

S16-4

Imaging analysis of rheumatoid arthritis by HR-pQCT

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Conflict of interest: None

HR-pQCT is a high resolution CT dedicated to human extremities with a voxel size of 0.06mm. It is installed in only three hospitals in Japan so far. Measurement parameters of HR-pQCT are bone mineral density (BMD), cortical bone microstructure (cortical thickness, porosity), and trabecular bone microstructure (trabecular thickness, number, separation). Although HR-pQCT has been mainly used for the research in osteoporosis, it is applied to the research in rheumatoid arthritis (RA) in recent years. It is useful in two aspects: evaluation of osteoporosis induced by RA and quantification of RA joint destruction (erosion, joint space narrowing, periarticular osteoporosis, osteophyte). It is expected to evaluate the efficacy of RA drugs against bone destruction more precisely than conventional assessments.

S16-5

Imaging-based strategy for dose-reduction/withdrawal of biologics

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Conflict of interest: Yes

Although the clinical outcomes of rheumatoid arthritis (RA) have substantially improved since biologics became available in practice, its cost and infection risk have been a great issue. Therefore, many studies have been performed on the dose reduction/withdrawal of biologics and the official guidelines/recommendations began to mention the dose reduction of biologics. On the other hand, the accuracy of the dose reduction/cessation strategies based on clinical composite measures has been shown to be limited. Musculoskeletal ultrasound directly visualizes synovitis, which is the central pathology of RA, and determines the severity of inflammation more accurately than does clinical assessment. Recently, ARCTIC Trial demonstrated that the addition of ultrasound information does not improve the short term clinical outcome in obviously active RA patients (Haavardsholm EA, et al. BMJ 2016), suggesting that the benefit of ultrasound can be limited to RA at lower disease activity. Our 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). Although this is currently under scrutiny in a large-scale multicenter trial, our data suggest that achieving “deep remission”, which can be determined only by highly sensitive imaging modalities, is necessary for successful dose reduction/withdraw of biologics without worsening the clinical outcome.

S17-1

Livelihood support with rheumatoid arthritis patients -Inter-professional collaboration perspective of the occupational therapist-

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Conflict of interest: None

The purpose of occupational therapy for patients with rheumatoid arthritis (RA) is to self-support and improvement of activities of daily living (ADL) and instrumental activities of daily living (IADL). To support their life as their wishes, it is important for occupational therapy intervention to have improved the quality of movement, reduce the pain and burden of joints. In this way, we aim to improve long term health-related quality of life to the maximum, which is one of principles of T2T (Treat to Target). It is important to livelihood support RA patients by inter-professional collaboration. For example, occupational therapists (OT) select self-help devices in cooperation with nurses for RA patients with the problem of the feet, and they select footwears for RA patients to reduce their pain in walking in cooperation with physical therapists and prosthetist and orthotists. In addition, we select sprints in cooperation with rheumatologists, nurses and pharmacists. Using these sprints, RA patients with deformity of fingers can self-inject biological agents or osteoporosis drugs more easily. Due to biological agents, RA patients could be better controlled disease activities, and they could keep high the ADL /IADL abilities. Meanwhile, overuse and misuse, which are induced by an increasing the overall activity, or change of family roles and social roles which depending on the life events are burden to their joints. Even if the clinical remission has been obtained, symptoms may remain in small joints such as fingers. It has never changed the necessity of patient education joint protection and using sprints temporarily. Furthermore, the elderly patients who need nursing care suffer from RA for a long time, and they have a history of joint surgery and progressed joint deformity, and their ADL/IADL abilities will further decline over time. It is necessary to share information about RA with local staff for maintenance of physical functions, and fall prevention.

S17-2

The role of the nurse in the team medical care for rheumatoid arthritis -Aiming an improvement of the patient satisfaction-

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Conflict of interest: None

In recent years there have been significant advances in the treatments for rheumatoid arthritis (RA) by the spread of methotrexate and biologic disease-modifying antirheumatic drugs (bDMARDs) therefore patient satisfaction for the treatment has improved. As reported in JCR 2016 the ratios of patient satisfaction increased from 33% before bDMARDs to 92% after bDMARDs in our hospital however it was revealed that about half of RA patients were worried about side effects of the medicine and/or large amount of medical expenses. It is difficult to deal with these physical, mental and social problems only by the doctors so the collaborative medical care with many professionals so called the team medical care is required. Serious complications sometimes develop in RA patients. Because we experienced several cases of severe complication we reviewed our methods of the patient instruction and made stronger cooperation with other clinical departments especially with emergency and respiratory medicine. Besides it is essential to cooperate with the pharmacists and the social workers etc. Such a cooperation will raise the patient satisfaction much more. To achieve this, we continuously held cross organizational conferences and we gave lectures in the societies and meetings. In this activity a nurse is the most familiar person to the patients and their family. On this account the nurse is regarded as key person of the team medical care. And the nurse has to respond to extremely high needs of not only the patients but also the various medical stuffs. To accomplish this role, the nurse must understand physical and mental pain of patients, learn knowledge to cope quickly without overlooking the change of patient's condition and acquire the skills such as the self-injection. In this way the nurses can contribute to further improvement of the patient satisfaction in RA treatment while snuggling up to the patients and their family.

S17-3

Pharmacist's involvement in patients with rheumatism at general hospital

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Conflict of interest: None

According to the Paper on Rheumatism 2015, it is reported that about 40% of patients who are prescribed 4 to 6 drugs for treatment of rheumatoid arthritis (RA) account for 40%. Furthermore, there are many elderly people with RA patients, and many cases are taking internal medicine in addition to RA treatment medicines due to comorbidities. The average number of oral dosage types in our hospitalized RA patient (July 2014 - April 2016) is 8.8, and about 25% of patients are taking 11 or more drugs. In this report, we will report on patient taking medicine and taking medication situation, medication status and medications, medication complaints and practical consultation. Many patients are hospitalized for surgery purpose and many referral patients from other hospitals. It is difficult for such patients to change RA medication during hospitalization. However, for internal medicines other than RA remedy drugs, it is considered that medicinal intervention by offering information such as proposal of weight loss / withdrawal, change of dosage form from interview with patient and examination value is possible. Indeed, it is often a case that patients are consulted for drug reductions, and it is considered a great merit that the hospital charge pharmacist can deal with it during hospitalization. Treatment of RA has undergone significant changes in recent years, and options such as biologics and molecular targeted therapeutic agents have increased in addition to conventional antirheumatic drugs. Among these therapeutic agents, many medications such as MTX and biological preparations, patient education and periodic monitoring are very important. However, pharmacists confirm whether drugs used by RA patients are inconvenient not only for RA remedies, but also for other medicines, or for incorrect medications, and to share in many occupations We believe that it will contribute to improving the adherence of the whole medicine including RA remedy.

S17-4

A multidisciplinary team approach to improve RA patient satisfaction from a viewpoint of rehabilitation

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Conflict of interest: None

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 the standard RA pharmacotherapies with methotrexate and biologic agents, followed by newly available tsDMARDs, enable most of the patients with RA to reach the complete remission as long as they have neither complications nor financial difficulties. However, patients with advanced RA have been still suffering from disabilities caused before the commencement of therapy with such aggressive pharmacotherapies. Therefore, a multidisciplinary team approach to RA based on patient education and self-care and composed with four main therapies including pharmacotherapies, orthopedic surgeries, care, and rehabilitation, is demanded to achieve the goal of remission in the total management of RA. Rehabilitation of RA should be performed not only by therapists including physical therapists, occupational therapists, and speech therapists, but also rheumatologists, nurses, prosthetists, dental hygienists, medical social workers, pharmaceutical chemists, and dieticians in a share or collaboration in response to individual disease activities and disabilities. Meanwhile, the subjects of rehabilitation of RA has transferred from social rehabilitation for heavily disabled patients to the education for less disabled or healthy patients. In other words, patients of RA are encouraged to switch their rehabilitation in hospital supported by health insurance to self-supported home exercises for healthy patients, or visited or attending rehabilitation supported by care insurance for disabled patients. In the presentation of this symposium, current rehabilitation for patients with RA including joint protection education, daily exercise program, and foot orthoses will be illustrated and discussed from the viewpoint of improving patient satisfaction.

S17-5

Usefulness of Patients-Reported Outcomes in Rheumatoid Arthritis

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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 change and better outcomes. Biologics are effective, but biological therapy can have a high cost and significant adverse effects associated with long-term use. We reported that positive Power Doppler signal detected by ultrasound (US) was associated with joint destruction, even in RA patients with clinical remission. US improves many aspects of RA diagnosis and management in daily clinical practice. However, no consensus has been reached as to the optimal approach for the management in RA. Recently, patient reported outcomes (PROs) have become increasingly important in the evaluation of RA. Quantifiable measures of PROs provides the physician with quantifiable information of subjective symptoms experienced by patients, thus helping us to give better care to our patients with RA. A multidisciplinary team approach plays a valuable role to achieve higher patient satisfaction in RA.

S17-6

Efficacy of collaborations for rheumatoid arthritis treatments with paramedical staff and physicians in nearby clinics

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Conflict of interest: None

To prescribe effective and safe treatments for our rheumatoid arthritis (RA) patients, we conducted a few trials shown below. "Efficacy of educating visiting pharmacists in RA drug administration to improve adherence to treatment regimens" Patients may not adhere well to RA treatment and may understand little about biological agents. This study evaluated an intervention educating visiting pharmacists regarding administration of oral and injectable RA medications for patients with poor adherence to treatment regimens. In total, 19 patients did not experience changes in their treatment, including dosage or intervals between drug administration before and after pharmacist visit. The mean values ± SD of disease activity score (DAS) 28-erythrocyte sedimentation rate (ESR), simplified disease activity index (SDAI), and clinical disease activity index (CDAI) before and after pharmacist visit showed improvements; they were 3.56 ± 1.46 and 3.12 ± 1.16 ($p = 0.084$), 7.99 ± 6.88 and 4.39 ± 3.47 ($p = 0.0176$), and 6.85 ± 5.74 and 3.90 ± 3.18 ($p = 0.0148$), respectively. Education regarding oral and injectable medications may be useful control RA activity and to avoid any adverse effects due to consumption of wrong medication. "Challenge of switching biologics' administration from the intravenous (i.v.) to the subcutaneous (s.c.) route" We tried to switch the mode of administration of tocilizumab and abatacept from i.v. to s.c. to save time and space of our hospital and reduce the burden of visits of RA patients themselves. But only half of the patients were able to switch to s.c. route. "Staff meetings at our hospital to share RA patient histories and treatment goals and to communicate with nearby medical clinics" We hold our monthly inter-institutional meetings on first Wednesday of every month to communicate with physicians in nearby clinics by sharing RA patient cases, which have been so fruitful that we recommend other institutions to follow our example and organize such events.

S17-7

Our Strategies in Comprehensive Care for Patients with Rheumatoid Arthritis - To Maximize Patients Benefits -

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Conflict of interest: None

There might be a high degree of regional variation in the strategies for comprehensive care in patients with rheumatoid arthritis (RA). Our team started working towards shared goals of total management of RA in 2011 when three orthopaedics specialized for RA participated in the existing team. Following visits of the advanced teams in the successful total management of RA, learn from the lectures of many RA teams delivering total management and the knowledges from literatures worked up our strategy into transdisciplinary team model for patients with RA. Rapid progress both in science and economy and rapid improvement of longevity in the elderly including aged patients with RA inevitably affects the goal and concept of RA treatment. We must aim not only for the improvement of recent activity of daily living but also for long-term normal living activity of over thirty or forty years. So we should have bird's eye view of the whole life of patients with RA and be aware of every problem such as the remaining disease activity of RA, damaged function of joint, the loss of physical activity, the subsequent social handicap, the care for the reproductive-age female population, unmet needs for the child-rearing by physically handicapped patients, immunocompromised events including pneumonia and infection of foot, long-lasting economical burden, socio-psychological problems, age and disuse related sarcopenia, frequently overlooked insufficiency fracture, and malnutrition. Whenever the each problem arise, we should cope with them to maximize patients benefits with expertise in any field. To keep up with developments in their field, we must be lifelong learner and master new skills in all fields. It is difficult, however, for static team. So team should not be static but be fluid in network of interconnected individuals working against each pathological condition or social problem occurred in patients with RA. This concept corresponds with cross-disciplinary teamwork that is "teaming" coined by Amy C. Edmondson. We consider the transdisciplinary team model Edmondson's teaming, then we work and learn together to incorporate transdisciplinary/cross-disciplinary teaming within an organizational setting.

S18-1

Advanced Genetics on Systemic Lupus Erythematosus

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Conflict of interest: None

Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder characterized by diverse clinical manifestations. Significant genetic contribution on the liability to SLE was well validated in twin studies since ~70% of the phenotypic variance of SLE was explained by genetics factors. For the last decade, large-scale, genome-wide association studies (GWAS) have efficiently scanned human disease genomes to identify the individual SLE loci in multiple ancestral populations, especially in Asian and European populations, bringing the SLE loci to ~100. The associations in majority of the SLE loci were accounted for by common variants with modest effect sizes that explained ~25% of heritability. A large fraction of genetic causes is still missing so that even more active collaborative works and challenging approaches are required to ensure a better detection power for genetic factors (including common low-risk variants and rare high-risk variants) and the epistatic interaction between causes. Along with the effort in the identification of SLE-associated loci, many research groups have actively investigated the potentially causal variants in the associated regions, SLE-relevant immune cell types and signal pathways based on GWAS results with other new omics data and public knowledge/omics databases using appropriate statistical methods. This talk will briefly summarize recent advances in our understanding of new SLE loci, some critical variants, population-specific association heterogeneity, and variant-highlighted biology in SLE development in recent genetic studies.

S18-2

Immunophenotyping in systemic lupus erythematosus

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Conflict of interest: Yes

Increasing evidence points to immunological heterogeneity in the pathogenesis of systemic lupus erythematosus (SLE). Indeed, targeted therapy for SLE showed considerable variability of efficacy. Therefore, it seems to be important to stratify the patients based on immunological heterogeneity in this disease. Flow cytometery is the powerful technology for proving cellular phenotype and function in the immune system by measuring multiple parameters on various individual cells. The data provide the following information: i) differentiation stage of lymphocytes such as naïve cells and effector memory cells, ii) differences in lineage or functional differences, and iii) activation status or involvement cellular signaling molecules in the pathological process. We have used an immunophenotyping approach to categorize patients with SLE into distinct subgroups by comprehensive 8-color flow cytometric analysis for human immune system termed "the Human Immunology Project" by NIH/FOCIS. Peripheral blood mononuclear cells from 143 patients with SLE and 49 healthy individuals were analyzed by flow cytometry to characterize circulating B cells, T cells and dendritic cells. The data were analyzed by use of principal component analysis. The cluster analysis subsequently revealed three distinct subgroups based on T cell heterogeneity, including a T cell-independent group, a T follicular helper (Tfh) cell-dominant group and a T regulatory cell-dominant group. The percentage of patients who were resistant to immunosuppressive treatment was highest among the Tfh cell-dominant group. Thus, this heterogeneity should be taken into consideration not only in basic research but also in patient selection in clinical trials for development of new drugs. The peripheral immunophenotyping might be useful in evaluating the pathogenesis and in determining the therapeutic target of each patient.

S18-3

Remission Induction by Biologics in Lupus: What Will it Take?

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Conflict of interest: Yes

Achievement of very low disease activity or remission are supreme objectives for lupus treatment. Recent data from clinical trials of three targeted biologics, anifrolumab, blisibimod and atacicept, suggest that these goals are attainable, and may additionally provide discriminatory endpoints for trials. What will it take to expand this treatment mission to more than a subset of lucky patients? In a disease as complex and heterogeneous as SLE, most targeted treatments are unlikely to help all patients, and, even in a group of likely responders, one dose may not be optimal for all. Identification of the role of type I interferons in SLE pathogenesis has allowed a very useful categorization of lupus patients to high and low interferon signatures. This distinction had helped in predicting discrimination between drug and placebo with anti-type I IFN therapies, and may become useful in predicting response to treatments that modulate interferon-dependent targets such as BLyS. However, this is not the only way to differentiate between meaningful subsets of lupus patients. In an ideal treatment development program, investigation of pathway-specific pharmacodynamic markers of response could help to define patients most likely to respond and provide guidance to adjust therapy in order to increase the chances of remission. Where a good pharmacodynamic response is found without clinical response, blood samples can then be interrogated for additional pathways that might need to be addressed in targeted polypharmacy. Although lupus is a complicated disorder and polypharmacy, which is often necessary, introduces an extreme degree of incongruity that defies advances in precision medicine, our current technology does make a *somewhat more precise* approach possible in our quest for remission.

S18-4

Long-term outcome of biopsy-proven lupus nephritis and novel insight of autoantibodies to erythropoietin receptor for prognosis

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Conflict of interest: None

A considerable diversity in prognosis is seen in Japanese systemic lupus erythematosus patients with biopsy-proven lupus nephritis (LN). We studied retrospectively 61 subjects with LGN (9 males, 52 females, mean age of 36 years old) who under- went renal biopsies and were followed from 1 to 531 months, with a mean of 188 months. Class IV was selected as the most significant risk factor for renal outcome. In addition, treatment including methylprednisolone pulse therapy was selected as a significant improving factor for renal outcome. In addition to immunosuppressants, apheresis therapy may be a good therapeutic tool for lupus nephritis patients with anti-phospholipid syndrome. We examined the clinical significance of autoantibodies to the erythropoietin receptor (EPOR), which we newly-identified, in patients with LN. Forty-six Japanese patients with SLE with LN who had undergone renal biopsy were enrolled in this study and followed for a mean of 83 months. Anti-EPOR antibodies using ELISA were detected in 18 (39%) of the 46 patients with SLE with anemia. Anti-EPOR antibodies were associated with low hemoglobin concentrations and reticulocytopenia. In addition, anti-EPOR antibodies were positively correlated with SLE disease activity. Further, anti-EPOR antibodies were associated with active lesions including cellular crescents in glomeruli. Serum levels of the antibodies as well as renal response to immunosuppressive treatment were significant risk factors for progression of renal dysfunction, providing the evidence that anti-EPOR antibodies may be a predictor for renal injury.

S18-5

Long Term Organ Damage in Lupus Patients

Ian N Bruce
The University of Manchester, UK

Conflict of interest: Yes

Mortality in SLE patients has improved a lot in the past 60 years and currently, the 10-year survival is reported to be >90% although this may have reached a plateau. Relative to the general population, the Standardise Mortality Ratio (SMR) associated with SLE has fallen from >10.0 in the 1970's to 2.5-3.5 in the new millennium. In addition to mortality, other key long-term outcomes have also been more widely studied in an attempt to further improve survival and quality of life. Such outcomes include overall damage. Damage increases over time in SLE cohorts and damage predicts both further damage and also mortality. In many studies, musculoskeletal, CNS and renal damage are the commonest systems that accrue damage. The frequency of individual damage items does however vary across the world. In international cohort studies, factors associated with a poorer prognosis in SLE include demographic characteristics e.g. older age, race/ethnicity and male gender. Lower socioeconomic status also adversely affects survival and risk of damage. Recent data has demonstrated that SLE factors such as persistently active disease, flares and renal involvement are also risk factors for damage and mortality. In addition glucocorticoid use has been noted to increase the risk of overall damage and may also predispose to specific complications such as osteonecrosis, cataracts, cardiovascular events and infections. In contrast, antimalarial drugs tend to mitigate the risk of a range of co-morbidities and overall damage. There is also some evidence that biologics may also help reduce damage accrual in SLE. In managing SLE, preventative strategies should therefore include addressing better disease control and managing individual risk factors such as hypertension and hyperlipidaemia. In addition, minimizing steroid use, optimising antimalarial drugs and recommending vaccinations, cancer screening and smoking cessation programmes and all important to improve long-term outcomes in SLE.

Special Symposium

SS1

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

Yuko Nagaya, Yusuke Miwa
Gender Equality Committee, Japan College of Rheumatology

Conflict of interest: None

In 2015, the Japanese House of Councilors 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 contextualized 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) explain how they took action for the gender equality.

SS2-1

Synovial pathogenesis - Teaching us new lessons!

Iain B McInnes
Institute of Infection, Immunity and Inflammation, University of Glasgow, UK

Conflict of interest: None

The advances in the last two decades in the treatment of rheumatoid arthritis (RA) have been remarkable - considerable unmet needs remain however reflected in incomplete responses in a majority of patients and still relatively low rates of remission. In this lectruie I will focus on the lessons that have been learned that inform the pathogenesis of RA from therapeutic interventions that are highly specific in terms of their molecular targeting. I will address synovial pathogenesis studies that particularly lay out a role for the myeloid lineages in defining the transition to, and maintenance of chronicity of synovitis in inflammatory arthritis. I will thereby look to how future therapeutics can be generated that could increase the maintenance of remission in patients.

SS2-2

Rheumatoid arthritis in 2028?

Gerd R Burmester
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Conflict of interest: None

Rheumatology is one of the most interesting disciplines in medicine, and barely any medical specialty has been so successful in the last two decades, especially with regard to integrating novel diagnostic and therapeutic tools. These along with the Treat to Target concept with the aim of remission employing constant monitoring and adaptation of treatment has dramatically changed the course of diseases such as rheumatoid arthritis (RA), psoriatic arthritis and ankylosing spondylitis. Many previously deadly diseases such as granulomatosis with polyangiitis and severe systemic lupus erythematosus can now be managed by modern immunosuppressive therapies. Nevertheless, there are tremendous medical needs, especially in osteoarthritis, fibromyalgia and systemic sclerosis where we frequently lack effective drug treatment. Also in inflammatory joint diseases such as RA, we increasingly see patients who have cycled through all available therapies and are still active. So - what does the future hold in 2018? There are many aspects of this question. First of course the dramatic new developments in systems biology with new technologies hoping to successfully utilize "big data" for complex biological systems which we encounter in the multifactorial rheumatic diseases. These approaches will allow insights into disease mechanisms and may lead to new diagnostic and therapeutic tools. Novel approaches of early diagnosis (even before clinically evident disease onset?) and immediate treatment will hopefully be routine in early arthritis clinics and will prevent damage of joints and bones. The combination of clinical signs, novel biomarkers and imaging techniques will make diagnosis much easier, and telemedicine approaches will allow access to specialists around the world. Of course, we will need a strong work force in order to make these advances available to our patients, and dedicated non-physician health professionals will be key here. Also the integration of the patients with shared decisions will be important. This lecture will address some of these items and hopefully raise enthusiasm for our exciting discipline.

SS3-1

Recent pharmaceutical regulatory framework to contribute early development of innovative medicines

Yasuhiro Araki
Pharmaceutical Evaluation and Licensing Division, Pharmaceutical Safety and Environment Health Bureau, Ministry of Health, Labour and Welfare, Tokyo, Japan

Conflict of interest: None

SS3-2

Current situations in New Drug Application of Rheumatism region

Hisashi Koike
Office of New Drug IV, Pharmaceuticals and Medical Devices Agency

Conflict of interest: None

SS3-3

Clinical study design and data analysis

Satoshi Morita
Department of Biomedical Statistics and Bioinformatics, Kyoto University Graduate School of Medicine

Conflict of interest: None

Basic statistical knowledge may be required to understand statistical methods. What clinical investigators need, however, is to appropriately interpret data/results observed in clinical trials, not statistical knowledge. This lecture will provide fundamental and useful statistical "skills" to design clinical trials and analyze data from them.

SS3-4

Interpretation of the safety profile of DMARDs in real world database

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Conflict of interest: Yes

Disease-Modifying Anti-Rheumatic-Drugs (DMARDs) play a central role for the management of the patients with rheumatoid arthritis. They not only reduce the inflammation/pain but can improve the morbidity related with joint destruction, altering the natural history of RA. Clinical trials have proven their safety profile, but only in the highly selective groups of the patients. Nowadays, the RA patients, as well as the general population, are getting older. In parallel, the older the patients get, the more frequent they have organ complications. It would not be surprising to see the discrepancy in the safety-profile between clinical trials and real-world management. The specialists should always offer the best treatment for any kind of RA patients, therefore, it is mandatory for us to watch real-world database to recognise the real safety-profile of DMARDs.

SS3-5

For the safe use of anti-rheumatic drugs: from an orthopaedic point of view

Sakae Tanaka
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Conflict of interest: Yes

Recent progress in the treatment strategy prominently improved the control of the disease activity of rheumatoid arthriti (RA). We recently reported using National Database of Rheumatic Disease in Japan (NinJa) that the number of major surgeries such as total knee arthroplasty and total hip arthroplasty in RA patients was markedly decreased during the last decade, while surgeries on small joints such as ankle, foot, wrist, and hand did not appear to differ. In addition, the number of osteoporosis-related surgeries, mainly fracture surgeries, have not changed, either. Recent treatment strategy of RA is early and aggressive immunosuppressive treatment, which necessarily leads to the increase in the number of infection. Swedish National Registry also demonstrated that the number of revision of total knee arthroplasty caused by infection is increased, which is considered to be related to immunosuppressive strategy. Recent studies have demonstrated that the osteoclast differentiation factor receptor activator of NF-κB ligand (RANKL) plays a critical role in osteoclast differentiation and bone destruction in RA. Denosumab, an antibody against human RANKL, efficiently suppressed the progression of bone erosion in RA patients in a randomized controlled study, and is considered as a putative therapeutic option for preventing bone destruction in RA. However, denosumab did not affect the inflammation of RA, and therefore, combination of anti-rheumatic drugs and anti-osteoporosis drugs are required to treat osteoporosis in RA patients.

SS4-1

Diagnostic opinion from pathologists who specialize in vasculitides

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Conflict of interest: None

Subcommittee of Clinical Pathology in the Japan Research Committee of the Ministry of Health, Labour, and Welfare for Intractable Vasculitis has established the system in which doctors can get a diagnostic opinion from pathologists who specialize in vasculitides. For each case, 2 pathologists take charge of the consultation. From February 2017 to November 2017, 8 cases with 10 biopsy specimens obtained from the kidney (2 specimens), nasal mucosa (2 specimens), skin (2 specimens), lung (1 specimen), temporal artery (1 specimen), brain (1 specimen), and pituitary gland (1 specimen), were subjected for the consultation. The major question was the validity of diagnosis of vasculitis. The required time for answer was diverse case-by-case (10-62 days). We hope this system could contribute to the advancement of the diagnosis and treatment of patients with vasculitis.

SS4-2

Update of large-vessel vasculitis and clinical observational studies

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Conflict of interest: None

Giant cell arteritis (GCA) is characterized by vasculitis due to lesions in the superficial temporal artery, the maxillary artery, and the ophthalmic artery. Aortitis due to the aorta or its branches is a common clinical feature of GCA and Takayasu's arteritis (TAK), although the two disease groups of large-vessel vasculitis are quite different in terms of epidemiology and genetic factors. However, clinical features, especially the large-vessel (LV) lesions, of Japanese patients with GCA are unclear. Differentiation and commonality of clinical features and treatment outcomes of GCA and TAK should be investigated in Japan. To accomplish the goals, a nationwide, retrospective cohort study was established. Thirty facilities (Japan Research Committee of the Ministry of Health, Labour, and Welfare for Intractable Vasculitis, and the Japan Agency for Medical Research and Development) participated in the study. Patients who had been diagnosed with GCA or TAK from 2007 to 2014, and started PSL at a dose of 0.5mg/day or greater were enrolled. Eligible patients included patients who were diagnosed with GCA and LV lesions, even if the ACR GCA classification criteria were not met. Differential diagnosis of GCA and elderly-onset TAK was by the discretion of the site investigators. The interim reports of clinical features of TAK and GCA in Japan will be presented in this symposium. Over the last decade, LV lesions of GCA are reported more frequently in line with progression of diagnosis by imaging tools, and the studies describe the clinical features and imaging findings. However it is unclear whether the large-vessel (LV) lesions are associated with treatment outcomes. Clinical features of GCA with LV lesions and their associations with treatment outcomes will be reported in the presentation.

SS4-3

Biological Treatment in Large Vessel Vasculitis

Yoshikazu Nakaoka
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Conflict of interest: Yes

According to the classification criteria of Chapel Hill Consensus Conference 2012 (CHCC2012), large vessel vasculitis (LVV) consists of Takayasu arteritis (TAK) and giant cell arteritis (GCA). Glucocorticoids (GCs), the first-line therapy for the treatment of TAK and GCA, are often associated with adverse effects when used long-term, and patients frequently relapse during GC tapering. Other immunosuppressive agents, including methotrexate, azathioprine and mycophenolate mofetil, may be used if relapse occurs while the patient is receiving GCs; however, these agents have not demonstrated consistent clinical benefits or steroid-sparing effects. With recent advance in the understanding of pathological mechanisms of the LVV, clinical trials of anti-interleukin-6 receptor antibody, tocilizumab (TCZ), for LVV were conducted. TCZ has been approved for TAK and GCA in Japan, and for GCA in the United States and Europe. In other inflammatory diseases such as rheumatoid arthritis and inflammatory bowel diseases, new therapeutic era with biologics totally changed the landscape and provided unprecedented clinical benefits to the patients. How can we make it happen for patients with LVV? We need to deepen our understanding of the above diseases. In this talk, I would like to review the recent progress in the treatment for LVV mainly focusing on TCZ and discuss about the current issues of this therapy.

SS4-4

New Guideline for Large Vessel Arteritis

Mitsuaki Isobe
Sakakibara Heart Institute

Conflict of interest: None

The first clinical guideline for management of vasculitis syndrome had been published in 2008 from Japanese Circulation Society Joint Working Group. Since the publication of this guideline classification, definition, and nomenclature of vasculitis were changed and big advances for the clinical management of these diseases have been made. Based on these development the Japanese Circulation Society organized a new team to revise this guideline which was published in 2018. In the part of large vessel arteritis Takayasu arteritis and giant cell arteritis are expounded in detail. Buerger disease is also included according to the content in the previous version of the guideline. Classification by Chapel Hill Consensus Conference (CHCC2012) integrated many vasculitis syndromes into middle vessel and small vessel arteritis. The description of these diseases is also taken up in the guideline. Since these vasculitis are relatively rare, large scale randomized clinical trials are not popular and the objective clinical evidence for treatment is quite limited. Therefore, this guideline adopted explanation and extensive review of the diseases instead of employing MINDS system. It is our hope that this new guideline promotes investigation of vasculitis and helps better clinical management of patients with vasculitis.

SS4-5

Treatment strategy for antineutrophil cytoplasmic antibody-associated vasculitis with rituximab; Results of RemIRIT study

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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 April 2017, 16 GPA and 35 MPA patients were registered. Among 16 GPA patients, 8 male and 8 female were included. Ten male and 35 female were included in MPA. The mean age was 67.9 years-old in GPA and 69.9 years-old in MPA. Thereafter, the number of registered cases increased steadily. In October 30, 2017, 28 GPA and 47 MPA were registered. At this point, the most common protocol of RTX was 500 mg/body or 375 mg/m 2 × 4 (22 cases), but various methods were used, indicating the diversity of RTX treatment strategy. At 3 months (n = 44), there were 37 survivors, 5 deaths and 2 withdrawal, 17 remission and 4 relapse cases. Serious adverse events or infections were found in 10 cases. At 6 months (n = 27), 15 cases were in remission, and the number of vasculitis injury index (VDI) = 0 was 9 cases. At 6 month, 13 cases continued the administration of RTX. The case registration is completed on December 31, 2017.

SS4-6

The future subject of the 2017 clinical practical guideline for ANCA-associated vasculitides

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Conflict of interest: None

In Japan, clinical management for ANCA-associated vasculitis (AAV) is usually shared by some departments such as rheumatology, pulmonary medicine, and nephrology. To date, the guideline (GL) for management of vasculitis syndrome (JCS 2008), clinical practice GL for ANCA-associated vasculitis (2014), and the evidence-based GL for rapidly progressive glomerulonephritis (RPGN) (2014) were published. In 2015, we use the online questionnaire system for collecting individual opinion of rheumatologists (The Japan College of Rheumatology, 925 councilors), pulmonologists (the Japanese Respiratory Society, 631), and nephrologists (The Japanese Society of Nephrology, 399), who are involved in the management for AAV in Japan. In this study, we found that both the remission induction protocol and usage of glucocorticoid and/or immunosuppressive agents were different among rheumatologists, nephrologists and pulmologists (reported in the 60th Annual Meeting of Japan College of Rheumatology). In the last year, the 2017 CPG for AAV was developed by collaboration of the Research Committees on Intractable Vasculitides, Renal Diseases, and Diffuse Pulmonary Diseases. This CPG developed using GRADE system showed 3 clinical questions for the treatment in patients with microscopic polyangiits (MPA) and granulomatosis with polyangiits (GPA) and approved by the Japanese Society of Internal Medicine, the Japan College of Rheumatology, the Japanese Respiratory Society, the Japanese Society of Nephrology, and the Japanese Dermatological Association. In this symposium, we will show a usage and observance situation in the 2017 CPG for AAV. Also, the future subjects including evidence-practice gap will be discussed to contribute to wide spread of the 2017 CPG for AAV in Japan.

Educational Lecture

EL1

Clinical significance of airway diseases in rheumatoid arturitis, with emphasis on its participation to the developement of interstitial lung disease

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Conflict of interest: None

Although the high prevalence of airway diseases in patients with rheumatoid arthritis (RA) has been recognized for decades, their clinical significance and treatment strategies have not been well discussed. With the introduction of potent disease-modifying treatments for RA, respiratory complications have emerged as the most important obstacle impeding the safe implementation of these therapies and improvement of patient prognosis. Along with interstitial lung disease, airway diseases are now regarded as one of the major risk factors of these complications and result in their own problems such as airway obstruction and lung destruction. The significance of airway disease can be summarized as follows. 1. It can predispose patients to infectious diseases such as pneumonia and nontuberculous mycobacterial disease. 2. It may cause progressive impairment of lung function, leading to obstructive changes and ultimate respiratory failure. 3. In some cases, airway inflammation can result in the destruction of bronchioles and surrounding lung parenchyma, leading to the formation of cysts mimicking a honeycomb lung, conventionally diagnosed as interstitial pneumonia, UIP (usual interstitial pneumonia) pattern, which is deemed as of poor prognosis. The last possibility has never been documented before. We shall present typical cases of such pathological process and, based on this recognition, mention the possibility of new therapeutic approach to this type of lung lesion, judged as intractable interstitial pneumonia up to now.

EL2

Imaging Pulmonary Diseases in Collagen Vascular Disorders

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Conflict of interest: None

Ground-glass opacity (GGO), consolidation, reticular opacities, traction bronchiectasis, honeycombing, and centrilobular nodules are important and commonly used descriptors in diffuse lung diseases. These words will be explained. Lung disorders in collagen vascular diseases include interstitial pneumonia, airway diseases, vasculitis, and malignancies. Drug-induced lung injury is also important in clinical managements. In terms of interstitial pneumonia, UIP, NSIP, OP, DAD and LIP are common. DAD is the acute serious lung injury with worst prognosis, while OP is subacute and usually shows benign clinical course although it can recur. NSIP and UIP are chronic diseases with different prognostic implication with NSIP showing better course, except in SSc, in which the two histologic patterns seem to carry little clinical difference. In RA, UIP, NSIP, OP and DAD are common, while in PM/DM, NSIP, OP and DAD are major lung diseases. In SSc, NSIP followed by UIP are the main diseases. UIP usually shows reticular opacities in the periphery of lower lobes mixed with traction bronchiectasis and often with honeycombing. NSIP is the disease mainly with GGO and traction bronchiectasis but rarely with honeycombing. The opacities usually predominate in peripheral or peribronchovascular locations. OP shows consolidation along bronchovascular bundles or subpleurally. DAD initially develops diffuse GGO, which rapidly progresses to consolidation with traction bronchiectasis. Airway disease comprises bronchiectasis, mosaic perfusion and centrilobular nodules. They are usually seen in RA and SjS. In vasculitis, diffuse hemorrhage appears as centrilobular GGO. Drug-induced lung injury usually takes the form of interstitial pneumonia, Infection such as tuberculosis and PCP are important complications in patients treated with anti-TNF drugs and steroids. Malignancy, especially lymphoma, occurs significantly more common in RA and SjS than in normal subjects.

EL3

Rehabilitation treatments for patients with Rheumatoid Arthritis

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Conflict of interest: None

The motor system is an important organ system that enables voluntary locomotion, which is essential in maintaining one's independence and dignity. Rheumatoid arthritis causes an abnormal condition that disables the motor system, and its treatment consists of medication, surgery, lifestyle management and rehabilitation. Rehabilitation medicine encompasses various disorders of almost all fields in medicine, increasingly so because of our super ageing society. The Japanese Association of Rehabilitation Medicine defines rehabilitation medicine as the stimulation of activities that is the heart of human endeavor, based on its traditional definition of overriding the physical and emotional function that has deteriorated from disease or injury. This concept of "promoting activities" must be applied to rheumatoid arthritis patients as well. The therapeutic approach for rheumatoid arthritis is adjusted to each phase of rehabilitation medicine. The acute phase rehabilitation medicine includes recovery of bone strength, range of motion and muscular strength weakened by inflammation, orthotic treatment, and patient education for joint protection. In the recovery phase after remission, preventing of deformity progression by overuse or misuse is integrated into the activities of daily living. The living phase consists of the follow-up of these points, as well as screening for compound disability caused by the addition of ageing-based frailty and sarcopenia. With the progression of drug therapy with biological agents, it is more important than ever to treat rheumatoid arthritis envisioning the long-term prognosis, activities of daily living as well as quality of life. Rheumatologists must incorporate this "promoting activities" through rehabilitation medicine into the treatment of rheumatoid arthritis.

EL4

Fractures in patients with Rheumatoid arthritis

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Conflict of interest: None

In patients with rheumatoid arthritis, osteoporosis occurs jointly and systemically, and the risk of fracture increases. Specifically, osteoclasts are activated by inflammatory cytokines, bone resorption increases and bone density decreases. Inflammatory cytokines also suppress bone formation signals. In addition, bad collagen crosslinking increases with inflammatory cytokines, collagen strength decreases, bone quality also decreases. Patients with rheumatoid arthritis are said to have a higher risk of fractures compared to non-patients regardless of age or by site. Factors that increase the risk of fractures are low BMI, disease duration of over 10 years, use of oral corticosteroids, J-HAQ score, history of joint arthroplasty, over 70 years old, history of fractures, serum CRP value, serum 25 (OH) value. 170 patients (293 fractures) with rheumatoid arthritis treated in our department from 2006 to 2015 were investigated. 16 males, 154 females, the average age at injury was 68 years. The fracture site, the number of fractures, the corticosteroids preparation, the medication of osteoporosis drugs, and the fractures chain were investigated in these cases. The fracture site is 97 fractures in the spine, 30 in the proximal femur, 18 in the proximal humerus, 15 in the distal end of the radius, 12 in the rib, 10 in the olecranon, 10 in the ankle joint, 91 in other sites. There were 83 cases with one fracture site, 57 cases for 2 sites, 24 cases for 3 sites and 6 cases for 4 sites. There were 100 patients (59%) with corticosteroids oral administration at the time of injury, 37 patients (22%) with medication for osteoporosis drugs. After the first fracture, 67 cases (40%) of the patients did not prevent the chain fractures another site again. The spine was the most common as the site of the first fracture. Many patients were not found treated with osteoporosis and failed to prevent the fracture chain from the initial fracture of the spine and seemed to be a future task.

EL5-1

Diagnosis of ankylosing spondylitis in Japan

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Conflict of interest: None

Ankylosing spondylitis (AS) is a chronic inflammatory disease and a member of a group of diseases called the spondyloarthropathies (SpA). AS usually affects the sacroiliac joints, spine, and large peripheral joints, with onset typically occurring during the second or third decade of life. The prevalence of AS is approximately 0.2-1.0%, with the majority of patients positive for HLA-B27. A review of the literature showed that the prevalence of HLA-B27 positivity in general population differs significantly among races, from over 30% to less than 1%. Japanese have low prevalence of HLA-B27 positivity with approximately 0.5%. Japanese are thought to have relatively low prevalence of AS. The diagnosis of AS is often missed and markedly delayed. In our seventy-two consecutive patients with AS, the mean patient ages at disease onset and diagnosis were 25.6±11.3 and 33.3±13.2 years old, respectively, resulting in diagnostic delay of 6.7 years. The number of medical institutions to which patients were referred before diagnosis was 2.4, and orthopedic surgeons were most commonly visited (62%). Non-specific low back pain or lumbar spondylitis (33%) and degenerative arthritis (28%) were the primary diagnoses preceding that of AS. Absence of articular symptoms significantly correlated with diagnostic delay. The patients with disease onset on Year 2000 or later had significantly shorter periods until diagnosis than those before 2000 (3.6 versus 7.5 years). The present study showed a marked diagnostic delay among Japanese patients with AS. Although it has been improved, continuing medical education focusing on inflammatory back pain in adolescent is required for early diagnosis of AS.

EL5-2

Surgical treatment of ankylosing spondylitis

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Conflict of interest: None

Kyphotic deformity of the thoracolumbar spine is the most frequent indication for surgical interventions in ankylosing spondylitis patients who have significant spondyloarthropathies. When surgical correction is concerned, the surgeons should select an appropriate osteotomy technique for a patient according to the pathology of his spine. When the intervertebral disc is still mobile, the Smith-Peterson osteotomy (SPO) is chosen. When dense syndesmophyte formation has developed and the disc becomes immobile, a pedicle subtraction osteotomy (PSO) is the technique of choice. When the severity of the deformity is beyond what an ordinary SPO or PSO can correct, enhanced techniques, such as two-level PSO or two-stage SPO, should be employed to achieve sufficient correction. In Anderson lesion, which is also called spondylodiscitis, in addition to correct the global kyphosis using either SPO or PSO, transforaminal grafting is suggested as an adjunct if a significant anterior column defect presents. Less often, the patients may have cervical kyphosis and require surgery. A C7 SPO or PSO may provide satisfactory results and are the standard techniques. On some occasions, such as C1-2 subluxation, lateral tilting deformity, or other unusual manifestations, the above-mentioned osteotomies may not be applicable. Traction management, either longitudinal or halo-Ilizarov style may be tried as an alternative and possible solution. The hip is second to the spine as the site of frequent involvement in ankylosing spondylitis. A total hip replacement surgery brings about satisfactory results. In addition to the regular cases, the surgeons should also know 1. how to evaluate the degree of the flexion contracture of the affected hip; 2. how to determine the sequence of surgeries on a patient who requires both hip and spine surgeries; 3. how to operate on a fully ankylosed and extremely deformed hip.

EL6

Multi-professional Team Approach for Patient Safety

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Conflict of interest: None

It is said, "a human error is not the cause of the accident, but a result". Because the human being is existence to commit a mistake, the environment and the system are the reason of the problem which let we cause the mistake. The human being can handle information processing highly, that is why we make a mistake. If it depends on these characteristics of the human, we should catch it as "human factor", not as "human error". In order to prevent an accident caused by a human factor, after understanding the behavior of the man, still it's necessary to build the error prevention countermeasures as effective and simple as possible. In addition, it is proposed that we should build a system on the premise "a man makes a mistake". "Fail-safe system" which operates in a safe way even if an error occurs, and "fool proof system" which can be performed safely whoever does are good instances. However, the human being is incomplete in essence and the various prevention systems that we made cannot be perfect. In the medical field, patients with same disease will each need the different approach, so it is limited to make them fix and standardize. We should be conscious that we must precisely rely on human power including the flexible measures to circumstances by the on-site staff. Because medical care is offered to the patient by a team comprised of the multi-professional staff. Therefore a team came to prevent an accident and team medical care is regarded as important from the angle of patient safety. It is essential in future to establish methodology to make team medical care function more effectively. In particular, we need to consider about how important the communication and the leadership are for the multi-professional team management. I want to present in this lecture concretely what the communicative ability required is and what is necessary to train the leadership for team medical care.

EL7

IgG4-related disease: diagnosis and treatment

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Conflict of interest: Yes

IgG4-related disease (IgG4-RD) is a recently recognized disease entity that is characterized by tumefactive and hyperplastic lesions in various organs including the lacrimal and salivary glands (so-called Mikulicz's disease), pancreas (autoimmune pancreatitis: AIP) and kidneys. Because patients with IgG4-RD have elevated serum IgG4 levels and characteristic histopathological features including dense infiltration of IgG4-positive plasma cells and storiform fibrosis, such lesions are assumed to have a common etiology and pathogenesis. Organ dysfunction is rarely severe in patients with IgG4-RD at diagnosis and responsiveness to glucocorticoids (GC) therapy is frequently positive. Rheumatologists have got familiar with this disease entity over the last ten years and it is easy to make diagnosis of IgG4-RD for patients with typical physical findings and imaging results, elevated levels of serum IgG4. However, a lot of challenges remain in diagnosis in case of patients presenting with atypical organ involvements or any fibroinflammatory condition without IgG4-related findings. Although the results of two prospective clinical trials using GC in Japan demonstrated the efficacy of GC for IgG4-RD, it has been confirmed that relapse occurred at a high rate following tapering or withdrawal of GC. The long-term prognosis of IgG4-RD is still unknown despite an increase in long-term observation cases because IgG4-RD itself shows a diverse course. Accordingly, determination of therapeutic indication and intensity are often difficult. In this lecture, I will review the basic knowledge about IgG4-RD and present a practical response based on our experience while answering the clinical questions.

EL8

Immune-related adverse events by immune checkpoint inhibitors

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Conflict of interest: Yes

In recent years, immune checkpoint inhibitors have attracted great at-

tention in the field of cancer treatment. These drugs have an effect different from conventional anti-cancer drugs and immunotherapy. Immune checkpoints are negative regulatory mechanisms of the immune system that prevents occurrences of excessive immune responses and autoimmunity. Typical molecules include PD-1 and CTLA-4 in T cells. In cancer, immune checkpoints are often activated to suppress anti-cancer immune responses. This has led to the development of immune checkpoint inhibitors that have been approved for several cancers. However, it was found that immune checkpoint inhibitors frequently cause new side effects, namely, immune-related adverse events, which had not been observed in conventional anti-cancer therapy. Autoimmune disorders, such as thyroid dysfunction, interstitial pneumonia, inflammatory bowel disease, liver disorder, rash, vitiligo, hypophysitis, type I diabetes, renal dysfunction, myasthenia gravis, peripheral neuropathy, myositis and uveitis are the representative events. Furthermore, these adverse events have characteristics different from ordinary diseases, such as having a rapid progress, so sufficient attention is required. It is thought that activation of autoreactive T cells as well as dysfunction of regulatory T cells have occurred, causing these adverse events. When they are expressed, it is necessary to promptly consult with experts, evaluate the grade of these adverse events and respond accordingly. It is desirable to implement intrahospital cooperation between a group of experts from various fields for countermeasures against immune-related adverse events.

EL9-1

Evidence of treatment for steroid-related osteonecrosis of the femoral head by the Clinical Guideline

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Conflict of interest: None

Treatment of steroid-related osteonecrosis of the femoral head (ONFH) is broadly divided into two therapies: conservative and surgical therapies. For the surgical treatment of ONFH, osteotomy, total hip arthroplasty (THA), core decompression, vascularized bone graft or cell therapy using autologous bone marrow graft are often performed. The Japanese Study Group for Idiopathic ONFH is now developing the Clinical Practice Guideline on the Management of Osteonecrosis of the Femoral Head. In this presentation, we will introduce the results of evidence analysis on several treatment methods of ONFH. One of the conservative treatment is non-weight bearing with crutches that is effective for pain reduction; however, there has been no clear evidence to support its prevention effect on femoral head collapse. Several authors have reported the effectiveness of bisphosphonate on prevention of femoral head collapse; however, the long-term effect is still unknown. In surgical treatments, long-term results of core decompression are still controversial. There is moderate evidence that vascularized bone graft has relatively good result especially for early stage ONFH. Autologous bone marrow cell implantation has good short-term results for early stage ONFH patients without femoral head collapse. Varus osteotomy and transtrochanteric rotational osteotomy of the femoral head have good long-term results on pain relief and prevention of femoral head collapse when the osteotomy is performed during the early stage of necrosis and in the absence of an advanced collapse. THA or hemiarthroplasty is one of the most effective procedures for patients with advanced collapse and extensive lesions even though several papers have reported the groin pain and outer-head migration after hemiarthroplasty. There are no long-term results for either hip resurfacing arthroplasty or THA for young patients. Further studies and more evidence are needed to establish the standard treatment of ONFH.

EL9-2

Recent advances in the diagnosis, pathophysiology, and prevention of corticosteriod-associated osteonecrosis of the femoral head

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Conflict of interest: None

Osteonecrosis of the femoral head (ONFH) is one of the intractable diseases, which causes irreversible destruction of the hip joint. Since ONFH generally occurs in young adults, the prevention as well as useful joint preserving procedures are necessary. To prevent ONFH, our project is designed to evaluate the efficacy of existing drugs against the development of ONFH. Based on the results of previous experimental studies, we hypothesized that triple therapy (including clopidogrel sulfate, pitavastatin calcium and tocophenol acetate) can prevent the development of steroid-related ONFH in SLE patients. This clinical study was officially approved as "Advanced medical treatment" by Minister of Health Labour and Welfare in Japan, in which those three drugs are prescribed for three months to prevent ONFH.

EL10

Basic notes and today's points of view on renal pathology for collagen disease

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Conflict of interest: None

Patients with collagen disease often present with renal involvement, and renal histology is useful as a diagnostic tool and to evaluate disease activities. Pathologically the kidney is the most suitable organ for the evaluation of active vasculitis because of the vascular rich structure. Since 2012, using the Systemic Lupus International Collaborating Clinics (SLICC) classification system, we have been able to diagnose SLE with only renal histology matched with lupus nephritis and serum ANA or anti-ds-DNA. The histological features of lupus nephritis manifest in various light microscopic patterns and in a full house immunofluorescence (IF) pattern. In the Chapel Hill Consensus Conference (CHCC) 2012, vasculitis category was revised. Small vessel vasculitis (SVV) category includes microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with polyangiitis (EGPA), anti-GBM disease, cryoglobulinemic vasculitis, IgA vasculitis, and hypocomplementemic urticarial vasculitis. MPA, GPA, and EGPA are called antineutrophile cytoplasmic antibody (ANCA) associated vasculitis. *Berden et al.* proposed a glomerular histological classification for ANCA-associated nephritis in 2010. Several studies were used to verify the classification, inconsistent results for the prognosis in mixed and crescentic classes remained. In our longitudinal study of 36 cases in ANCA-associated nephritis based on Cox-regression analysis adjusted with baseline eGFR, cases with severe interstitial inflammation showed significantly worse prognosis than cases with mild inflammation. These results suggest an additional role of tubulointerstitial injury to the glomerular class. SVVs are divided into pauci-immune, and immune-complex type, therefore IF analysis is essential for handling these diseases. Here I will present basic notes and today's points of renal injury in classic collagen disease and related conditions.

EL11

Diagnosis and Treatment of Lupus Nephritis

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Conflict of interest: Yes

Lupus nephritis (LN) is one of the major organ injuries in systemic lupus erythematosus (SLE). Urine findings are important for the diagnosis of LN. According to ACR classification of SLE, renal lesion is defined as "persistent proteinuria > 0.5 g/day, or cellular casts". Because the histological features of LN are varied and the therapeutic response and renal prognosis differ depending on the tissue type, renal biopsy is recom-

mended and the histological diagnosis should be made based on the ISN/RPS classification. Using the data in our department, we have identified the risk factors for poor renal outcomes: high serum Cr at renal biopsy, combination of proliferative and membranous lesions (mixed type), combination of acute and chronic lesions (A/C lesions). In some cases, renal biopsy cannot be performed due to bleeding tendency or poor general condition. Therefore, attempts have been made to find urinary biomarkers for histological diagnosis and prognosis of LN. As for the treatment of LN, treatment guidelines were published in 2012, such as from ACR. For the induction treatment of active Class III/IV LN, IVCY or MMF is recommended as the first-line drug. To achieve higher response rate, clinical trials using various biologics (rituximab, ocrelizumab, atacicept, abatacept, etc.) have been conducted. So far, no superiority of the addition of biologics to the standard treatment of MMF or IVCY has been demonstrated. Clinical trials using new biologics (obinutuzumab, belimumab, anifrolumab, BI 655054, etc.) are in progress. In contrast, the combination therapy using pre-existing immunosuppressants, MMF and tacrolimus, was reported to show superiority in rate of inducing remission compared to IVCY. In addition, a phase II trial of the combination therapy with MMF and voclosporin, a derivative of cyclosporine, also demonstrated better response rate compared to MMF alone. In this lecture, the recent update of diagnosis and treatment of LN will be presented.

EL12

Perioperative management of csDMARD, bDMARDs, and tsDMARDs in patients with rheumatoid arthritis

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Conflict of interest: Yes

Surgical intervention is one of the crucial treatments in rheumatoid arthritis. Surgeons and physicians should know perioperative complications and meticulously plan the countermeasures against these complications. Previously several important studies were published from Japan, in which bDMARDs significantly increase the risk of postoperative infection more than csDMARDs, even though the difference is not wide. Therefore, most of guidelines recommend perioperative discontinuation of bDMARD. On the other hand, MTX is not recommended to discontinue perioperatively because it does not increase perioperative complications even if the patient takes it. Rather the discontinuation may induce flare-up afterward. However, one should take all of the situation of the patient and the operation into consideration and judge how to manage accordingly. Other perioperative complications include delayed wound healing, deep vein thrombosis, flare-up, and so on. RA is a universal risk factor for these complications, and one should pay the greatest attention to perioperative management for patients who undergo an orthopaedic surgery.

EL13

The management of family planning and pregnancy in patients with rheumatic diseases

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Conflict of interest: Yes

The most important issue as the pre-conception care for patients with chronic diseases is evaluating whether their conditions are good or not for pregnancy, as well as, their medication is whether safe or not. Poor outcome of pregnancy tend to result from patients with active diseases. Therefore, a desirable outcome by safely using medicine must be achieved. It is common advice for women with and without disease to take folic acid and keep one's ideal body weight is important. Many rheumatoid arthritis (RA) patients in remission can stop medication after conception because RA tends to improve during pregnancy. However, patients with systematic lupus erythematosus (SLE) are usually advised to continue medication throughout pregnancy. It is imperative that attention is payed to 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. Furthermore, we would like to introduce the findings of the research team for surveillance concerning the pregnancy outcomes of anti-SS-A antibodies and antiphospholipid antibodies-positive mothers.

EL14

New classification criteria and concept of idiopathic inflammatory myopathy

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Conflict of interest: Yes

The long-standing classification criteria of polymyositis (PM) and dermatomyositis (DM) was set by Peter and Bohan 43 years ago. In Japan, Tanimoto and his colleagues in the MHLW set their own criteria at 1995, which was modified at 2014 and has been used to identify the patients with PM and DM for the medical subsidization. Last October, the International Myositis Classification Criteria Project team published new criteria to classify IIM. This international project has been supported by many international centers including 4 Japanese ones. It collected clinical and laboratory information from 976 IIM patients and 624 comparator patients, selected the most important information variables, and weighted them for the formula in classification criteria. Physical findings, laboratory data for muscle-derived enzymes and muscle-specific autoantibodies, and muscle pathology findings were selected. Validation with a Japanese cohort is underway. As for subset classification, we have no consensus. Muscle pathology is useful but not perfect. A part of PM is called as immune-mediated necrotizing myopathy (IMNM) because of paucity of inflammatory cell infiltration in the necrotic muscles. Anti-SRP antibody or anti-HMGCR antibody positivity have been often found in the IMNM patients. However, anti-SRP antibody positive cases can present typical PM while anti-HMGCR antibody positive cases can present DM. In this regard, some researchers propose the subset classification based on the antibody profile. Based on our basic research, we propose that inflammation should be evoked in the muscles, skin and lungs when the local innate immunity in these tissues is activated locally with the background activation of the systemic autoimmunity. Difference in involved tissues should depend on the different activation patterns of the local immunity.

EL15

Regulation and ethical issues of clinical research in Japan

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Conflict of interest: None

Belmont report is one of the famous fundamental ethic concept of clinical research. Three concepts are written in this report which are "Respect of person", "Beneficence" and "Justice". It is important to put these concepts into practice when we run clinical research. Though this great report is written in just a few pages, there are few researchers who had read this report before starting their research. After "Clinical trial ethical guidance" has taken effective in Japan since 2003, clinical trial environment has change dramatically. The guidance had requested PI high data quality control, but it could not avoid misconduct in clinical research. Now the regulation of clinical research is moving from guidance to the clinical research law. Under the law, there is a possibility that researcher would inflict a penalty when they do violate the law. Two types of clinical research have to observe the law. One is the clinical research using drug without approval and another is the contract clinical research. The law request researcher guarantees the data of clinical research. Researcher has to have a dialogue with the community of patients and citizen better then now to acquire their confidence to the clinical research. The law also requests the system of central IRB system certificated by the government. "Act on the Protection of Personal Information" has made many changes in the clinical research. For example, the concept of methods for anonymization in a linkable fashion has changed because of the development of science. Informed consent and opt out system also make confusion to the researcher. These issues are not easy to resolve researcher

themselves, but have to be resolved by the government, community of medicine or University. When the clinical trial act has started in EU, the number of clinical trials had decreased but now it has increased. Same thing is starting in Japan and we need to resolve these issues to come up to the requirement of society.

EL16

Assessment and treatment of rheumatoid foot and ankle

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Conflict of interest: None

Rheumatoid arthritis is a systemic disease, and doctors need to take care of many parts of the body. Foot and ankle lesion is prone to be neglected by doctors, and patients reluctantly accept the impairment of their foot and ankle without telling anyone. But, when a doctor sees and touches the foot of the patient and ask what trouble the patient have, a good treatment option might be found. The first step of treatment is to clarify what annoys the patients. In many cases, deformity and/or pain due to deformity annoy them. The knowledge of several typical patterns of deformity and pain sites is useful in the assessment process. Finding the way to relieve the problem of the patients is the next step. The treatment goal varies from patient to patient and shared decision-make process should be employed. In this process, doctors' knowledge of conservative and surgical treatment options is critically important. The aim of the current lecture is to provide information of assessment and treatment options for rheumatoid foot and ankle.

EL17

Pediatric to Adult Rheumatology Care Transition

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Conflict of interest: None

Advances in medicine have dramatically improved the prognosis of childhood-onset chronic diseases, allowing patients to survive and reach adulthood. The transition from pediatric to adult healthcare systems has recently received worldwide attention. Transitioning patients with childhood-onset rheumatic diseases that persist into adulthood can be complex and challenging. The burden of musculoskeletal disease continues to increase throughout childhood and adolescence, with approximately 70% of all patients with juvenile idiopathic arthritis (JIA) not achieving treatment free remission within 10 years of diagnosis. Surveys of the attitudes of Japanese non-pediatric rheumatologists regarding transitional care were conducted performed in 2016 concluded that transition to non-pediatric institutes was supported by about 90% of respondents, however, only 32% of non-pediatric rheumatologists had no hesitation about caring for adults with childhood-onset rheumatology disorders. Two main factors prevented smooth transitions to non-pediatric care were inadequacy of non-pediatric care and lack of independence from parents/family. Reflecting these results, supportive guidelines for the transition of patients with pediatric rheumatologic diseases to adult medical care is in progress in Japan.

EL18

Skin manifestation of rheumatic diseases

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Conflict of interest: Yes

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

EL19

Attracive features of orthopedic rheumatologist: abilities of successful diagnosis and differential diagnosis, operative/non-operative treatment, and rehabilitation in patients with rheumatoid arthritis

Hisaaki Miyahara
NHO Kyushu Medical Center

Conflict of interest: None

Attracive features of orthopedic rheumatologist are disscussed. Orthopedic rheumatologist can manage rheumatoid arthritis very well by their capability of successful diagnosis, differential diagnosis, operative/non-operative treatment, and rehabilitation in patients with musculoskeletal disorders including rheumatoid arthritis. The most important playing role of orthopedic rheumatologists is the combination of medication and surgical intervention which provides dramatic improvement of quality of life in patients with rheumatoid arthritis.

EL20

Surgical Treatment for Spinal Disorders in RA Patients

Morio Matsumoto
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Conflict of interest: Yes

Spine is often affected by rheumatoid arthritis (RA), causing various disorders. Cervical spine was most frequently involved, and atlantoaxial subluxation (AAS), vertical subluxation (VS) or subaxial subluxation (SAS) and combination of these pathologies may occur. The occurrence of cervical lesions has been decreasing since good control of RA has become possible with use of DMARDs and biological drugs. However, these drugs have been reported to be ineffective for preexisting RA lesions. Because spontaneous fibrous or osseous fusion often occurs in AAS, conservative treatment is treatment of the choice for patients without myelopathy or intractable pain. But, for those with progressive neurological symptoms, posterior fusion surgery is indicated. Recent development of spinal instrumentation allows for powerful reduction and fixation of sub-luxated cervical spine, but postoperative development of dysphasia and SAS yet remain problematic. In the thoracic and lumbar spines, spondylolisthesis and scoliosis causing back pain and neurological deficits in the lower extremities, osteoporotic vertebral body fractures are serious problems for patients. If adequate conservative treatment fails, decompression with or without fusion surgery is indicated. For those with an isolated osteoporotic vertebral fracture, balloon kyphoplasty or injection of bioactive cement may be considered. Fusion surgery for RA patients with lumbar spinal disorders has been reported to be as effective as for non-RA patients, but adjacent segment disease or fracture of proximal vertebra occurs more frequently in RA patients, and these problems occur equally for patients with and without good control of RA.

EL21

Total care of rheumatoid arthritis by nurses

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Conflict of interest: None

In 1947, the International Health Organization (WHO) defined in its health charter that health is not merely the absence of disease, but physical, psychological and social well-being. When it comes to rheumatoid arthritis, it is necessary to achieve clinical, structural and functional remission. To achieve these remissions, patients' participation in "shared decision making", described as the basic idea of T2T recommendation, is essential. In order to maximize the therapeutic effect, it is necessary to

maintain adherence and to take measures against side effects and infection, as well as to detect side effects in the early stages. In order to carry out these measures, educational support such as providing patients with knowledge about diseases, treatments and side effects is important. Teaching skills of the nurse, self-management guidance and educational support are also essential to accomplish "shared decision making". The patients' own understanding of their disease and participation in their treatment will enable the prevention of a decline in adherence, taking effective measures against side effects and participate in daily care, will result in optimal effective treatment for each patient. Regarding the psychological aspect, patients with rheumatoid arthritis often have anxiety, and, therefore, may self-adjust their medications due to anxiety, resulting in a decrease in therapeutic effect. It is important to talk about the patient's point of view and to acquire the gesture necessary for mutual communication such as listening, empathy, acceptance and open questions. It is reported that patient satisfaction is significantly higher as more information provided by healthcare provides is given to patients, with more patient satisfaction and more communication time and words. As for social aspect, support not only for patients, but also for family members and surroundings is necessary. Kuroe et al. said, " what people with chronic illness ask for is to continue everyday life as usual, and if there is anything else, it is to support them so they can live as they hope". Taking these physical, psychological and social aspects into consideration, care aimed to improve quality of medicine is necessary. We aim to improve the quality of medicine and the quality of life while combining the viewpoint of the health care worker who maximizes the treatment effect and the viewpoint of the patient who continues to be a living person while having a disease.

EL22

Role of group 2 innate lymphoid cells in type 2 immune responses

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Innate Immune Systems, RIKEN IMS

Conflict of interest: Yes

Recent studies have revealed new types of lymphocytes functioning in innate immune responses that are collectively called innate lymphoid cells (ILCs). Unlike T and B lymphocytes, ILCs lack Rag-dependent antigen-specific receptors and are activated by cytokines produced by other innate immune cells or epithelial cells. ILCs have been divided into 3 groups based on their cytokine production profiles; group 1 ILC including NK cells and ILC1 produce IFNγ, group 2 ILC (ILC2) including natural helper cells, nuocytes and innate helper type 2 cells produce type 2 cytokines such as IL-5, IL-6 and IL-13, and group 3 ILC including lymphoid tissue inducer (LTi) cells and ILC3s produce IL-17 and IL-22. ILCs play important roles in protection against various invading microbes including multicellular parasites, and in the maintenance of homeostasis and repair of epithelial layers. In particular, ILC2 produce a large amount of IL-5 and IL-13 in response to IL-25 or IL-33, and induce eosinophilia and goblet cell, both of which act to protect against helminth infection and exacerbation of allergy.

EL23

Legal pitfalls and patient safety in the management of rheumatoid arthritis: negligence and accountability

Yasuhiro Otaki
General Medical Education and Research Center, Teikyo University

Conflict of interest: Yes

In 1999, a sensational report was published by the Institute of Medicine entitled "To Err is Human: Building a Safer Health System" suggesting that medical errors could be responsible for the deaths of between 44,000 and 98,000 hospitalized patients annually in the United States. This report served as a wake-up call for many countries including Japan. In Japan, the Japanese Supreme Court has made it known that civil medical lawsuits have increased dramatically since the late 1990s. Recent significant paradigm shifts in the diagnosis and treatment of rheumatoid arthritis (RA) have led to increases in unforeseen clinical issues, such as interstitial pneumonia or infection mediated by methotrexate and/or biologics. Inevitably, the utilization of both traditional and novel treatment modalities has considerably increased the complexity of current RA management. Here, I give an outline of situations in daily practice where an understanding of the medical errors or malpractice claims associated with the management of RA can be increased.

EL24-1

Optimum Laboratory Tests for Diagnosing Periprosthetic Infection in a Patient with Suspected Inflammatory Arthropathy

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Conflict of interest: None

Infection is a rare but important complication of total joint arthroplasty. Although many studies have calculated the sensitivity and specificity of various tests to diagnose or rule out periprosthetic infection, most of those studies have excluded patients who have an underlying inflammatory arthropathy. This presentation will summarize the diagnostic thresholds for commonly used laboratory tests for diagnosing infection, including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), synovial fluid cell count with differential, and use of an intraoperative gram stain. We will also summarize several new tests that have been applied to diagnosing or predicting risk of infection, including alpha-defensin, serum or synovial fluid IL-6, procalcitonin, fructosamine, and d-dimer. Advances in molecular diagnostics are also likely to improve sensitivity and identify resistant organisms. While some of these tests can help diagnose or rule out periprosthetic infection before or after the operation, a frozen section (FS) is one of the few tests with turnaround time fast enough to use during an operation. Although we might anticipate that patients with rheumatoid arthritis have inflammation that reduces specificity of a FS diagnosis, we will present results of a study that documents good specificity (94.7%) but poor sensitivity (55.6%) for FS used during the second stage re-implantation after periprosthetic infection in patients with rheumatoid arthritis. Improved sensitivity to 88.9% on permanent sections of the same cases suggests that acute inflammation may be patchy at re-revision arthroplasty and therefore subject to sampling errors. The search for new and better laboratory tests to diagnose periprosthetic infection continues, but we need additional studies that include patients with an underlying inflammatory arthropathy, and that document overall disease activity, involvement of the specific joint, and peri-operative medication history.

EL24-2

Characteristics of PJI organism and role of molecular diagnosis

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Conflict of interest: None

There are a variety of species and characteristics included in the organism causing PJI. As we already know from the previous reports, *Staphylococcus* is one of the major species in PJI; however, it is important to approach the detailed characteristics of *staphylococcus* as etiologic agents including methicillin resistance, the percentage of coagulase negative *staphylococci* (CNS), minimum inhibitory concentration (MIC), and other minor organisms in order to improve clinical outcomes. In fact, the MIC of VCM in *Staphylococcus species* from orthopaedics isolates was higher than that of respiratory medicine samples especially in MRCNS from implant related samples in our study. Particularly in biofilm isolates in orthopaedics infections, many antibiotics including vancomycin and rifampin were proved to have insufficient minimum biofilm eradication concentrations. In addition, insufficient antibiotic pressure can induce the viable but non-culturable (VNC) state in *Staphylococcus* biofilm. Here, we confront the difficulty in diagnosing culture negative PJI. The molecular diagnosis based on polymerase chain reaction has a certain role for such VNC organisms. In fact, the PCR is the only available method for identifying the MRS in VNC state. In this session, we will present the re-

cent investigation concerning detailed characteristics of bacterial profile causing PJI, including MIC distributions in Staphylococcus species for several antibiotics. In addition, we will review the current concept of diagnosing PJI and status of our PCR accuracy.

EL25

The rheumatic diseases and stem cell transplantation

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Conflict of interest: Yes

Rheumatic diseases generally have a good prognosis as compared to malignant diseases. However, some cases show poor prognosis due to resistance to conventional treatment and irreversible organ damages. To reconstruct the immune system in such cases, hematopoietic stem cell transplantation (HSCT) has been tried since the mid-1990s, and it has shown good long-term remission rates. On the other hand, reduction of transplant-related death from the viewpoint of treatment risk-benefit balance is left unsolved. Mesenchymal stem cells (MSC) have the differentiation potency into a variety of tissues. Because MSC differentiate into vascular endothelial cells at the ischemic site and improve blood flow, MSC transplantation for intractable skin ulcer in scleroderma is promising. MSC transplantation has also been performed for patients with systemic lupus erythematosus or Crohn's disease in an attempt to utilize an immunosuppressive effect of MSC. Endothelial progenitor cells (EPC), which are contained in the mononuclear cell fraction of bone marrow or peripheral blood, have the ability to differentiate into vascular endothelial cells at the site of ischemia. We have transplanted EPC-containing bone marrow mononuclear cell fraction to an ischemic area of the limb in patients with scleroderma with intractable skin ulcers, and got good results in reducing ulcer area and improving pain. Since human induced pluripotent stem cell (iPS cell) was first reported in 2007, regenerative therapy using iPS cells has been actively studied. The application of iPS cells to treatment for rheumatic diseases is expected. Since 2013, the Japanese government has established a system of law as to regenerative therapy. As the environment surrounding the research on regenerative medicine including stem cell transplantation is changing drastically. In this lecture, I would like to overview the existing circumstances and problems of stem cell therapy in rheumatic diseases.

EL26-1

Recent progress in diagnosis and treatment for Sjögren's syndrome: 2018 Update-For the best clinical practice based on guideline-

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Conflict of interest: Yes

Sjögren's syndrome (SS) is an autoimmune disease which affects salivary and lacrimal glands, accompanied with various autoantibodies and extra-glandular manifestations (EGM). In this lecture, we introduce 1) comparison of different sets of criteria, 2) worldwide present situation for clinical practice guidelines for SS and development of "SS clinical practice guideline 2017" in Japan, and 3) evidences of topical and systemic therapies for SS shown in the guideline, to discuss the best clinical practice for SS. 1) The research team of Japan Ministry of Health, Labor and Welfare (MHLW) (chaired by Takayuki Sumida) revealed that new 2016 ACR-EULAR classification criteria for primary SS had significantly higher sensitivity and lower specificity in diagnosis of Japanese primary SS, compared with the currently available three sets of criteria such as revised Japanese Ministry of Health criteria, American-European Consensus Group criteria, and ACR criteria. 2) Recently the treatment guideline by SS Foundation in USA and the management guideline by British Society for Rheumatology have been published for SS. Moreover the guideline committee of MHLW performed the systematic review of evidences for 38 clinical questions, and has developed "SS clinical practice guideline 2017" which was approved by JCR and Japanese society for SS, according to the procedure proposed by Minds. 3) In "SS clinical practice guideline 2017", it is recommended that rebamipide, diquafosol sodium, and hyaluronate sodium eye drops, and lacrimal point plug are effective for dry eye, and cevimeline and pilocarpine are effective for dry mouth. It is suggested that corticosteroid could not improve salivary and lacrimal secretion, while mizoribine and methotrexate could improve sicca symptoms. Both corticosteroid and cyclophosphamide are suggested to be effective for EGM. For biologics, it is suggested that rituximab and abatacept might be effective for both glandular and EGM, while belimumab only for EGM.

EL26-2

Adult-onset Still's disease

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Conflict of interest: None

Patients with adult-onset Still's disease manifest with the triad of high-grade fever, arthritis, and skin rash. The disease is now considered one of the autoinflammatory diseases presenting similar phenotype to systemic juvenile idiopathic arthritis. Although the etiology of adult-onset Still's disease is still uncertain, genetic susceptibility such as HLA genotypes and abnormal macrophage activation possibly triggered by infection may play a role. Activated macrophages produce inflammatory cytokines such as IFN-γ, IL-6, and IL-18, and proteins involved in iron metabolism including ferritin, CD163, and heme oxygenase-1. Some of these proteins are useful for biomarkers and potential treatment target for the disease. Yamaguchi's criteria has been widely applied in the clinic worldwide, but it has some limitations. We are currently developing a collaborative study to improve the criteria. Now new guidelines for the management of adult-onset Still's disease is in the process of development in Japan. In the current presentation, I will discuss topics and future perspective of adult-onset Still's disease.

EL27

Ten common mistakes in the diagnosis and management of systemic sclerosis

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Conflict of interest: Yes

Prognosis of patients with many connective tissue diseases has been much improved by standard management in accordance with practical guidelines. In contrast, systemic sclerosis (SSc) remains an intractable disease with poor outcomes. This is primarily due to lack of understandings of natural disease course and highly variable clinical presentation of the disease by healthcare providers. It is useless and meaningless without full understandings of unique features of SSc, and discussion of treatment responses in observational cases without adequate controls is always inadequate and often leads wrong prejudice. Recent advances in basic researches successfully lead to implementation of a number of clinical trials of potential anti-fibrotic agents in SSc patients. Before the dawn of SSc-treatment era, this lecture features basic knowledge required for daily clinical practice of SSc patients, highlighting 10 common mistakes in the diagnosis and management of SSc, listed below: 1. Performing skin biopsies for the purpose of SSc diagnosis 2. Forcing patients to expose to cold water for assessing the presence of Raynaud's phenomenon 3. Ordering anti-topoisomerase I, anticentromere, and anti-RNA polymerase III antibody tests without prior ANA test (indirect immunofluorescence) 4. Use of 2103 ACR/EULAR classification criteria for making diagnosis 5. Not initiating treatment until functional impairment becomes apparent 6. Considering that treatment employed is efficacious when skin sclerosis is improved 7. Use of corticosteroids for the purpose of treating skin sclerosis 8. Assuming that intravenous cyclophosphamide is the gold-standard treatment for ILD 9. Use of ACEI/ARB for the purpose of preventing renal crisis 10. Use of bosentan when skin ulcer is present on a finger.

Meet the Expert

MTE1

Therapeutic strategy for the multiple joint disorders in the patients with rheumatoid arthritis

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Conflict of interest: None

Recently, the classification criteria of rheumatoid arthritis (RA) enabled us to diagnose RA in the early stage. The composite measures for the disease activity and the newly developed medication (bDMARD, tsDMARD etc.) made us possible to control the disease activity tightly. Thus it was not a dream to allow the patients to go about an ordinary life. However, there were still some patients whose joint deterioration progressed due to a delayed diagnosis and an insufficient medication. Other patients in the clinical remission might have the secondary osteoarthritic change due to overuse of the painless joint after the acute inflammation. Some patients could not be treated by a strong medication because of their infectious diseases and other comorbidities. Such patients had the multiple joint disorder. Before making the treatment strategy for the disabled patients, it was important to assess the patient's disease activity, ADL, QOL and comorbidities, and to get the sufficient information about the patient's background including age, gender, family, job and interest etc. For the disease whose radical cure was impossible, total management should be adopted. Systemic treatment was built on the basic therapy and 4 columns of medication, rehabilitation, surgery and care of the patient. It was also important to allow the patient to select the treatment options depending on the various disease conditions and the surroundings.

MTE2

The key points of rehabilitation for Rheumatoid Arthritis

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Department of Rehabilitation Medicine, Chiba Rehabilitation Center

Conflict of interest: None

Recently drug treatment for Rheumatoid Arthritis is improving, patients who suffer the daily life looks like decreasing. But there are still patients who have joint contracture for long time or patients who are not effective to the drug treatment or cannot use the proper drugs by the side effect. Those patients have to take rehabilitative approaches. In this session, I will speak about the joint protection teaching and rehabilitation for the upper and lower extremities as the key points of rehabilitation for Rheumatoid Arthritis. For the joint protection, we have to teach the proper method in accordance with the joint inflammation status and the work load in the daily life. If inflammation is severe, the patients refrain to work. Thus, we have to take care disuse. On the other hand, if inflammation is light or none, we have to take care overuse. We use the orthosis for rest, and we teach the proper movement in the daily life. For the wrist and finger deformity, we make the wrist supporting orthosis. For the ulnar deviation, we make soft or hard type correcting orthosis. For the swanneck or buttonhole deformity, me make 3-point supporting finger orthosis. For the light type finger deformity, we use the self-adhesion elastic taping method. I will introduce main selfcare devices such as the long handle hair brush, the reaching device, the socks-aid, the button-aid, the long and bending spoon and fork, the tweezer type chopsticks. For the foot and toe deformity, we instruct the Prosthetist to make the custom-made insole and shoes. The patient can take the financial support from the medical insurance and the law to help the disabled. For the ankle eversion and flat foot, we use the medial longitudinal arch supporting pad and the sole device. For the claw toe and the forefoot tyrosis, we use the metatarsal pad and the forefoot depressurization. If the patient is difficult to use the conventional type cane, we use the special Rheumatoid Cane, and the walker.

MTE3

Treatment strategy for elderly rheumatic diseases

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Conflict of interest: None

Elderly-onset is common in polymyalgia rheumatic (PMR), giant cell arteritis (GCA), and microscopic polyangiitis (MPA). The age of onset also shifted to elderly side in rheumatoid arthritis (RA). The prevalence rates of elderly rheumatoid diseases such as systemic lupus erythematosus, systemic sclerosis, and dermatomyositis/polymyositis increase in line with the increasing life expectancy. Elderly-onset cases are not rare in these rheumatic diseases. Induction therapy of elderly rheumatic diseases is challenging, because adverse events are common in elderly patients receiving corticosteroids, immunosuppressive drugs, or biologics. Maintenance therapy is also critical problems for elderly patients. The primary physicians are balancing risk of adverse events and relapse of the elderly patients with rheumatic diseases in clinical practice, however clinical data of randomized controlled studies are scarce and observational studies are few. In this seminar, I will discuss these challenging clinical questions, especially about treatment of PMR, GCA, RA, and MPA.

MTE4

Fibromyalgia Practice in Japan

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Conflict of interest: None

Fibromyalgia (FM) is a rheumatic disease to be suffered most commonly on middle-age women (the prevalence in Japan: about 1.7%). 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 area of brain in patients with FM, and it is thought that neuroinflammation would be the important pathophysiological mechanism 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 important clinical questions (CQs) for Japanese rheumatologists participating in this seminar, for the improvement of QOL of patients with FM. CQ-1: What is classification or diagnostic criteria? CQ-2: What is activity or severity criteria? CQ-3: What drugs are prescribed in Japanese real world practice? CQ-4: What regimens are selected for non-drug treatment in Japan? CQ-5: How are the clinical course and prognosis (functional or vital)?

MTE5

A paradigm shift in the management of SLE: from "steroid first" to "hydroxychloroquine first"

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Conflict of interest: None

After the introduction of hydroxychloroquine (HCQ) and mycophenolate mofetil in 2015, a paradigm shift from "steroid first" to "HCQ first" occurred in the management of SLE in Japan. As a consequent, use of glucocorticoids was decreased in our department (Abstract of Shimada K) A randomized controlled trial of HCQ demonstrated a reduction of SLE flares in 1991 and a clinical trial in Japan showed the favorable effect of HCQ on lupus-specific skin lesions and joint pain. 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 in numerous observational studies. Accordingly, recent guidelines recommend lifelong HCQ use for all lupus patients. In our department about two-thirds of SLE patients (about 250 patients) were using HCQ. One-year continuation rate of HCQ was about 90% in our department (Abstract of Takamasu). Skin hypersensitivity reaction is not uncommon and may be very severe Cases of Stevens-Johnson syndrome were reported. HCQ retinopathy will be reported probably in 2020s. Early detection by regular eye screening and withdrawal of HCQ can prevent the progression of retinopathy and preserve visual acuity. Establishing collaboration with reliable ophthalmologists

who own SD-OCT is ideal for safety management. Identifying the features and risks of HCQ retinopathy in Japanese population is important as a future research. Industry-government-academia should cooperate to broaden the indication of HCQ to rheumatoid arthritis (Keio University) and other unmet medical needs. An investigator-initiated clinical trial of HCQ to prevent the recurrence of anti-SSA antibody-associated congenital heart block is ongoing (Abstract of Yokogawa).

MTE6

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.

MTE7

Basic knowledge essential for utilizing joint ultrasound examination for RA monitoring

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Conflict of interest: None

In routine practice, we mainly refer to the number of tender and swollen joint, CRP, ESR, patient`s VAS, which are components within the composite measure such as DAS, SDAI, CDAI. and investigate the condition of rheumatoid arthritis. It is common to judge roughly, however, each component can not judge the disease condition of RA properly, such as when the findings of affected joints are mild, when suffering from infection, individual difference in pain range value, etc. In such a case, using joint ultrasound examination, it becomes possible to detect abnormal findings such as synovitis with high sensitivity through high-resolution ultrasound images and correct disease activity judgment. On the day of lecture, tips and pitfalls of ultrasound examination, how do you select and judge joint position and number of ultrasound examination necessary for RA activity evaluation? The inspection timing and interval? How do you interpret the obtained findings? How to strengthen treatment using ultrasound image? We will acquire the fundamental knowledge that is indispensable for exploiting the joint ultrasound examinaiton in RA monitoring.

MTE8

Diagnosis and treatment for pain in extremities in children

Shuichi Ito
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Conflict of interest: Yes

Pain in extremities in children is common chief complaint in outpatient clinic. However, diagnosis and physical examination is often challenging. Orthopedic trauma and growth pain are major causes, but infection, rheumatic diseases, metabolic diseases, hemato-oncological diseases, congenital bone, cartilage and connective tissue diseases could be the cause. Anatomically-based careful physical examination and radiological evaluation are useful to focus on site of the pain, leading to the diagnosis. Additionally, family and developmental history taking is essential to diagnosis inborn disorders. Meanwhile, somatoform disorder, malingering and fibromyalgia syndrome are also put in the list of differential diagnosis. Psychosocial problems are frequently associated with such disorders, so-called "heart pain". In this lecture, you can learn physical examination, differential diagnosis and treatment of pain in extremities in children.

MTE9

Total joint arthroplasty for elbow and finger in RA patients

Takuji Iwamoto
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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) 4) Total wrist arthroplasty; surgical technique of DARTS total wrist arthroplasty

MTE10

Iatrogenic immunodeficiency-associated lymphoproliferative disorders in patients with rheumatic diseases

Masayoshi Harigai
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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. Publication of the 2016 classification by WHO is eagerly anticipated. 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.

MTE11

My personal opinion of the recommendations for the management of rheumatoid arthritis with biological DMARD 2018, especially the selection with long-term strategy

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Conflict of interest: None

1. The important principle of the selection and the treatment long-term strategy of bDMARDs is, if a first bDMARD has failed, more successful treatment with another bDMARD by another mode of action should be considered. 2. TNF pathway inhibitors should be considered to divide two mode of action. One is anti-TNF monoclonal antibody, and another is soluble TNF receptor fusion protein. If it is possible the combination therapy with MTX, the first bDMARD should be considered one of anti-TNF monoclonal antibody. 3. The possible bDMARD of dose-up or the shortening of interval may have some advantages compared with other bDMARD. 4. The initial bDMARD treatment with loading dose may have little advantage because the next step should be dose down. 5. The switching of bDMARDs from anti-TNF monoclonal antibody to soluble TNF receptor fusion protein is usually successful, however the switching from soluble TNF receptor fusion protein to anti-TNF monoclonal antibody and from anti-TNF monoclonal antibody to anti-TNF monoclonal antibody is not. In long-term strategy, it should be considered the first bDMARD should be selected in anti-TNF monoclonal antibody, if it is failed, the second bDMARD should be selected soluble TNF receptor fusion protein. 6. The ineffectiveness of TNF inhibitors is influenced by anti-drug antibody or by the ineffectiveness of MOA of TNF pathway. 7. Which the first bDMARD should be considered, TNF inhibitors or IL-6 inhibitor? In current EBM, TNF inhibitors may have some advantages as first bDMARD in long-term strategy. 8. However, in patients who cannot use MTX or who can only use low dose MTX as comedication, IL-6 inhibitors may have some advantages by less immunogenicity. 9. In the selection of bDMARD, if the safety is more important considered, abatacept may have some advantages, especially elderly patients. 10. The bDMARD therapy should not be stopped except early RA, and the physician should not inform the stopping of bDMARD before the treatment. 11. By gently warmth to patients, the physician should recommend the subcutaneous injection of bDMARDs with the longer interval and not self-injected. 12. I hope about the medical economic statement of bDMARD, the bio-free should be unsolved, and the price down of bDMARD should be very important.

MTE12

Pathological aspects of vasculitides

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Conflict of interest: None

Vasculitis is a disease in which vessels are affected primarily. Since vasculitis is apt to affect vessels segmentally, it is desirable to cut the vessels in round slices as many as possible for histological examination. By the same reason, it is recommended to examine deeper sections when there is no remarkable finding in the first section in spite of the clinical suspicion. The major histological aspects of vasculitis are granulomatous vasculitis and necrotizing vasculitis. The specific stain of elastic fibers can be useful to elucidate the vascular injury. Granulomatous vasculitis is characteristic of Takayasu arteritis (TAK) and giant cell arteritis. Multinuclear giant cells that capture the degraded elastic fibers in the cytoplasm are sometimes present in the lesion. In TAK, the granulomatous inflammation characteristically invades the tunica media from the adventitial side. On the other hand, necrotizing vasculitis occurs in polyarteritis nodosa, anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis, anti-glomerular basement membrane disease, IgA vasculitis, etc. Infiltration of neutrophils (eosinophils in case of eosinophilic granulomatosis with polyangiitis) is present, and leukocytoclastosis is sometimes observed. Additionally, the presence of neutrophil extracellular traps in the lesion is the feature of ANCA-associated vasculitis. These histological characteristics are considered to reflect the pathogenesis. Thus, an exact recognition of pathological findings is important for understanding the pathophysiology of vascilitides. In this lecture, I will introduce the web-edition of the Pathology Atlas of Vasculitides and the consultation system of Pathological Diagnosis of Vasculitides, which have been established by the Subcommittee of Clinical Pathology in the Japan Research Committee of the Ministry of Health, Labour, and Welfare for Intractable Vasculitis. I hope to contribute useful information for diagnosis of patients with vasculitis.

MTE13

How to use X-ray images in clinical practice of rheumatoid arthritis

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Conflict of interest: Yes

In this lecture, I would like to show representative and specific X - ray images in diagnosis and treatment, and to deepen knowledge for X - ray interpretation. Rheumatoid arthritis (RA) is characterized by arthritis which causes bone destruction. And it is thought that bone destruction will occur from the strength of arthritis and its duration. Therefore, if bone destruction is occurred early period of disease, it is judged to be poor prognosis. The classification criteria for rheumatoid arthritis of ACR / EULAR, which was revised in 2010 as the basis of current diagnosis, is aimed at early intervention before the appearance of bone destruction. Although the sensitivity of X - ray examination is not high, it is a very useful method for detect bone destruction in routine practice. Diagnosis of rheumatoid arthritis is easy if the structural destruction of the joint is detected. For understanding changes in X-ray image well, we have to compare left to right, and check the changes with the time course. 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, surgical therapy should be performed at an appropriate timing if there is a rapid destruction progress. Joint stability is essential for joint function. With simple x-rays, it is possible to detected by confirming the abnormal mobility of the joint by functional imaging. Cervical spine function imaging is very useful for detecting the stability of the cervical spine, especially the annular joint. RA affects, not only for one joint, but also for the relationship with adjacent joints, overall alignment and balance in the spine and lower limb need to be considered.

MTE14

Practical Approach to Neuropsychiatric Systemic Lupus Erythematosus (NPSLE)

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Conflict of interest: None

Central nervous system (CNS) lupus is a serious and potentially life-threatening manifestation of systemic lupus erythematosus (SLE), occurring in 37-95% of cases, and is associated with an increased risk of death. Despite its frequency and severity, the lack of a diagnostic gold standard makes it challenging to differentiate primary CNS lupus from secondary neuropsychiatric (NP) manifestations unrelated to SLE at their onsets. The American College of Rheumatology has developed a standardized nomenclature system that provides case definitions for 19 NP syndromes associated with SLE, including reporting standards and recommendations for laboratory and imaging tests. Although this standardized nomenclature has helped to clarify a complicated situation, its usefulness as a clinical diagnostic criterion remains to be determined. EULAR have recommended that the diagnostic work-up of suspected NPSLE should be comparable to that in patients without SLE who present with the same manifestations, and aims to exclude causes unrelated to SLE. Investigations include cerebrospinal fluid analysis (to exclude central nervous system infection), EEG (to diagnose seizure disorder), neuropsychological tests (to assess cognitive dysfunction), nerve conduction studies (for peripheral neuropathy) and MRI (T1/T2, fluid-attenuating inversion recovery, diffusion-weighted imaging, enhanced T1 sequence). Glucocorticoids

and immunosuppressive therapy are indicated when NPSLE is thought to reflect an inflammatory process (optic neuritis, transverse myelitis, peripheral neuropathy, refractory seizures, psychosis, ACS) and in the presence of generalized lupus activity. Antiplatelet/anticoagulation therapy is indicated when manifestations are related to antiphospholipid antibodies, particularly thrombotic CVD. In this workshop, practical approached to NPSLE is to be discussed.

MTE15

The excellent imaging procedure for detecting the connective tissue diseases ~Ultrasound-probe can tell the precise findings led to diagnosis~

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Conflict of interest: None

Ultrasound technique have played a pivotal role for diagnosis and evaluation of treatment efficacy since 1949 when K.T. Dussik firstly introduced it in clinical settings. The reason why ultrasound is surprisingly spread in clinical field is that it is easy and non-invasive imaging procedure to patients. Remarkable innovative revolutions for ultrasound probe make it possible for Rheumatologists to put into clinical setting. However many patients also including co-medicals are no where insight about adaptations of ultrasound to connective tissue disease (CTD). Musculoskeletal ultrasound (MSKUS) is mostly used for Rheumatoid arthritis (RA) in Rheumatology. The contribution of MSKUS for both diagnosis and evaluation of treatment efficacy is quite high as expected. In particular, high specificity (93.7%) in 2010 ACR/EULAR-RA classifications was shown by using MSKUS compared with that (79.4%) of palpation method from our country. The algorism for RA diagnosis also including the validation of therapeutic effect and remission was reported from EULAR recently. These excellent reports suggested that MSK is crucial examination for daily medical practice, moreover MSKUS is very useful to not only RA but also the differential diagnosis similar to CTD. In this session, I am going to introduce the latest evidence of MSKUS in addition to the real-cases diagnosed by MSKUS, and focus upon the educational systems to sonographers and nurse in our institution.

MTE16

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 IIM includes other clinical condition such as inclusion body myositis (IBM) besides PM/DM, 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 IIM. Therefore, prompt correct evaluation and subsequent appropriate treatment of muscle and other symptoms are important. In this context, autoantibodies found in patients with IIM are useful for diagnosis, selection of treatment, evaluation of treatment and prediction of prognosis in each patient.

MTE17

Footwear and custom orthotic interventions for rheumatoid foot in combined-modality therapy of surgical, pharmaceutical and rehabilitation

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Conflict of interest: None

Principle of footwear and custom orthotic interventions for rheumatoid foot is simple. Cautious selection of shoes, prevention of concentrated plantar pressure and sliding induced plantar friction, stabilization of damaged joints and realignment of the shifted mechanical axis are important. Principle of shoes selection is also simple. Big toe box that is provided by shoes 2-3 cm bigger than foot length, well-fixation of foot in shoes by fixing belt or shoestring and well-fitting of heel to quarter are required. After cautious selection of shoes, we prescribe the insole for various pathological condition of rheumatoid foot. The difficulty of footwear and custom orthotic interventions lies in point other than these principles. Despite the prevalence of footwear and custom orthotic interventions, unrecovered or remaining gait disturbances are frequently overlooked. Their poor functional prognosis due to overlapping age-related disability could burden them sooner or later. We must aim not only for the improvement of recent activity of daily living but also for long-term normal living activity of over thirty or forty years. In the case of disabled patients using foot orthosis, we must return them to a lifestyle with less disability with timely indicated appropriate surgical intervention. Since we are now short of the specialists of foot and ankle surgery whose techniques catch up with rapidly advanced pharmacotherapy, the well-organized cooperation with foot and ankle surgeon who have high expertise in rheumatoid foot is possible solution. On the other hand, some patients tolerate the improper footwear or orthotics and are led into reduced walking distance and impaired health-related quality of life. Patients' reasons for this tolerance are complex but include high price of custom foot orthotics, impossible size and shape adjustment after purchase of ready-made shoes, strongly opinionated shoes size choice of foot length and low demand of recovery from disability. Provision of dedicated foot care service including shoes adjustment is required, however that remains to be prepared in our team. Rapidly advanced pharmacotherapy and rapid improvement of longevity in the elderly including aged patients with RA inevitably increase the importance of non-pharmaceutical management such as rehabilitation and surgery. I will introduce my strategy and review the literature in this course.

MTE18

Diagnosis and treatment for Behcet's disease

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Conflict of interest: Yes

Behcet's disease (BD) is an inflammatory disease affecting multiple organs such as eye, mucosa, and skin. The disease has a broad spectrum from mild cases having mucocutaneous lesions solely to serious ones presenting with blindness or severe organ damages in the intestine, large vessels, and CNS. The diagnosis relies on symptomatology based on the combination of clinical manifestations, because of lack of specific findings in blood, imaging, and histopathological examinations. There are some discrepancies between the Japan criteria and the International Criteria, especially in the diagnosis for patients with intestinal involvement. Recent studies have suggested several clinical clustering patterns among BD patients. For example, a cluster is found in male patients with HLA-B51, ocular lesion, and CNS involvement. Therapeutic approaches are different depending on clinical presentations. Topical corticosteroids and colchicine are given for mucocutaneous lesions and mild ocular lesions, whereas the posterior pole of ocular lesion is necessary for treatment with immunosuppressants such as cyclosporine or azathioprine (AZA), and anti-TNF antibody such as infliximab (IFX) and adalimumab (ADA). The first line therapy for acute and chronic progressive types of neuro-BD is corticosteroids and methotrexate (MTX), respectively, whereas IFX is indicated for refractory cases. Corticosteroids and IFX or ADA are chosen for acute intestinal ulcer as remission induction. 5-ASA, AZA, and MTX

are also used. Treatment with corticosteroids and immunosuppressive agents is principle for acute deep vein thrombosis and inflammatory aneurysms. Surgical operation and endovascular intervention for the intestinal and vascular involvement are optional. The procedures are associated with postoperative complications and recurrences, which are suppressed by concomitant immunosuppressive therapy.

MTE19

The Usefulness of Nailfold videocapillaroscopy

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Conflict of interest: Yes

In 2013, the collaboration of the American college of rheumatology and the European league against rheumatism (ACR/EULAR) proposed a new set of criteria for systemic sclerosis for the first time in 30 years. Of note, nailfold capillary abnormalities were one of the new items in these criteria. These morphological changes and progressions can be detected by nailfold videocapillaroscopy (NVC). Since microvascular damage and dysfunction represent early markers of systemic sclerosis, qualitative and semi quantitative assessment of video capillaroscopy images is expected in clinical application and treatment outcome assessment. Moreover, nailfold videocapillaroscopy may be useful in evaluating the pathogenesis of systemic sclerosis. Under these circumstances, the nailfold capillary abnormalities for not only in systemic sclerosis but also other autoimmune diseases have been investigated by the EULAR working group. However, in Japan, it is hard to say that this evaluation method using NVC has been fully penetrated. In this seminar, I will present about the significance and attractiveness of NVC and how to practice it, and outline the application to clinical research for autoimmune diseases.

MTE20

Polymyalgia rheumatica and giant cell arteritis

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Conflict of interest: None

Giant cell arteritis (GCA), previously known as temporal arteritis is classified as a large-vessel vasculitis. Almost all patients who develop GCA are over the age of 50. Common signs and symptoms of GCA due to the involvement of the temporal arteries and other medium-sized arteries of the head and the neck are visual disturbances, headache, jaw claudication, neck pain, and scalp tenderness. General manifestations, such as fatigue, malaise, and fever, are also present. GCA is diagnosed based on the American College of Rheumatology 1990 classification criteria. Because the disease is relatively uncommon and the disease can cause so many different symptoms, the diagnosis of GCA can be difficult. Actually, GCA is classified into three types: classic temporal arteritis type (cranial GCA); large-vessel type (LV GCA), affecting the aorta and its major branches without temporal arteries; generalized type, affecting both temporal arteries and large vessels. ACR 1990 classification criteria for large-vessel GCA were satisfied in only small portion of LV GCA patients. Polymyalgia rheumatica (PMR) is an inflammatory disorder characterized by pain and stiffness in shoulders, neck as well as girdles. PMR occurs in 30-50% of patients with GCA, and 15-30% of patients develop GCA, thus these two diseases might be the same disease with different clinical aspects. The markedly significant uptake of FDG has been reported in ischial tuberosities, greater trochanters, iliopectineal bursas and spinous processes, suggesting the grate value of FDG-PET/CT for the diagnosis with PMR. In this section, we would like to discuss the clinical subtype and characteristic manifestations of GCA, and the relation between GCA and PMR.

MTE21

Examination and treatment of rheumatic hands

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Conflict of interest: None

(Introduction) In rheumatoid arthritis (RA), wrist and finger joints are often affected. According to Rheumatic White Paper 2015, initial symptoms of RA are mainly wrist joint arthritis (37.7%) and finger joint arthritis (52.1%). Persistent arthritis could cause joint destruction or deformity. For this reason, the treatment of RA hand has become essential recently. (Examination of RA hand) As it is required to confirm the presence of finger or wrist joint synovitis, careful examination is essential. In addition, it is necessary to get in-depth information, joint destruction, range of motion, pinch power, and grip power. Ultrasound test is necessary for additional inspection. Tenosynovitis is important because of the risk of tendon rupture and should not be missed. (Conservative treatment of RA hand) Joint steroidal injection makes some synovitis improve, therefore it is important as conservative treatment of RA hand. It is desirable to consider resting-purpose orthotics for arthritis. Although it is ideal to be made through the cooperation of occupational therapist, may be used commercially available products. If an orthotic suitable for individual hand deformity is could be considered, the benefits were significant. (Surgical treatment of RA hand) In these days, small joint surgeries are predicted to increase, and joint-preserving RA hand surgery has been more indicated recently. If conservative treatment such as a joint injection is not effective, the synovial resection is recommended. For destructive joint cases surgical intervention is needed. We have to explain that surgical treatment is possible and effective for advanced hand deformity. (Conclusion) In addition to the RA drug treatment, a local approach to remaining arthritis is also thought to be essential. Especially for the problem of RA hand which is often a diseased part, combination of conservative and surgical treatment is thought to be even more important.

MTE22

How to Write a Paper in English - Unknown Tips and Tricks

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Conflict of interest: None

In medical science, research papers are published primarily in English. However, it is not easy for many Japanese researchers to write a paper in English, a non-native language. I provide some “tips and tricks” to write a paper in English in terms of logic, easy-to-understand figures and tables, and structural difference between English and Japanese. ***Logic*** In both English and Japanese, logical composition is most important in writing a paper. Scientific papers are not highbrow literature, esoteric philosophy, or advanced mathematics; required logical composition is very simple. The keys are: “abstract and specific,” “parallel and contrast,” and “comparison and integration.” For example, most cases of cerebrovascular diseases are either cerebral infarct or intracerebral hemorrhage (abstract and specific). While high prevalence of hypertension is common in these diseases, patients with cerebral infarct are more likely to have comorbidity, such as diabetes mellitus and dyslipidemia (parallel and contrast). Taken together, cerebrovascular diseases are strongly associated with lifestyle-related diseases such as hypertension, diabetes mellitus, and dyslipidemia (comparison and integration). ***Easy-to-understand figures and tables*** Presentations in journal clubs are often given with only figures and tables, which are sufficient to grasp the outline. This means that English itself has little role in understanding the outline of good papers. Providing easy-to-understand figures and tables is critical for writing a paper in English. ***Structural difference between English and Japanese*** English sentences have a definite subject and object in principle, while Japanese sentences do not. English is thus beneficial for providing a well-organized logical structure. Using a non-native language makes sentence structure simple and clear. Take advantage of this and focus on the simplest possible logic and easy-to-understand figures and tables to achieve sophisticated expression in English.

MTE23

Design and statistical analysis of exploratory clinical research

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Conflict of interest: None

In conducting clinical research, a research plan is obviously important. It is easy to make a scientifically ideal research plan without considering a reality of clinical practice if we have the template of a clinical research protocol. However, such a research plan will not fit into the clinical practice and become a research plan that cannot be implemented. In order to construct a good clinical research plan, education by experienced researchers is essential. In order to learn about the research plan, it is good to participate in seminars or workshops. Although seminars about research plan are widely held, it cannot be said that they are extensively provided according to the property of research, especially in research of exploratory stage. Therefore, this session focuses on the design of exploratory clinical research. For making an appropriate plan for exploratory research, it is necessary to understand p-value and hypothesis test appropriately, since it is not possible to set up a research just based on whether p-value is less than 0.05 or not. In addition, we also need to pay attention to the difficulty in estimating the group difference which is necessary for calculating sample size of the research. Next, it is necessary to take into account the interpretation of the statistical analysis results. It seems that over-interpretation of results has frequently be conducted. To avoid this, it is good to make the final product as specific as possible. In this session, for researchers who have little experience in clinical research, explanations and discussions about the clinical research plan will be provided while exchanging opinions.

MTE24

Treatment of shoulder pain for patients with rheumatoid arthritis-Surgical treatment in case of no efficacy of conservative treatment-

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Conflict of interest: None

Conservative treatments including NSAIDs, hyaluronic acid injection or rehabilitation for treatment of shoulder pain are performed in daily practice of RA. However disease activity depends on the efficacy of conservative treatment as limited issue. Arthroscopic synovectomy of shoulder is effective for the patients for disease duration with under 10 years and low usage prednisolon. However over 70 years with high joint destruction with more than 10 years disease duration, reverse shoulder arthroplasty (RSA) is selected to improve pain, ROM immediately compared with TSA. Clue of Surgical treatment beside conservative treatment is going to be explained in this lecture.

International Concurrent Workshop

ICW1-1

MicroRNA-34a: Role in the development of Osteoarthritis during Obesity

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Conflict of interest: None

OBJECT: We have previously reported that miR-34a is elevated in end-stage OA synovial fluid compared to early OA. Studies have shown that miR-34a is also elevated in obesity; however, no studies have examined the role of miR-34a in the development of OA during obesity. We hypothesize that during obesity expression of miR-34a is elevated and contributes to OA pathophysiology. **METHODS:** Mouse blood was collected at 9 weeks old (baseline) and at the end of a high-fat diet (HFD)/ lean-diet (LD). Human plasma was taken from end-stage OA patients undergoing total knee replacement. Patients with no comorbidities were segregated into non-obese (BMI=18.5-29.9 kg/m^2) and obese groups (BMI≧30 kg/m^2). Chondrocytes and synovial fibroblasts (SF) were transfected with 100nM miR-34a mimic or inhibitor for qRT-PCR or Western blot. *In-vivo* grade mir-34a mimic or inhibitor was injected intra-articularly in mouse knee joints. **RESULTS:** Human plasma miR-34a was significantly upregulated in obese end-stage OA patients compared to non-obese patients. HFD mice expressed sig. higher plasma miR-34a compared to baseline mice and LD controls. In-situ hybridization showed HFD mouse knee joints also expressed sig. higher levels of miR-34a than LD mouse knees and localized to cartilage and synovial membrane. Mir-34a mimic-treated chondrocytes sig. increased expression of catabolic markers and reduced expression of anabolic markers, while treatment with mir-34a inhibitor reversed these effects. Mir-34a mimic-treated SFs sig. increased expression of fibrotic and inflammatory markers, while mir-34a inhibitor reversed these effects. Interestingly, intra-articular injection of miR-34a mimic induced cartilage damage and loss of proteoglycan content; however, mir-34a inhibitor injections in surgically-induced OA mice was cartilage-protective. **CONCLUSIONS:** This study will be the first to elucidate a mechanistic role for miR34a in the development of OA during obesity and its potential as a therapeutic target.

ICW1-2

Intra-articular injection of microRNA-181a-5p inhibitor alleviates cartilage degeneration in both lumbar facet and knee osteoarthritis animal models

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Conflict of interest: None

Objective: We recently discovered miR-181a-5p as a mediator in destroying facet cartilage (Filed in US patent; No 62/299,305). This led us to hypothesize that inhibition of miR-181a-5p may be a therapeutic target in facet joint osteoarthritis (FJ-OA). In this study, we tested the effect of miR-181-a-5p inhibition on cartilage degeneration not only in FJ-OA but Knee OA animal model. **Methods:** Needle puncture-induced FJ-OA model in Sprague-Dawley rats and Knee OA model (DMM) in C57BL/6 mice were used. MiR-181a-5p inhibitor (anti-sense molecule; 5μg/μl) or control inhibitor (negative scramble) were injected into FJs (L4/5-L5/6) at 3 and 6 wks or mice knee joints at 2 and 4 wks (n=10 rats or mice/ group) post-surgeries. Histopathological analysis including safranin O, in situ hybridization (ISH) and immunohistochemistry (IHC) assessments (MMP13, PARPp-85, COLX and COLII cleavage markers) was performed at 12wks for FJs and 10 wks for knee OA models. **Results:** ISH showed a significant decrease in the expression of miR-181a-5p in both facet and knee cartilage injected with miR-181a-5p inhibitor compared to

those cartilage injected with control inhibitor. Blinded OARSI scoring revealed that, intra-articular injection of miR-181a-5p inhibitor resulted in a marked reduction in the severity of FJ-OA and knee OA associated with decreased degree of cartilage degeneration, proteoglycan loss and chondrocyte cellularity compared to control. IHC assessments further revealed markedly reduced catabolic/chondrocyte cell death activities and amount of collagen depletion in cartilage in miR-181-a-5p inhibitor-treated facet and knee joints compared to control. **Conclusion:** Our preclinical data strongly suggests that local inhibition of miR-181-a-5p is a potential therapy to halt both facet and knee cartilage degeneration during OA. We are currently focusing on identifying the most effective dose, injection frequency as well as safety profile of this miRNA inhibitor in pre-clinical animal models.

ICW1-3

Determination of a Method for Metabolite Signature Selection and Classification Modeling to Predict Knee Osteoarthritis

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Conflict of interest: None

Objective: Age, sex, and BMI can help to predict knee osteoarthritis (OA) patients from healthy adults (HV). The metabolome, an overall output of metabolic processes occurring within an individual, and specific levels of select metabolites can also be used to help with disease diagnosis. However, metabolite selection methods and modeling algorithms that best identify metabolites capable of predicting OA have not been well established. We sought to determine a method that was capable of effectively identifying metabolite signatures predictive of OA in demographically-stratified populations. Methods: Phosphatidylcholine (lysoPC) and lyso (PC) analogues from plasma of OA patients undergoing total knee replacement and HV were measured by metabolomics. Cohorts were stratified by age, sex and BMI. Analogue signatures were determined by generating univariate area under the receiver operator curve (UAUC) values from 1000 bootstrapped training and test sets. Metabolites with UAUC > 0.5 at the 2.5% quantile of the empirical distribution were selected as capable of predicting OA from HV within strata. Three multivariate classification algorithms were tested using each signature. The most consistent algorithm was determined by the minimum difference between training and test set AUC values, derived from 1000 resamplings. Results: The metabolite signature from males age > 50 years old encompassed the majority of identified metabolites in other strata, suggesting lysoPCs and PCs were dominant indicators of OA in older males. Principal component regression with logistic regression was the most consistent classification algorithm tested. Using this algorithm, the males age > 50 years old signature had fair power to differentiate OA patients from HV. Conclusions: Individual levels of lysoPC and PC analogues may be indicative of individuals with OA in older male populations. Our metabolite signature modeling method is likely to increase classification power in validation cohorts.

ICW1-4

High-Fat Diet-Induced or Surgically-induced Acceleration of Osteoarthritis (OA) is Attenuated by Inhibition of Autotaxin

Poulami Datta[1,2,3,4], Evgeny Rossomacha[1,2,3,4], Helal Endisha[1,2,3,4], Carolen Younan[1,2,3,4], Kaushik H Borada[1,2,3,4], Kathleen E Pritchett[1,2,3,4], Nizar N Mahomed[1,2,3,4], Rajiv Gandhi[1,2,3,4], Jason S Rockel[1,2,3,4], Mohit Kapoor[1,2,3,4]
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Conflict of interest: None

Objective: Obesity increases the risk of developing Osteoarthritis (OA). Recent evidence suggests that after weight loss, a metabolic adaptation persists long after alteration of body composition. In high fat diet (HFD)-fed mice, which show acceleration of OA, we identified a signature rich in lysophosphatidyl cholines (lysoPC) analogues that was sustained up to at least 9-months of age. We also identified that changes in leptin in the HFD-fed mice knee joints are sustained and that leptin increases the expression of MMP13 by an autotaxin (ATX)-dependent mechanism. ATX is an enzyme responsible for the conversion of lysoPC to the inflammatory mediator lysophosphatidic acid (LPA). Presently, we sought to identify if local pharmacological inhibition of ATX can attenuate diet or surgically-induced OA pathogenesis in vivo and the contribution of LPA to the catabolic phenotype of chondrocytes in vitro. **Methods:** Nine week-old mice were fed HFD for 18 weeks or 9 week-old mice were subjected to surgically-induced OA. ATX antagonist was injected intra-articularly in the knee joints and subsequent knee joint pathology was evaluated. Primary human chondrocytes were treated with various agents, including ATX antagonist, and the release/expression of selected metabolites or enzymes was determined. **Results:** Local injection of ATX antagonist reduced the degree of OA pathogenesis surgically induced OA models compared to saline injected controls. In vitro, we found that LPA increased the expression of MMP13, consistent with our previous observations that ATX antagonist blocks MMP13 expression. **Conclusion:** Inhibition of ATX attenuates surgically-induced OA, likely by modulating the production of catabolic MMP13 by blocking the conversion of local lysoPCs to LPA. We continue to examine pre-clinical efficacy of ATX inhibition in HFD-fed mice. Our data, to date, suggests pre-clinical efficacy of ATX to limit OA progression.

ICW1-5

The Relationship Between Human Cartilage glycoprotein 39 and Rapid Joint Destruction In Early Osteoarthritis

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Conflict of interest: None

Objective: This study aimed to correlate the levels of Human cartilage glycoprotein 39 (HC gp-39) in the serum and synovial fluid (SF) of patients with primary osteoarthritis (OA) with the cartilage thickness, osteophyte formation by ultrasonography (US) and other disease parameters. Methods: HC gp-39 levels were obtained from serum and SF of 60 early OA patients and from serum of 40 healthy controls using an enzyme-linked immunosorbent assay (ELISA) method. All patients underwent complete clinical assessment included The Western Ontario and McMaster Universities Arthritis Index (WOMAC) scores. The Kellgren and Lawrence (KL) grade was used to assess the severity of knee OA on a plain radiograph and US evaluation was performed to assess radiological progression. Results: Serum HC gp-39 levels (163±57.8 ng/ml) in patients group were significantly higher compared to the serum levels in the control group (62.8±16.9 ng/mL), ($p<0.001$). In patients group, SF levels of HC gp-39 were considerably higher (770.9±88.5 ng/mL) compared to the serum levels (66.3±5.7 ng/mL), ($p<0.001$). SF levels of HC gp-39 were strongly correlated with WOMAC ($r=0.51$, $p<0.05$) and serum levels of HC gp-39 were strongly correlated with reduced cartilage thickness on medial condyle of the femur ($r=-0.35$, $p<0.05$). There is a considerable difference in HC gp-39 levels mean values between the patients with shorter and longer osteophytes on tibia and femur condyles (p=0,000). Conclusion: Elevated serum and SF levels of HC gp-39 in OA patients is associated with more radiological progression and may give some idea about the pattern of joint destruction suggesting that it could be a useful marker to reflect OA severity. Moreover, significantly elevated HC gp-39 levels in SF compared to suggesting cartilage as a significant source of

HC gp-39 in OA and support a possible pathogenic role in OA.

ICW1-6

The association between osteoarthritis and sleep duration in Koreans: a nationwide study

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Conflict of interest: None

[Object] Osteoarthritis (OA) is the most common musculoskeletal disease in old age. OA causes chronic pain, which reduces the quality of life of patients. Sleep is an important factor in the recovery, and adequate sleep is important for quality of life. Several features of patients with OA can affect sleep time, and sleep also affects OA. We investigated the relationship between OA and sleep duration. [Methods] Data for 2010-2012 were collected from the Korea National Health and Nutrition Examination Survey. We included 11,546 participants (4,916 men and 6,630 women). Patients with OA were defined as participants with knee/hip joint pain and radiographic changes of the knee/hip joints. Sleep time was divided into 4 sections as follows: 1) 0-3 hours, 2) 4-5 hours, 3) 6-7 hours, and 4) ≧8 hours. Sleep time of 6 and 7 hours was the most frequent, and set as the reference time. [Results] In the multiple logistic regression model, the patients who slept for 0-3 and 4-5 hours had odds ratios (ORs) of 2.44 (95% confidence interval [CI] 1.22-2.36) and 1.41 (95% CI 1.03-1.93) for men, and 1.73 (95% CI 1.26-2.37) and 1.29 (95% CI 1.11-1.51) for women, respectively, for having OA. [Conclusions] The prevalence of OA was lowest in the participants who had 6-7 hours of sleep, and progressively increased with shorter sleep time. Thus, sleep duration was significantly associated with OA.

ICW2-1

Tumor necrosis factor inhibitors influence the apoptosis of inflammatory cells in rheumatoid synovial tissues

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Conflict of interest: None

[Object] Inflammatory cytokines were reported to increase in the blood and synovial tissue in the patients with rheumatoid arthritis (RA). They have potentials of powerful anti-apoptotic effects and relates to the failure of apoptosis in RA. Tumor necrosis factor inhibitor (TNFi) have been successfully used in the preventing of joint destruction in RA, however, 20-30 % of them using biologics are still non-responders or show only minor improvement. The aim of this study is to examine the effect of TNFi (infliximab, etanercept and adalimumab) in the synovial tissue samples of RA patients with TNFi (TNFi group) compared to them with non-biological therapy (Non-BIO group). [Methods] Synovial tissue samples of 40 RA (25 TNFi and 15 Non-BIO samples) were immunohistochemically stained with cleaved activated caspase-3 (casp-3) and TUNEL staining. Positive cells were counted per 10 fields (x 200) by microscopy. Casp-3 positive cells were analyzed by double immunofluorescent methods with DC-markers (DC-LAMP, CD123), Macrophage (CD68), T cell (CD2), B cell (CD20), fibroblast-like cell (5B5). Synovial inflammation was estimated by Krenn grading score. [Results] TNFi and non-BIO group was shown the similar grading scores (1.8 vs 1.7) and DAS28CRP4 (3.6 vs 4.0), CRP (1.2 vs 1.4). Casp-3 and TUNEL positive cells were observed significant higher counts per fields in lymphoid aggregation and lining layer in TNFi samples compared to non-BIO (16 vs 7 and 9 vs 1 in lymphoid aggregation, p< 0.01). Casp-3 immunoreactivity was also confirmed in T cells and fibroblast-like cells, macrophage cells by immunofluorescent staining. [Conclusions] TNFi influence the apoptosis of inflammatory cells in rheumatoid synovial tissues compared to that in non-BIO. BIO therapy including TNFi may improve abnormality of apoptosis in chronic inflamed-synovitis in RA inflamed-joints.

ICW2-2

The efficacy and safety of bDMARDs in 2917 patients with rheumatoid arthritis (RA) ~ a retrospective cohort study FIRST registry ~

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Conflict of interest: None

Objective: We conducted a retrospective analysis of the retention rates for 7 biological treatments and discontinuation reasons and verified the efficacy and safety of bDMARDs in real-world patients with RA. Methods: We used clinical data obtained from FIRST registry which comprises University of Occupational and Environmental Health hospital in Japan between September 2003 and May 2017. We included RA patients who fulfilled the ACR 1987 revised or 2010 ACR/EULAR RA classification criteria staring the biological treatment. The Kaplan-Meier survival curves were used to analyze retention rates. The Cox proportional hazards regression model was used to identify the influencing factors for adverse events. $P < 0.05$ was considered statistically significant. Results: In total 2917 patients (Infliximab (IFX) 668, Etanercept (ETN) 494, Adalimumab (ADA) 522, Tocilizumab (TCZ) 494, Abatacept (ABT) 493, Golimumab (GLM) 104, Certolizumab (CZP) 142) were included. The retention rates for each biologic treatment at 12 months after treatment were almost 80%. The ratio of remission and low disease activity were almost 60%. The major reasons of discontinuation among observation period were remission, inefficacy and adverse event. Infection included pneumonia were 30.9% in adverse event. It was almost onset within 2 years. In the Cox proportional hazard model, the risk of adverse event and pneumonia was significantly increased in patient receiving prednisolone; the hazard ratio (95%CI) was 1.14 (1.00-1.29) for adverse event (p=0.0351) and HR (95%CI) was 1.13 (1.02-1.26) for pneumonia (p=0.0256). Conclusions: Although bDMARDs showed high efficacy for real-world patients with RA, we should be aware of adverse events including pneumonia in RA patients with oral corticosteroids and assess their clinical profiles before biological treatment.

ICW2-3

Drug survival rates and reasons for discontinuation in elderly patients with rheumatoid arthritis (RA) treated with biologic disease-modifying antirheumatic drugs (bDMARDs)

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Conflict of interest: None

[Object] To investigate retrospectively the treatment continuation rate of bDMARDs therapy and to detect risk factors for discontinuation in elderly RA patients. [Methods] RA patients who received bDMARDs therapy over the age of 75 (abatacept [ABT], 147; etanercept [ETN], 80; tocilizumab [TCZ], 52 patients) were examined between February 2011 and November 2017 in our institute. In ABT and ETN groups, 59 patients each were statistically selected by propensity score matching method to accommodate selection bias. [Results] Continuation rate after 5 years of ABT, ETN and TCZ was 53%, 38%, and 20%, respectively (ABT vs ETN, p=0.03). Matched patient characteristics (ABT/ETN) were as follows: median age 80/79 years, median disease duration 53/48 months, use of corticosteroid (CS) in 30/33%, use of MTX in 58/59%, median DAS-CRP of 5.03/5.38, pre-existing lung disease in 54/54%. Continua-

tion rate after 5 years of ABT (54%) was significantly higher compared with that of ETN (34%) (p=0.02). The cause of discontinuation (ABT/ETN) included inadequate response in 42/37%, adverse events (AEs) in 25/48%, and bio-free after remission in 17/4%. ETN group have more AEs compared with ABT; injection site reaction and drug eruption accounted for about half of the AEs. In the both groups, the use of CS was an independent risk factor for discontinuation (hazard ratio 2.5, p=0.01). [Conclusions] ABT therapy showed the high continuation rate and fewer AEs in elderly RA patients. The use of CS probably reduces the continuation rate of ABT and ETN therapy.

ICW2-4

The Analysis of Successful Down-titration of Biological DMARDs among RA Patients in the real world

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Conflict of interest: None

[Object] Clinical trials have shown that if a patient is in sustained remission, biological disease-modifying anti-rheumatic drugs (bDMARDs) therapy can be tapered in rheumatoid arthritis (RA). However, little is known about tapering bDMARDs in the real world. We investigated the predictive factors associated with the successful down-titration of bDMARDs in RA patients. [Methods] This study included consecutive RA patients who fulfilled 1987 ACR and/or 2010 ACR/EULAR classification criteria and treated with bDMARDs (infliximab, adalimumab, etanercept, golimumab, certolizumab-pegol, tocilizumab, and abatacept) for longer than 6 months followed at two Yokohama City University Hospitals. The patients receiving stable and standard dose treatment were defined as SD group, while the patients receiving down-titration were defined as DT group. Among the DT group, we divided patients into two groups: FL group who flared after tapering bDMARDs and SR group who sustained remission. We retrospectively analyzed clinical characteristics, treatment regimen between two groups respectively. [Results] 347 patients (SD 251, DT 96) were recruited. The mean age was 63 ± 14 years and 84% were female. A univariate analysis showed that patients with biologics naïve (p = 0.001), younger age at onset (p = 0.019), younger age at the beginning of bDMARD (p = 0.022), and low CRP levels (p = 0.001) could challenge to tapering bDMARDs. A multivariate analysis revealed that the low CRP at baseline was associated with successful tapering bDMARDs (OR 1.24, p = 0.041). Among DT group, FL group was 29 (30%). There were no significant differences between FL Group and SR Group. Among the FL group, the duration from tapering bDMARDs to flare was 21 [15-31] months. [Conclusions] Tapering bDMARDs might be achieved in RA patients who have low CRP at the baseline. Although we should continue to monitor the activities after tapering bDAMRDs, most of the patients could sustain the remission over one year.

ICW2-5

Long term outomes after discontinuation of adalimumab in rheumatoid arthritis patients with achieving remission: 5-year data of the HONOR study

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Conflict of interest: None

[Object] Purpose of this study is to investigate the possibility of discontinuing adalimumab (ADA) for 5 years without flaring, and to identify enabling factors with RA patients to remain ADA-free. [Methods] Patients receiving ADA and methotrexate (MTX) who maintained disease activity score 28 (DAS28)-erythrocyte sedimentation rate (ESR) remission (<2.6) for 6 months and who subsequently agreed to discontinue ADA were enrolled. 52 patients who went on ADA discontinuation were studied for 5 years. The effect of discontinuation ADA on clinical disease activity, functional disability and radiographic progression were evaluated by DAS28-ESR, by a health assessment questionnaire-disability index (HAQ-DI) and by the modified total Sharp score, respectively. [Results] Out of the 46 patients who were completed 5 years follow up, 11 (24%) were maintained in DAS28-ESR<2.6 and 15 (33%) in DAS28-ESR≦3.2. Among the patients who sustained DAS28-ESR≦3.2 during ADA discontinuation, 89% remained in structural remission and 91% in functional remission. A logistic regression analysis showed that DAS28-ESR at baseline significantly predicted a DAS28-ESR<2.6 maintained after discontinuation of ADA, and a receiver-operating characteristic (ROC) analysis showed that the cut-off value of DAS28-ESR at discontinuation was 1.61. Comparison between mild (1.61<DAS28-ESR<2.6) and deep (DAS28-ESR≦1.61) remission, 50% patients with deep remission were significantly achieved sustain remission during ADA discontinuation (p=0.022). A sub-analysis of compare early (≦2 years) and established (>2 years) RA revealed that higher proportion of remission were identified in early RA patients. ADA readministration to patients with flare was effective in returning DAS28-ESR≦3.2 within 1 year in 70% patients. [Conclusions] These data indicate that the possibility of remaining ADA-free for 5 years in RA patients who had done early intervention and deep remission at the timing of ADA-free.

ICW2-6

Factors associated with the maintenance of biological DMARDs-free remission in rheumatoid arthritis - ANSWER cohort study -

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Conflict of interest: Yes

Objectives: Clinical remission can be maintained after discontinuation of biological DMARDs (bDMARDs-free remission; BFR) in some patients with rheumatoid arthritis (RA). However, it is not known which bDMARDs is advantageous for achieving BFR, or in what condition BFR can be considered. The aim of this study is to determine the factors that are associated with the maintenance of BFR in typical clinical practice. Methods: RA patients were enrolled from the multicenter observational registry in Japan. RA patients who has achieved clinical remission (DAS28 CRP<2.6) at the time of bDMARDs discontinuation were included. Serial disease activities and treatment changes were followed up and BFR failure was defined if the disease activity exceeded the remission cutoff or bDMARDs were restarted. Results: A total of 181 patients were included. BFR was maintained in 21.5 % of the patients at one year after the discontinuation of bDMARDs. BFR was more successfully achieved after discontinuation of anti-TNF antibodies (IFX, ADA, and GLM; median BFR survival 98 days; 95% CI, 70-178)), followed by CTLA-4Ig (ABT; 73 days, 95% CI: 32-245), anti-TNF receptor/PEG (ETN, and CZP; 63 days, 95% CI: 35-105), and anti-IL-6 receptor antibody (TCZ; 42 days, 95% CI: 29-56). After multivariate analysis, sustained remission (>6 months) (Hazard ratio for BFR failure 0.50, 95% CI: 0.31-0.77, p<0.01), Boolean remission at the time of discontinuation (HR 0.62, 95% CI: 0.42-0.92, p=0.02), non-use of glucocorticoids at the time of bDMARDs discontinuation (HR 1.54, 95% CI: 1.08-2.20, p=0.02) remained as independent factors associated with BFR. Conclusion: BFR

can be achieved in some RA patients after discontinuation of bDMARDs in daily clinical practice. Anti-TNF antibodies are advantageous for achieving BFR than anti-TNF receptor/PEG or other bDMARDs. Sustained remission, Boolean remission, and free of glucocorticoid use at the time of bDMARDs discontinuation are important for achieving BFR.

ICW3-1

Th17 cell migration and CCL22/17-CCR4 axis are crucial in the crescentic glomerulonephritis model: the translational research from bedside to bench

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Conflict of interest: Yes

[Object] We have recently reported that CCL22/17, specific ligand of CCR4 significantly increased in remission patients with ANCA associated vasculitis (AAV) after monotherapy of anti-IL-6 receptor antibody (Tocilizumab). Recently, it has been reported that immuno-pathogenic Th17 cells migrate to the kidney via CCL20-CCR6 axis in crescentic glomerulonephritis models. The objective of this study is to elucidate the mechanism of amelioration/deterioration by the chemokines and cytokines in the crescentic glomerulonephritis model (Masugi nephritis), which is the main symptom of AAV. [Methods] We established the accelerated crescentic glomerulonephritis model and analyzed various strains of single knock out (KO) mice (IL-23p19-/-, IL-22-/-, IL-17A-/-, CCR6-/-, and RORgt-/-) and CCR4/6 double KO (DKO) mice. The outcome was evaluated by crescents formation, interstitial inflammation, renal function and flow cytometry analysis of mononuclear cells isolated from the kidney. [Results] IL-23p19-/-, IL-17A-/-, CCR6-/-, and RORgt-/- mice developed less severe nephritis, frequency of glomerular crescent formation and interstitial inflammation. However, CCR4/6 DKO mice developed more severe nephritis compared with CCR6-/- mice and wild type mice. Flow cytometry analysis revealed that the proportion of IL-17A+ cells infiltrated into kidney were significantly increased, whereas that of FoxP3+/CD4+ cells was decreased in CCR4/6 DKO mice compared to wild type mice. [Conclusions] Our results suggested that Th17 cell is the major immuno-pathogenic cells in the crescentic glomerulonephritis model and CCL22/17-CCR4 axis plays a crucial role in the amelioration of disease activity.

ICW3-2

Sema6D reverse signaling controls lipid metabolism in macrophage polarization, linking mTOR to PPARg

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Conflict of interest: None

[Object] Polarization of macrophages into the pro-inflammatory M1 or alternative M2 states has distinct metabolic requirements. Emerging evidence points to a critical role of mTOR signaling in macrophage polarization. However, it remains unclear how mTOR regulates metabolic status to promote the activation and polarization of these cells. This work aims to elucidate the precise mechanism of mTOR-regulated M2 macrophage polarization. [Methods] We first performed a microarray analysis to explore the precise molecular mechanisms by which mTOR activation states regulate M2 macrophage polarization. Next, we examined the role of the identified molecule in M2 macrophage polarization. Finally, we investigated whether the identified molecule is required for maintenance of immune tolerogenic properties *in vivo*. [Results] Inhibition of mTOR or loss of Sema6D blocked M2 macrophage polarization, concomitant with severe impairments in PPARγ expression, uptake of fatty acids, and lipid metabolic reprogramming. In addition, we found that a tyrosine kinase, c-Abl, which associates with cytoplasmic region of Sema6D, is required for PPARγ expression. Furthermore, Sema6D-dependent PPAR signals are crucial for generation of intestinal resident CX3CR1^{hi} macrophages and prevent development of colitis *in vivo*. [Conclusions] Sema6D reverse signaling controls M2 macrophage polarization, coupling immunity and metabolism via PPARγ.

ICW3-3

Canonical TGF-beta signaling via C-terminally phosphorylated Smad3 and Smad4 suppresses Th17 differentiation

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Conflict of interest: None

[Object] Interleukin (IL)-17-producing CD4$^+$ T helper cells (Th17) are responsible for the pathogenesis of autoimmune diseases including rheumatoid arthritis and IL-6 and transforming growth factor (TGF)-β are essential for the induction of Th17. We have previously reported that non-canonical TGF-β signaling via ERK-linker phosphorylated Smad2-STAT3 enhances, whereas unphosphorylated Smad3 suppresses STAT3-induced Th17 differentiation. However, the roles of canonical TGF-β signaling via C-terminally phosphorylated TGF-β receptor-regulated Smads (R-Smads) and Smad4 in Th17 differentiation remain largely unknown. We sought to determine the role of canonical TGF-β signaling in IL-6-induced Th17 differentiation. [Methods] The roles of Smad3 and Smad4 in STAT3 signaling for Th17 cell differentiation were investigated using *in vitro* Th17 cell polarization culture and *in vivo* murine collagen-induced arthritis (CIA) model with *Smad3*$^{+/+,\ -/-}$ mice and *Cd4Cre; Smad4*$^{+/+,\ fl/fl}$ mice. [Results] T cell-specific Smad4 deletion exacerbated CIA with increased Th17 in the arthritic lesions and draining lymph nodes, which phenocopied Smad3 deficient mice. Deletion of Smad3 or Smad4 resulted in enhanced phosphorylation of STAT3 at Y705 and S727 in Th17 cells. Smad4 in cooperation with pSmad3C, but not pSmad2C, transactivated the negative regulators of STAT3 such as the *Socs3*, *Shp1* and *Shp2* genes. Expression of SOCS3, SHP1 and SHP2 was significantly decreased in T cells infiltrated in the arthritic joints of T cell-specific Smad4 deficient mice. [Conclusions] Canonical TGF-β signaling rather suppresses IL-6-induced STAT3 phosphorylation and Th17 differentiation by upregulating the negative regulators of STAT3.

ICW3-4

The Role of Follicular Helper 17 T cells in Glucose-6-phosphate Isomerase Induced Arthritis

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Conflict of interest: None

[Object] Tfh in rheumatoid arthritis has drawn an attention recently, but its function remains unclear. In addition, little is known about the regulation of antibody desialylation, which causes autoimmune activation. The purpose of this study was to explore the role of Tfh in glucose-6-phosphate isomerase (GPI) induced arthritis (GIA), which mouse model was dependent on T cells, B cells and IL-17. [Methods] 1) Fluctuation of Tfh and its subsets in draining lymph nodes (dLNs) were analyzed by flow cytometry. Subsequently, expression of co-stimulatory molecules were assessed among these subsets. 2) Localization of Tfh and the subsets were analyzed by immunofluorescence (IF) staining. 3) Serial changes of plasmablast and plasma cell population in dLNs were analyzed by flow cytometry. 4) Anti-GPI antibody production from plasmablast was measured in the existence of Tfh. The titers in GIA sera were measured by ELISA. 5) The mRNA of ST6 beta-galactoside alpha-2,6-sialyltransferase 1 (st6gal1), the responsible protein of antibody sialylation, in plasmablasts was measured by quantitative PCR. [Results] 1) Tfh was increased in GIA. It was peaked at day 7; the onset of arthritis, and IL-17

producing Tfh (Tfh17) was specifically increased at the same time. Moreover, OX40 expression in Tfh17 was higher than other subsets. 2) IF showed that Tfh17 was accumulated in germinal center of dLNs. 3) Plasmablast and plasma cell were most increased at day 7, which was consistent with Tfh. 4) Anti-GPI antibody production was up-regulated in the existence of Tfh and GPI *in vitro*. However, its titer in sera was gradually elevated over time *in vivo*. 5) St6gal1 expression in plasmablast was decreased at day 7 and recovered at day 28. This fluctuation was inversely correlated with the arthritis course. [Conclusions] Tfh, particularly Tfh17, might have a crucial role in the development of arthritis via plasmablast activation and possibly regulating desialylation of autoantibody in GIA.

ICW3-5

Tofacitinib Facilitate the Expansion of MDSCs and Suppress the Progression of Interstitial Lung Disease in SKG Mice

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Conflict of interest: None

[Background] SKG mice, which are rheumatoid arthritis (RA) model, develop not only arthritis but interstitial lung disease (ILD) resembling RA-ILD. Myeloid-derived suppressor cells (MDSCs) are heterogeneous immature myeloid cells with suppressive functions. We previously reported that tofacitinib, which is JAK inhibitor, facilitates the expansion of MDSCs and ameliorates arthritis in SKG mice. [Object] To elucidate the effect of tofacitinib on ILD in SKG mice. [Methods] SKG mice were induced ILD by Zymosan A (ZyA) injection. Four weeks after the ZyA-injection, tofacitinib (20 mg/kg) or DMSO was intraperitoneally injected three times per week for eight weeks. We evaluated lung-infiltrating cells by flow-cytometry, and severity of ILD by HE staining. DC generation and T-cell proliferation assays were performed in vitro. [Results] Tofacitinib significantly suppressed the progression of ILD compared to control. Flow cytometry revealed that tofacitinib significantly increased MDSCs and suppressed Th17 cells, group 1 innate lymphoid cells (ILC1s), and GM-CSF^{+}ILCs in vivo. MDSCs expanded in the inflamed lungs also suppressed T cell proliferation in vitro. [Discussion] To our knowledge, this is the first report to show that tofacitinib is effective for RA-ILD model. Tofacitinib not only directly but indirectly suppress the pathogenic lymphocytes by facilitating the expansion of MDSCs. These results indicate a potential therapeutic effect of tofacitinib for RA-ILD. [Conclusion] Tofacitinib facilitate the expansion of MDSCs, which in turn suppress the progression of ILD in SKG mice.

ICW3-6

Inhibition of mTOR pathway and glutaminolysis facilitates the expansion of myeloid-derived suppressor cells and synergistically ameliorates arthritis in SKG mice

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Conflict of interest: None

[Object] Myeloid-derived suppressor cells (MDSCs) are a heterogeneous population of immature cells that increase in the pathological state such as tumor or inflammation and have the immunosuppressive ability. MDSCs have been reported to ameliorate arthritis in several mice models. mTOR pathway and glutaminolysis are known to be activated in the differentiation from myeloid progenitors to mature myeloid cells such as dendritic cells, macrophages, or osteoclasts. The aim of this study is to evaluate the effect of the inhibition of mTOR pathway and glutaminolysis on MDSCs in a mouse model of rheumatoid arthritis. [Methods] Bone marrow (BM) cells from untreated Balb/c mice were cultured for 5 days under GM-CSF stimulation with four patterns of drugs; 1) DMSO (control), 2) rapamycin, 3) 6-Diazo-5-oxo-L-norleucine (DON; a glutamine analogue), or 4) the combination of rapamycin and DON. Cultured BM cells were analyzed by flow cytometry. Cultured MDSCs were isolated by MACS and analyzed their immunosuppressive characters by co-culture with CFSE-dyed CD4^{+} T cells. The four patterns of drugs described above were administered intraperitoneally to arthritic SKG mice induced by Zymosan A injection. [Results] We found that DON (separately or in combination) suppressed the differentiation of dendritic cells in a dose-dependent manner and the addition of rapamycin on DON suppressed the differentiation of macrophage *in vitro*. Most DON-treated BM cells showed the phenotype of MDSCs, large part of which were Ly6G^{+} polymorphonuclear MDSCs (PMN-MDSCs). On the other hand, rapamycin (separately or in combination) significantly increased the TGF-β expression and the inhibitory capacity of Ly6G^{+} PMN-MDSCs. The combination of rapamycin and DON synergistically suppressed arthritis in SKG mice *in vivo*. [Conclusions] The combination of rapamycin and DON facilitates the expansion of PMN-MDSCs *in vitro* and synergistically ameliorates arthritis in SKG mice *in vivo*.

ICW4-1

Toll-like receptor 7 (TLR7) is upregulated on peripheral B cells and associated with disease activity and damage in primary Sjogren syndrome

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Conflict of interest: Yes

[Object] Primary Sjogren Syndrome (pSS) is characterized by activitition of B cells, increased production of RNA-associated antibodies and elevated proportion of transitonal B cell. Toll-like receptors 7 (TLR7) have been reported promoting the effects above in some murine models of SS. We took up this study to identify if TLR7 expression is associated with disease activity and the role of TLR7 in pSS. [Methods] 21 pSS patients and 12 healthy controls (HCs) were selected. The mRNA expression of TLR7 was determined by real-time PCR on peripheral B cells of both pSS patients and HCs. We measured BAFF serum concentrations by ELISA, and the BAFF-R, TACI and BCMA expression was analyzed on each B cell subset (CD27^{-}CD24^{hi}CD38^{hi}/transitional B cell; CD27^{-}CD24^{lo}CD38^{lo}/naive B cell;) by flow cytometry. The results were compared among patients with diversed degree of disease activity and damage to HCs. [Results] The expression level of TLR7 mRNA were elevated in pSS patients compared with HCs (p=0.004), and correlated with the SSDAI (SS disease activity index) (r=0.803; p=0.009) and the SSDI (SS damage index) (r=0.881; p=0.002). Serum BAFF concentrations increased in pSS patients compared with HCs (p=0.041), but not corrleted with TLR7 expression. TACI expression in pSS patients in total B cells and traditional B cells compared to HCs were elevated and are both associated with TLR7 expression (r=0.763, p=0.048, r=0.820, p=0.004, respectively). A lower BAFFR expression was seen in transitional B cell compared with HCs (p=0.018). BCMA expression was of no significance. [Conclusions] Increased TLR7 expression on peripheral B cells were associated with disease activity and damage, suggesting that TLR7 may play a role in the development in pSS. Increased serum BAFF concentrition and TACI expression were associated with TLR7 expression, indicating that BAFF may regulate TLR7 expression through TACI according to previous studies. TLR7 may be a potential treatment target of pSS and worth of further study.

ICW4-2

Comparison of clinical features between young and elderly onset in patients with primary Sjogren syndrome

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Conflict of interest: None

[Object] The onset of primary Sjogren's syndrome (pSS) varies in age. The aim of this study was to compare clinical features between re-

productive age and above onset in patients with pSS. [Methods] All patients with pSS diagnosed with 2016 ACR/EULAR classification criteria in our department from 1995 to 2017 were included. Patients were divided into 2 groups according to the age of diagnosis at 45 years old; young onset and elderly onset. The symptoms and laboratory findings were compared. [Results] Six hundred sixteen pSS patients were enrolled. Five hundred seventy four (93%) were female. One hundred fifty five (25%) were young-onset and the remaining 461 (75%) were elderly-onset. The mean age at pSS diagnosis was 34.9 and 62.5 years old, and the observation period was 5.20 and 4.75 years, respectively. At diagnosis, the positivity of anti-SS-A antibody (96.1 vs 78.2 %, p<0.001), anti-SS-B antibody (60.7 vs 39.8 %, p<0.001), and rheumatoid factor (56.6 vs 41.3 %, p=0.001) were significantly higher in the young-onset patients than the elderly-onset patients. Also, the levels of IgG (2126 vs 1852 mg/dl, p<0.001) and IgM (156 vs 143 mg/dl, p<0.001) were significantly higher in the young-onset patients. While the elderly-onset patients were more frequently complicated with pulmonary disease (7.4 vs 1.3%, p=0.003) and thyroid disease (14.3% vs 7.1%, p=0.02), the young-onset patients had higher rate of skin lesions (10.3% vs 2.2%, p<0.001). Anti-SSA and anti-SSB antibodies were more frequently seroconverted to negative. The increase in anti-SSA and anti-SSB titres during the observation period was 390 and 80 U/ml in the young and 233 and 25 U/ml in the elderly-onset patients. [Conclusions] Clinical and serological characteristics were different between young and elderly-onset patients with pSS, suggesting there may be difference in the pathogensis in pSS.

ICW4-3

Thymus and Activation-regulated Chemokine (TARC) as a Biomarker for IgG4-related Disease

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Conflict of interest: None

[Object] TARC, also known as chemokine ligand 17 (CCR17), is expressed in the thymus and is produced by dendritic cells, endothelial cells, keratinocytes and fibroblasts. TARC has affinity as a ligand for CCR4 and CCR8, which are predominantly expressed by Th2 cells. High serum concentration of TARC is determined in allergic diseases such as atopic dermatitis and bronchial asthma. Several studies have reported frequent atopic symptoms among patients with IgG4-related disease (IgG4-RD). We investigated the role of TARC as a biomarker in IgG4-RD, in which Th2 cytokines associate in disease states. [Methods] We evaluated the serum concentration of TARC from 29 IgG4-RD patients, 28 Sjogren syndrome (SjS) patients and 23 healthy controls (HC) by ELISA. We also analyzed the correlations between TARC concentration and clinical parameters. To investigate the biological effect of TARC toward pathogenesis in IgG4-RD, in vitro induction of plasmablasts from peripheral blood mononuclear cells (PBMCs) in patients with IgG4-RD by TARC was evaluated. [Results] We found that the serum concentration of TARC in the IgG4-RD was significantly higher than SjS and HC (IgG4-RD mean 486.1 pg/ml, SjS mean 121.3 pg/ml, HC mean 252.2 pg/ml). Serum concentration of TARC from IgG4-RD positively correlated with number of organ involvement whereas showed the correlation neither with serum IgG4 nor eosinophil number in peripheral blood. The patient groups which showed lung involvement had a high titer of TARC concentration. [Conclusions] Collectively, our data suggest that TARC is an essential Th2 cytokine in patients with IgD4-RD. TARC may be involved in the development of IgG4-RD through an aberrant induction of plasmablasts.

ICW4-4

T follicular helper cells and plasmablast axis promote the development of organ involvement in patients with IgG4-related disease

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Conflict of interest: Yes

[Object] To assess the role of an abnormal immune network in the pathology of immunoglobulin (Ig) G4-related disease (IgG4-RD). [Methods] Sixteen patients diagnosed with IgG4-RD at our institution were selected. Peripheral immunocompetent cells were immunophenotyped by multicolor flow cytometry to assess the association between clinical manifestation and pathological findings. [Results] Compared to healthy controls, IgG4-RD patients showed comparable proportions of T helper (Th) 1 and Th17 cells, but higher proportions of regulatory T (Treg) and follicular helper T (Tfh) cells. Further, the proportions of class-switched memory B cells and plasmablasts were higher in patients. Among all phenotypes, in particular, the plasmablast proportion increased from 4.2% (controls) to 16.5% (patients). The serum IgG levels were found to be correlated with the proportions of plasmablasts and Tfh cells, but not with those of other T cell subsets. In patients with extraglandular symptoms, only plasmablasts, Tfh cells, and memory Treg cells were increased. Histopathologic examination revealed a marked Tfh ($CD4^+$ $Bcl6^+$) cell infiltration; the increase of Tfh cells in the peripheral blood thus reflected the degree of Tfh cell infiltration into the tissue. Although steroid therapy reduced plasmablast and Tfh cell proportions, the memory Treg cell proportion remained unchanged. [Conclusions] The results of this study revealed that Tfh cells induced the differentiation of B cells into IgG- or IgG4-producing plasmablasts in patients IgG4-RD, which reflected the progression of organ damage. Our results also suggested that controlling the Tfh cell-plasmablast axis could be a novel therapeutic strategy for treating IgG4-RD.

ICW4-5

Evaluations of complement pathways in IgG4 related disease

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Conflict of interest: None

Objectives: In IgG4 related disease (IgG4-RD), hypocomplementemia is known to be seen. Complement pathways consist of three pathways, classical, alternative, and lectin pathways. We attempted to elucidate which complement pathway is mainly associated with IgG4-RD. **Methods:** Levels of complement elements and complement-associated elements, C2, C4b, C5, C5a, C9, factor D, factor I, and mannose-binding lectin (MBL) in preserved sera of patients with IgG4-RD at diagnosis were measured using multiplex bead-based assay. **Results:** This study included 28 IgG4-RD patients and age- and sex-matched 28 healthy donors. Patients with IgG4-RD had significantly lower levels of C2 and higher levels of C5 and C5a compared to healthy donors [33998 ng/mL vs. 54847 ng/mL (median), p=0.0123, 33347 ng/mL vs. 28153 ng/mL, p=0.0440, 16416 pg/mL vs. 9378 pg/mL, p=0.0066, respectively]. Levels of C2, C5 and C5a were not associated with clinical manifestations at diagnosis except for more lacrimal glands involvement in patients with lower C2 levels. There were no differences in factor D, which was associated with the alternative pathway, and MBL, which was associated with the lectin pathway. C2 There was no correlation between each CH50, C3 and C4, and levels of complement elements and complement-associated elements. In remission after the administrations of prednisolone, levels of C5a significantly decreased compared to levels of C5a at diagnosis (16305 pg/mL to 10029 pg/mL, p=0.0043). **Conclusions:** The classical complement pathway may be associated with IgG4-RD rather than the alternative pathway and the lectin pathway. We could not find associations between clinical manifestations at diagnosis and levels of C2, C5, and C5a.

ICW4-6

Clinical features of IgG4 related disease with hypocomplementemia

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Conflict of interest: None

[Object] To elucidate the clinical characteristics and prognosis of patients with IgG4-related disease (IgG4-RD) complicated with hypocomplementemia at diagnosis. [Methods] We included all patients who was diagnosed with IgG4-RD in Nagasaki University Hospital from July 2009 to September 2017 in the study. Baseline variables at diagnosis including clinical symptoms, laboratory data, imaging studies, and subsequent relapses were compared between the patients with and without hypocomplementemia. We defined hypocomplementemia as the status that serum C3 levels at diagnosis were below the lower normal limit. [Results] Excluded 9 patients because of loss of data regarding C3 levels at diagnosis, we finally included 35 patients with IgG4-RD. Fourteen patients (40%) had hypocomplementemia at diagnosis. Patients with hypocomplementemia had significantly more ocular and lacrimal glands involvement (10 [75%] vs. 5 [24%], p=0.01), lymph node involvement (12 [86%] vs. 9 [43%], p=0.02), lung involvement (5 [36%] vs. 1 [4%], p=0.03) and renal involvement (5 [36%] vs. 0 [0%], p=0.006). Patients with hypocomplementemia had more numbers of involved organs compared to patients without hypocompplemetemia (2 [IQR: 1-4] vs. 1 [1-2], p=0.0002). Patients with hypocomplementemia had significantly higher eosinophil (365 [238-723] vs. 148 [85-335], p=0.006), sIL2-R (1275 [650-2021] vs. 431 [305-526], p=0.0003), IgG (2902 [2181-4109] vs. 1731 [1268-2120], p=0.0017), IgG4 (1195 [622-1790] vs. 215 [160-498], p=0.0002) and IgG4/IgG ratio (41 [24-50] vs. 15.3 [10.4-23.9], p=0.0006). Assessed by a log-rank test, the difference of the relapse-free survival rate after remission between two groups was not seen (p=0.17). [Conclusions] Conclusions: The clinical characteristics of IgG4-RD differed depending on whether or not patients were complicated with hypocomplementemia at diagnosis.

ICW5-1

Discovery of Novel Long Noncoding RNAs in Rheumatoid Arthritis Based on Next-Generation Sequencing Approach

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Conflict of interest: None

[Object] Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by chronic inflammation and destruction of synovial joints, and occurring in approximately 1.0% of general population. Long noncoding RNAs (lncRNAs) have been received wide attention as key molecules that mediate a variety of physiological and pathological processes by regulating gene expression. However, the role of lncRNAs in the pathogenesis of RA is poorly understood. Here, we performed the analysis of lncRNA profiling in the synovium from the patients with RA. [Methods] High quality total RNAs were extracted from the synovium of RA (n=8) and osteoarthritis (OA) (n=4) patients, and the total RNAs quality and quantity were checked by Agilent 2100 Bioanalyzer (Agilent Technologies) and NanoDrop ND-1000 Spectrophotometer (Thermo Scientific). TruSeq RNA libraries generated from RA and OA synovium were sequenced using an Illumina HiSeq 2000 sequencer with paired-ends read length of 100 bases, following the manufacturer's instructions. The generated sequence reads were aligned to the *Homo sapiens* genomic DNA reference (UCSC hg19) using TopHat. Aligned reads were mapped and converted to fragment per kilobase of transcript per million mapped reads (FPKM) values using Cufflinks. [Results] Next-generation sequencing generated a total $12.8X10^8$ reads. For all samples, the number of filtered reads for a given total transcripts were normalized to the total mapped reads. After filtering the low quality reads, a total of 366,394,362 effective transcript reads in RA synovium and 187,367,061 transcript reads in the OA synovium were obtained. Next, using one-way ANOVA test, 16 lncRNAs were found to be differentially expressed between RA synovium and OA synovium ($P<0.05$). [Conclusions] This study suggests that several lncRNAs are differentially expressed in RA synovium compared with OA synovium and these lncRNAs could be implicated in the pathogenesis of RA.

ICW5-2

Lower serum hepcidin levels in patients with rheumatoid arthritis treated with tocilizumab than other biological DMARDs or non-biological drugs

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Conflict of interest: None

[Object] Hepcidin is a major regulator of iron metabolism and homeostasis. It is in turn regulated by IL-6 and causes the anemia of inflammation. This study investigated the serum level of hepcidin in patients with rheumatoid arthritis (RA) and sought to identify differences in hepcidin levels among patients treated with certain therapeutic drugs. [Methods] Two hundred and sixty-three patients with RA were included in this study. The mean patient age was 67.5±11.4 years, 77.6% were female, MTX was administered to 52.5% of patients, and biological DMARDs were administered to 33.5%. The serum hepcidin level in each patient was measured by liquid chromatography-tandem mass spectrometry. The disease activity of RA and laboratory findings were compared among three groups depending on treatment as follows: tocilizumab (TCZ group); biological DMARDs, except TCZ (non-TCZ group); and treatment with other than biological DMARDs (non-Bio group). Statistical analyses were performed using the Spearman's rank method and *t*-test. [Results] Serum hepcidin levels were positively related to serum ferritin levels ($r=0.818$, $p<0.001$), serum iron levels ($r=0.314$, $p<0.001$), CRP levels ($r=0.249$, $p<0.001$), and DAS28-CRP ($r=0.127$, $p=0.039$). Serum hepcidin levels were negatively related to unsaturated iron binding capacity ($r=-0.711$, $p<0.001$), platelet count ($r=-0.180$, $p=0.003$), and RBC count ($r=-0.132$, $p=0.032$). Among 217 patients with low disease activity ($CDAI \leqq 10$), only lower WBC count was observed in the non-TCZ group compared with the non-Bio group. Otherwise, higher serum albumin level, higher RBC count, lower platelet count, and lower serum hepcidin level were observed in the TCZ group compared with the non-TCZ or non-Bio group. [Conclusions] Serum hepcidin levels were related to the anemia of inflammation in patients with RA. Even if low disease activity was achieved, the anemia of inflammation was more strictly suppressed by TCZ than other biological DMARDs or non-biological drugs.

ICW5-3

Old and new biomarkers in Rheumatoid Arthritis-same problem. Can they predict the response to anti-tumor necrosis factor therapy?

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Conflict of interest: None

Objectives: to test the possible predictive role for the response to treatment of RF type IgM and IgA, anti-CCP, anti-MCV,14-3-3 eta pro-

tein and COMP on a group of patients treated with anti-TNF α agents. **Methods:** prospective and observational study including 64 patients followed 12 months with active RA, uncontrolled by csDMARDs. Clinical assessment was performed at 0,6 and 12 months according to ACR criteria and evaluation of treatment response according to EULAR criteria (good/moderate/nonresponder). **Results:** 59 patients (92.2%) were women and 5 (7.9%) men, mean age 57.5±9.4 years. Following baseline immunological parameters titres and the response at 6 months, tests for identifying differences between the groups showed that lower titres of both RF isotypes (IgM 51.36±95.35 U/ml, p=0.016, IgA 22.45±61.25 U/ml p=0.033), anti-CCP (60.82±26.331ng/ml, p=0.001),14-3-3 eta protein (0.51±0.580ng/ml, p=0.045) and COMP (746.04±130.09ng/ml, p=0.000) had predictive value on achieving a good EULAR response at 6 months. Grouping patients in 2 categories (responders/nonresponders), just 14-3-3 eta protein and anti-CCP had predictive value for the response at 6 months For 12 months visit, lower baseline titres for RF type IgM (92.93±120.22U/ml, p=0.002) and IgA (49.96±98.08U/ml, p=0.002) had predictive value for achieving a good response at 12 months. We didn't obtain other informations grouping patients in 2 categories. The status pretreatment influenced the good response for COMP at 6 months (p=0.001) and RF IgA at 12 months (p=0.004). Using multivariate logistic regression methods we obtained a statistical model for predicting the response at 6 months including normal values for 14-3-3 eta protein, anti-CCP and COMP (Hosmer and Lemeshow according test lambda^2 =5.795, p=0.67 more or equal than 0.05 with a predictive response accuracy of 89.1%). **Conclusion:** in the future a version using multiple biomarkers could increase accuracy for identifying pretreatment patients who will respond to anti-TNF therapy.

ICW5-4

Semaphorin 4A and 4D were elevated in patients with rheumatoid arthritis and associated with antibody production

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Conflict of interest: None

Objective: Semaphorin 4A (Sema4A) and 4D have been found to be involved in regulation of immune responses. The aim of this study was to investigate clinical significance and potential role of Sema4A and 4D in rheumatoid arthritis (RA). **Methods:** Blood samples were obtained from 93 patients with RA and 20 healthy controls. Serum levels of Sema4A and 4D were analyzed by enzyme-linked immunosorbent assay. The association of Sema4A and 4D with clinical features and laboratory parameters were analyzed. **Results:** Serum Sema4A and 4D levels were significantly increased in RA patients compared with healthy controls (718.6 ± 75.58 *vs* 142.3 ± 24.42 pg/ml; 8.46 ± 3.1 *vs* 0.06 ± 0.01 ng/ml, $P<0.001$ and $P<0.01$ respectively). Stratified analyses revealed that both Sema4A and 4D were higher in RF positive patients than RF negative counterparts (789 ± 95.9 *vs* 358.3 ± 87.3 pg/ml; 12.95 ± 4.72 vs 0.16 ± 0.03 ng/ml, $P<0.01$ both). Although there was no association of Sema4A with TJC, SJC, VAS, DAS28, PLT, ESR, CRP, IgA and IgG, we found a positive correlation of Sema4A with RF titer ($r=0.275$, $P<0.05$), IgM ($r=0.287$, $P<0.05$) and IL-6 ($r=0.223$, $P<0.05$). Similarly, serum level of Sema4D was positively correlated with SJC ($r=0.222$, $P<0.05$), RF titer ($r=0.587$, $P<0.001$), IgM ($r=0.39$, $P<0.01$) and IL-1β ($r=0.258$, $P<0.05$). **Conclusion:** Our findings suggest that Sema4A and 4D might serve as pro-inflammatory biomarkers and be associated with antibody production in RA.

ICW5-5

Change in CD8 and CD4 T-lymphocyte cytokine subsets on treatment with methotrexate in rheumatoid arthritis

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Conflict of interest: None

[Object] To look at the effect of methotrexate on circulating CD8 and CD4 cytokine subsets and levels of circulating cytokines. [Methods] Patients who were 18 to 65 years of age and having active rheumatoid arthritis (ACR 1987 criteria) were treated with methotrexate for 24 weeks. Disease activity was measured using the disease activity score and response to treatment assessed by EULAR criteria. At 0 (baseline) and 24 weeks (post methotrexate), PBMCs were isolated using density gradient centrifugation and stimulated with PMA /Ionomycin (with Brefeldin) for 5.5 hours. Surface staining was done using anti CD3/ anti CD8 and intracellular cytokine staining with anti Interferon gamma, IL17 and IL4. Cytokine bead array was used to determine levels of IFNgamma, IL12, IL10, IL4 and IL17 in plasma at 0 and 24 weeks. Cell frequencies and cytokine levels described by using median (IQR=interquartile range) and compared using wilcoxon signed rank. [Results] This study included 67 patients (F:M=4:1) with rheumatoid arthritis, 57 (85%) being RF positive and 20 receiving prednisolone at baseline. They were treated with methotrexate for 24 weeks, with mean dose at completion of study being 22.9+/-3.0 mg per week. CD8+IFNgamma+ cells declined from 37.2 (IQR 19.4-60.2) to 22.7% (IQR 8.5-49.7), p=0.04 and there was marginal increase in CD8+IL17+ cells from 0.3 (IQR 0.1-0.6) to 0.4 (IQR 0.2-1.2), p=0.006. THere was no signficant change in the CD4 cytokine subsets. There was a significant decline in the circulating levels of IL-12 [(519 (40.4-2336.1), 124.7 (23.5-771.9) pg/ml, p<0.001] and IL-17 [556.6 (19.5-21341), 118.4 (0-1930.9) pg/ml, p<0.001] and increase in IL-4 with treatment. In non-responders, there was a significant increase in CD8-IL17 (p=0.01) that was not seen in responders. [Conclusions] Methotrexate leads to changes in circulating CD8 subsets, predominantly decline of the CD8+IFNgamma+ subset, that may be explained due to reduction in the polarising cytokine IL12.

ICW5-6

Identification of immunophenotypic subgroups and differential responses to molecular targeted therapies in patients with rheumatoid arthritis (RA)

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Conflict of interest: Yes

[Objective] In the treatment of RA, different targeted therapies induce different effects in immune cell phenotypes. This forms the basis for subgroup identification for precision medicine. We stratified RA patients based on immunophenotyping and investigated the response for targeted therapies. **[Methods]** 224 bio-naive, active RA patients were enrolled. Circulating B, T, NK and dendritic cells (DCs) were defined based on flow cytometric analysis termed "the Human Immunology Project". **[Results]** The proportions of T effector and activated Tfh cells, but not Th17 and Treg cells, were higher in RA than the age matched control. Likewise, the proportions of B effector cells and plasmacytoid DCs were higher. None of them correlated with disease activity. Cluster analysis stratified RA patients into 2 groups: patients without immune abnormality and patients with immune abnormality. The group with immune abnormality was further divided statistically into 3 groups (with high proportions of B effector and Tfh cells in all groups): patients with less T cell abnormality (T cell low dependent group), patients with high percentage of Tfh and Treg cells (Tfh/Treg dominant group), and patients with conspicuously high proportion of T effector cells (T effector dominant group). Baseline disease activity was similar among the groups. After treatment with biologics, the number of patients with insufficient response was more frequent in the group with immune abnormality. In addition, TNF inhibitors were numerically more effective in the group without immune abnormality. In contrast, abatacept was more efficacious in T cell low dependent group and Tfh/Treg dominant group, and tocilizumab was more effective in Tfh/Treg dominant group. However, the poor clinical efficacies were seen in T effector dominant group for all biologics. **[Conclusions]** The identification of immunophenotypic subgroups may enhance treatment effect of molecular targeted drugs and serve as a step towards precision medicine.

ICW6-1

MicroRNA-10b Plays Role on Th17 Cell via Suppression of MAP3K7 in Ankylosing Spondylitis

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Conflict of interest: None

[Object] We recently reported a novel Th17 regulator miR-10b-5p that is present in Th17 cells from patients with Ankylosing Spondylitis (AS). IL-22 is closely related to Th17 cells and also regulated by IL-23, a key cytokine for IL-17A production. Moreover, IL-22 has been implicated in the regulation of new bone formation in experimental models. Therefore, we wonder whether miR-10b-5p affects IL-22 production in AS. [Methods] Primary CD4+ T cells were negatively isolated from PBMCs from AS patients (Miltenyi Biotec). Transfection was performed with the Neon transfection system (Thermos Fisher Scientific, Germany) according to manufacturer's instructions. The transfection efficiency was evaluated by monitoring FAM (Fluorescein) positive cells using flow cytometry, and qPCR at 24 h after transfection. miR-10b-5p function was determined by overexpression of miR mimic in CD4+ T cells followed by intracellular cytokine staining, cytokine measurement, and qPCR. Statistical analysis was performed using Prism 5.0 Software (GraphPad Software, San Diego, USA). A $p < 0.05$ was considered statistically significant. [Results] Overexpression of miR-10b-5p reduced both IL-22+CD4+ T cell frequencies and IL-22 production in CD4+ T cells from patients with AS. To identify the cellular targets of miR-10b-5p, we previously performed RNA-sequencing of CD4+ T cells transfected with miR-10b-5p together with in silico Target Scan analysis. MAP3K7 was selected as a target gene because of its known role in cytokine regulation. We then silenced MAP3K7 in CD4+ T cells using siRNA and found the suppression of IL-22 response, mimicking the effect of miR-10b-5p overexpression. [Conclusions] Our data suggest that miR-10b-5p suppress IL-22 production by targeting MAP3K7. miR-10b-5p might be a potential therapeutic candidate for regulation of new bone formation in patients with AS.

ICW6-2

The effect of extraarticular manifestations on tumor necrotic factor alpha inhibitor drug survival in patients with ankylosing spondylitis: nationwide data from the Korean College of Rheumatology BIOlogics (KOBIO) registry

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Conflict of interest: Yes

Objectives: The objective of our study was to assess the predictors of tumor necrosis factor alpha inhibitor (TNFi) drug survival in patient with ankylosing spondylitis (AS) including extraarticular manifestions, using nationwide registry of Korea. **Methods:** Data were obtained from the Korean College of Rheumatology BIOlogics (KOBIO) registry which is multi-center based national wide data from 53 tertiary care hospitals in Korea. Demographics, clinical features, laboratory findings, disease activity indices, and extraarticular manifestataions (uveitis, enthesitits, dactylitis, psoriasis, inflammatory bowel disease) were studied in patients with AS during the TNFi therapy. We analyzed the drug survival of 5 TNFi agents (etanercept, infliximab, infliximab biosimilar, adalimumab, and golimumab) and the factors affect drug survival especially in terms of extraarticular manifestations. To verify affecting factors, univariable and multivariable cox regression analysis were performed. **Results:** Of 1482 AS patients starting TNFi drugs from Dec 2012 to Jan 2017 were included. The effect of extraarticular manifestations on TNFi drug survival was not statistically significant. But peripheral arthritis was statistically significantly associated with TNFi drug survival (unadjusted HR: 2.21 95% CI 1.66 to 2.95, adjusted HR 1.38 95% CI 1.01 to 1.88). Of disease activity indices, higher level of ASDAS-ESR showed statistical significance in TNFi drug survival (unadjusted HR: 1.87 95% CI 1.73 to 2.03, adjusted HR: 2.23 95% CI 2.00 to 2.63). Golimumab had higher retention rate to TNFi therapy than etanercept during 3 years of follow-up period (unadjusted HR: 0.46 95% CI 0.31 to 0.68, adjusted HR: 0.65 95% CI 0.43 to 0.99). **Conclusion:** In national wide KOBIO registry, extraarticular manifestations including uveitis could not affect TNFi drug survival. But the development of peripheral arthritis during TNFi therapy had higher risk of discontinuance of its treatment in AS patients.

ICW6-3

Precision medicine using different biological DMARDs based on characteristic phenotypes of peripheral T helper cells in patients with psoriatic arthritis

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Conflict of interest: None

[Object] Biological DMARDs became available and efficacious in patients with psoriatic arthritis (PsA). However, it remains unclear how we can differentially use bDMARDs to individual patients. We evaluated the peripheral immune cell phenotypes using 8 color flow cytometry, and tried to optimize bDMARDs therapy to individual patients. [Methods] Among 64 patients with PsA, 26 underwent bDMARDs therapy selected based on phenotypic differences of peripheral helper T cells on 8-color flow cytometry. The efficacies of this strategic bDMARDs treatment and the standard bDMARDs treatment administered to the other 38 patients were evaluated at month 6. [Results] The patients with PsA were classified into the following 4 types based on the peripheral blood analysis: a CXCR3+CCR6-CD38+HLA-DR+ activated Th1 cell-predominant type, CXCR3-CCR6+ CD38+HLA-DR+ activated Th17 cell-predominant type, Th1/Th17-high type, and Th1/Th17-low type. At 6 months of treatment, PASI score was significantly decreased in both group (standard: 9.9→3.9, strategic treatment: 8.4→2.4). SDAI were also significantly decreased at month 6 in both group (standard: 18.5→9.41, strategic: 16.2→3.5). The rate of low disease activity achievement according to SDAI at month 6 was significantly higher in the strategic bDMARDs treatment group compared with that of the standard bDMARDs treatment group (standard: 55.2 %, strategic: 92.3 %). [Conclusions] Our study indicated the potential for precision medicine via the strategic treatment of different bDMARDs based on the phenotypic differences in peripheral T helper cells.

ICW6-4

The relationship between SAPHO syndrome and malignancy

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Conflict of interest: None

[Object] The relationship between SAPHO syndrome and malignancy is unclear, as only one case report of SAPHO syndrome induced by intravesicular injection of BCG to treat bladder cancer exists. Here, we examined the relationship between SAPHO syndrome and malignancy. [Methods] Twenty-five patients with SAPHO syndrome diagnosed in or out hospital from January 2000 to June 2017 were examined retrospectively; the age of SAPHO syndrome onset, sex, medical history, allergy history, presence of skin or osteoarthritis symptoms, and blood results were collected. [Results] Malignancy was documented in 9 cases (36%), of whom 7 developed malignancy within 6 years before or after the diagnosis of SAPHO syndrome. The age of SAPHO syndrome onset was significantly older in those with malignancy than those without malignancy (55.2 ± 10.5 vs. 44.7 ± 10.6 years: $p<0.05$). Those diagnosed with SAPHO syndrome before age 50 years had no malignancies ($p<0.05$). There were significantly fewer patients with a history of allergy among those

with than those without malignancy (p<0.05). The two osteitis cases at the time of SAPHO syndrome diagnosis had a malignancy (p=0.12). There were no significant differences in terms of other clinical features between those with and those without malignancy. [Conclusions] No differences in the clinical features of SAPHO syndrome were apparent according to the presence of malignancy. The risk of malignancy was significantly greater in cases diagnosed with SAPHO syndrome at age 50 years or older.

ICW6-5

Newly identified prognostic factors in patients with polymyalgia rheumatica

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Conflict of interest: None

[Object] Polymyalgia rheumatica (PMR) is sometimes refractory, and some cases are finally diagnosed as rheumatoid arthritis (RA). The purpose of this study is to elucidate predictive factors for clinical course of PMR. [Methods] Newly diagnosed PMR patients at our hospital from July 2006 to June 2017 were enrolled. All patients fulfilled the EULAR/ACR 2012 Provisional Classification Criteria for PMR but not the EULAR/ACR 2010 Classification Criteria for RA. The primary endpoint was the rate of remission within the first month after commencement of treatment. For evaluation of composite outcome with refractory PMR and development of RA, secondary outcome was defined as requirement of additional treatment and/or relapse during the observation period. Categorical variables with a possible relation to the outcomes such as clinical characteristics, criteria items, articular symptoms and laboratory data were compared by using the nonparametric chi-square test. [Results] The mean age of enrolled 61 patients was 70.6 years and 67% were female. 38 (62%) patients failed to achieve remission by one month. Proportion of patients showing elevated ESR (>100 mm/h) at baseline was higher in patients without remission than those with remission more frequently (62% vs. 30%, p = 0.017). Patients without remission also showed lower decreasing rate of CRP after a week (76% vs. 89%, p = 0.026) compared to those with remission. Furthermore, 30 (49%) patients required additional treatments and/or had relapse during the observation period. These patients showed higher platelet counts at baseline (42.9 ± 1.9 vs. 36.3 ± 2.0 $\times 10^4/mm^3$, p = 0.023) and lower proportion rate of achievement of low CRP (<1.0 mg/dl) after a week (44% vs. 80%, p = 0.009). [Conclusions] ESR and platelet counts at baseline and early treatment response might be useful for prediction of refractory PMR and/or transition to RA.

ICW6-6

Biomarkers for relapse in adult Still's disease patients using tocilizumab

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Conflict of interest: None

[Background] Symptoms and laboratory data in patients with adult Still's disease patients (ASD) at relapse are often non-specific. Especially in ASD patients treated with tocilizumab, IL-6 receptor inhibitor, inflammatory markers are normal despite the flared disease activity. [Object] To identify useful biomarkers for diagnosing relapse in ASD patients treated with tocilizumab. [Methods] Consecutive ASD patients diagnosed by Yamaguchi's criteria in our institution from January 2007 until September 2017 were reviewed. Clinical information was collected from their medical chart. Relapse was defined as a case who required immunosuppressive treatment intensification for ASD according to their attending physicians. Biomarkers at relapse were analyzed. [Results] Seventy six patients with ASD were enrolled, and 21 relapses were identified. Eighteen patients were treated with tocilizumab experienced 5 relapses. At relapse, CRP, WBC, serum ferritin, ESR and LDH were significantly higher at relapse than before relapse. In patients treated with tocilizumab, while CRP was within the normal range (CRP<0.30 mg/dL) in all cases at relapse, LDH was significantly elevated at relapse compared to before relapse (211.2 IU/mL vs 451.2 IU/mL, P=0.04). WBC and serum ferritin tended to increase but with no significant difference (WBC: 9500/μL vs 14620/μL, P=0.21, serum ferritin: 49.2 ng/mL vs 236.4 ng/mL, P=0.091). [Conclusions] In addition to WBC, serum ferritin and ESR, LDH was a useful biomarker for relapse of ASD, especially in those treated with tocilizumab.

ICW7-1

Role of single nucleotide polymorphisms in primary Sjogren's syndrome -associated pulmonary arterial hypertension

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Conflict of interest: None

Objective: The biomarker of primary Sjogren's syndrome -associated pulmonary arterial hypertension (pSS-aPAH) has not been well investigated. This study aimed to identify the single nucleotide polymorphisms predicting PAH in patients with pSS. **Methods:** Both pSS patient with PAH and those without PAH were enrolled in our study. All pSS patients were fulfilled the 2002 AECG or the 2016 ACR/EULAR classification criteria. PAH was diagnosed based on ESC/ERS guidelines by right heart catheterization. Candidate genes were selected based on previous studies involving pSS or PAH. Single nucleotide polymorphism (SNP) genotypes of candidate genes were determined by polymerase chain reaction (PCR). We further evaluated its association with PAH susceptibility in a case-control study. **Results:** 43 patients with pSS-associated PAH and 92 pSS patient without PAH (pSS-nonPAH) were enrolled. Fifteen SNPs in 11 genes were identified. Among them, fourteen SNPs were in Hardy-Weinberg equilibrium. Further case-control study showed that genotypes of EBF1 rs3843489 (p=0.042, OR=2.37, 95% CI [1.02, 5.50]) and STAT4 rs10168266 (p=0.012, OR=0.38, 95% CI [0.18, 0.82]) were significant between pSS-aPAH and pSS-nonPAH group. **Conclusion:** EBF1 rs3843489 and STAT4 rs10168266 polymorphisms were significantly associated with the PAH susceptibility in patients with pSS, indicating that inflammation and B cell development may be evolved in the pathogenesis of pSS-aPAH. The potential clinical and basic research significance needs further investigation.

ICW7-2

Musculoskeletal manifestations occur predominantly in patients with older onset Familial Mediterranean Fever

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Conflict of interest: None

Background. Our previous nation-wide survey showed the clinical manifestations and prevalence of Japanese Familial Mediterranean Fever (FMF) patients. However, the clinical differences between young-onset

FMF (YOFMF), adult-onset FMF (AOFMF), and late-onset FMF (LOFMF) have not been yet clarified. **Objectives.** We sought to compare between the clinical profile of patients with AOFMF, LOFMF and YOFMF and to determine the clinical characteristics of them. **Methods.** We enrolled consecutively 395 patients in 2006-2017. Mutation detection in exons 1, 2, 3, and 10 of the *MEFV* gene was performed. We defined YOFMF, AOFMF and LOFMF as the onset of FMF <20, 20-39 and ≧40 years of age, respectively. We compared clinical manifestations and mutations in *MEFV* gene among these three groups. **Results.** The median age at the onset of YOFMF, AOFMF and LOFMF were 12.5, 28 and 51 years old respectively. A family history of FMF and a mutation in exon 10 of the *MEFV* gene were significantly more frequent in groups with younger onset ([YOFMF 28%, AOFMF 17%, LOFMF 12%; $p<0.01$], [YOFMF 51%, AOFMF 33%, LOFMF 19%; $p<0.001$], respectively). In the accompanying manifestations during the attacks, abdominal pain and chest pain were significantly more frequent in groups with younger onset ([YOFMF 64%, AOFMF 56%, LOFMF 30%; $p<0.001$], [YOFMF 45%, AOFMF 33%, LOFMF 24%; $p<0.01$], respectively), whereas arthritis and muscle pain were significantly more frequent in groups with older onset ([YOFMF 32%, AOFMF 48%, LOFMF 62%; $p<0.001$], [YOFMF 8%, AOFMF 18%, LOFMF 26%; $p<0.01$], respectively). There was no significantly difference in the response to colchicine among the three groups. **Conclusion.** Our results suggest that older onset FMF had a lower percentage of mutations in exon10 of the *MEFV* gene and predominantly presented arthritis and muscle pain during the attacks. It is thus important to distinguish them from other inflammatory diseases such as gout, adult Still's disease, and infectious arthritis.

ICW7-3

Functional analysis of the novel G58V mutation in the TNFRSF1A gene identified in a family with TNF receptor-associated periodic syndrome (TRAPS)

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Conflict of interest: Yes

[Object] TNF receptor-associated periodic syndrome (TRAPS) is an autoinflammatory disease characterized by intermittent episodes of fever. Mutations in the *TNFRSF1A* are associated with TRAPS. T50M mutation and cysteine mutations cause decreased cell surface expression of TNFR1 and exhibit severe disease phenotypes. Single nucleotide polymorphisms such as T61I and R92Q are associated with TRAPS-like phenotypes, but the molecular pathogensis is not fully understood. Recently we have identified a novel G58V *TNFRSF1A* mutation with intermittent fever in a family. They also had T61I mutation. In this study, we functionally characterized the novel G58V *TNFRSF1A* mutation. [Methods] The pathogenicity of the G58V mutation was analyzed by the online prediction tools (SIFT, Polyphen2, PROVEAN and PANTHER). Wild-type (WT) or mutated *TNFRSF1A* (T50M, G58V, T61I, G58V/T61I, R92Q) constructs were transfected into HEK293 cells. Surface and intracellular expression of TNFR1 in the cells was analyzed by flowcytometry. NF-κB promotor activity was measured by dual-luciferase reporter assay. [Results] The G58V mutation was predicted to be a damaging amino acid substitution that could impair the TNFR1 function. Western blotting analysis showed expression levels of the WT and mutant TNFR1 proteins were comparable in the whole cell lysates. TNFR1 expression on the cell surface was decreased in the T50M, G58V and G58V/T61I TNFR1-transfected cells compared to WT TNFR1-transfected cells. In contrast, the R92Q and T61I mutation did not affect it. NF-κB promoter activities in the T50M or G58V mutation were significantly decreased (T50M 21.5 ± 3.6%; G58V 34.8 ± 4.4%; G58V/T61I 56.7 ± 23.9% vs. WT). The R92Q and T61I mutation did not suppress the acitivities. [Conclusions] As with the pathogenic T50M mutation, the novel G58V mutation suppressed the cell surface expression of TNFR1 and spontaneous NF-κB promoter activity. This indicated that G58V could be a responsible mutation causing TRAPS.

ICW7-5

Integration of disease genetics and miRNA-target gene network identified pathogenesis implicated in tissue specificity

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Conflict of interest: None

[Object] MicroRNA (miRNA) regulates transcription of specific target genes, and is related to pathogenesis of human diseases. Development of an *in silico* miRNA screening method utilizing human genetics-driven resources is warranted. Moreover, integration of tissue-specific miRNA expression profiles should be necessary to elucidate miRNA impact on disease pathogenesis. [Methods] We implemented a method to quantitatively evaluate enrichment of GWAS signals on miRNA-target gene networks (MIGWAS). We obtained expression profiles of 2918 miRNAs in 180 cell types from FANTOM5 consortium and integrated them into the MIGWAS pipeline. For each cell type, we defined a subset of highly expressed miRNAs and partitioned MIGWAS results. We applied MIGWAS to the GWAS summary statistics of 22 human traits comprising of in total approximately 2,470,000 samples. [Results] MIGWAS identified human traits with significant enrichment of association signals on miRNA networks, such as rheumatoid arthritis (RA) and diabetes. Tissue specificity analysis showed that miRNAs enriched in the GWAS association signals of the disease showed specific expressions for the tissues implicated in biology of the corresponding disease (e.g., immune cells and respiratory epithelial cells for RA, gastrointestinal cells for Crohn's disease, and adipocyte for high LDL-cholesterol). [Conclusions] MIGWAS demonstrated that miRNA-target gene network contributes to human disease genetics in the context of cell type-specific expressions, and successfully identified miRNA as promising biomarkers and therapeutic targets.

ICW7-6

Genetics of hematological and biochemical biomarkers links cell types to human autoimmune diseases

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Conflict of interest: None

[Object] Clinical biomarkers are useful intermediate phenotypes to understand complex human diseases. Elucidation of genetic landscapes of such intermediate phenotypes and its relationships with cell type specificity contributes to understanding of biology of human complex diseases. [Methods] To acquire comprehensive insights into their genetics, we a conducted genome-wide association study (GWAS) of 58 hematological and biochemical biomarkers in 162,255 Japanese subjects. We further incorporated additional Japanese GWAS results of 30 complex diseases including autoimmune diseases such as rheumatoid arthritis (RA) and Graves' disease (GD). We comprehensively evaluated pleiotropy, polygenetic correlation, and cell-type specificity related to human phenotypes. As for polygenic correlation, we introduced a novel method of statistical genetics, named linkage disequilibrium score regression (LDSC), which incorporated epigenetic histone motifs of >200 cell types and empirically evaluate polygenic correlation of the genetic backgrounds of the human traits. [Results] We identified 1,407 trait-associated loci ($P < 5.0 \times 10^{-8}$), 680 of which were novel findings. Without prior biological knowledge of cross-phenotype relationships, our findings demonstrated that genetics of clinical measurements successfully recapture their relevance to diseases, and thus could contribute to elucidation of unknown etiology and pathogenesis (e.g., strong causal relationships of human regulatory T cells with GD, rather than RA). [Conclusions] Our study provided many insights into the genetic basis of various biomarkers and illuminated the complex genetic links between clinical measurements, human autoimmune diseases, and relevant cell types.

ICW8-1

Rheumatoid Arthritis GWAS SNP in the CD83 Gene May Increase Disease Susceptibility by Decreasing the Expression of CD83 on B Cells

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Conflict of interest: Yes

[Object] Genome-wide association studies (GWAS) have identified many SNPs associated with the risk of autoimmune diseases; however, the role of those SNPs in disease pathogenesis is often not clear. It has been reported that many GWAS SNPs contribute to disease pathogenesis by influencing gene expression; therefore, examining the relationship between genotype and gene expression may help elucidate the role of those SNPs in disease pathogenesis. In this study, we focused on rs12529514, an intron SNP in the CD83 gene associated with rheumatoid arthritis (RA), and we sought to determine possible mechanisms by which this SNP contributes to the pathogenesis of RA using a recently published eQTL database. [Methods] The effect of rs12529514 on gene expression was examined in an eQTL database of peripheral blood mononuclear cells (PBMC), as well as publicly available epigenomic databases. In addition, the effect of this SNP on peripheral blood B cell compartment was analyzed. [Results] rs12529514 RA risk allele significantly decreased the expression of CD83 on B cells but not in other PBMC subsets. An examination of this locus using publicly available database suggested that the RA risk haplotype might decrease the expression of CD83 by decreasing the binding of nuclear factor-kappa beta in a regulatory site nearby. As CD83 has been reported to influence B cell development in mice, we hypothesized that this RA risk SNP might contribute to the risk of RA by influencing B cell development. Peripheral blood B cells of healthy individuals with the RA risk SNP showed certain characteristics of RA patient B cells, such as an increase in the frequency of CD27-IgD- B cells, suggesting that this SNP may influence the differentiation of B cells. [Conclusions] The RA risk SNP in the CD83 gene decreases the expression of CD83 on B cells, and thus, by influencing the differentiation of B cells, contribute to the development of RA.

ICW8-2

Association of single nucleotide polymorphisms in omentin-1, adiponectin and resistin genes with systemic lupus erythematosus in Chinese population

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Conflict of interest: None

[Object] The aim of our study was to evaluate the association of single nucleotide polymorphisms (SNPs) in *omentin-1, adiponectin*, *resistin* genes with systemic lupus erythematosus (SLE) susceptibility. [Methods] In this study, we genotyped four SNPs (rs2274907, rs35779394, rs79209815, rs13376023) of *omentin-1*, two SNPs (rs16861194, rs266729) of *adiponectin* and three SNPs (rs1862513, rs3745368, rs3745367) of *resistin* in 593 SLE patients and 643 normal controls recruited from Chinese population. The genotyping was conducted using TaqMan SNP genotyping assays. [Results] No significant differences were observed for the distribution of allele and genotype frequencies of the above SNPs between SLE patients and controls. Notably, we found an increased risk of in rs3745368 polymorphism under the dominant model (GG vs. AA + GA, $P = 0.026$). We also reported that the GG genotype frequency of the rs13376023 in *omentin-1* was associated with oral ulcers in SLE patients ($P = 0.021$). In *resistin*, the GG genotype and G allele frequencies of rs3745368 were found to be related to discoid rash in SLE patients ($P = 0.037$, $P = 0.011$, respectively), and the GG genotype and G allele frequencies of rs3745367 were associated with renal disorder in SLE patients ($P = 0.034$, $P = 0.016$, respectively). Haplotype analyses indicated that the haplotype CGA for *resistin* was significantly associated with SLE susceptibility ($P = 0.005$). [Conclusions] In summary, no significant evidences were found to support the hypothesis that *omentin-1, adiponectin* and *resistin* SNPs may contribute to SLE susceptibility. While *omentin-1*, *resistin* genetic variations maybe associated with the occurrence of several specific clinical phenotypes in SLE.

ICW8-3

Identification EP300 as a Novel Therapeutic Target for Rheumatoid Arthritis by the Comprehensive Analysis of Fibroblast-like Synoviocytes

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Conflict of interest: Yes

[Object] Fibroblast-like synoviocyte (FLS) cooperatively expresses matrix metalloproteinases, chemokines and cytokines in a response to various cytokines, which leads joint destruction in rheumatoid arthritis (RA). The objective of this study is to identify a fundamental molecular machinery which confers the inflammatory phenotype of RA-FLS. **[Methods]** FLS from RA patients (n = 30) were stimulated with cytokines (TNF-α, IL-1β, IL-6/sIL-6R, IL-17A, IL-18, IFN-γ, IFN-α, TGF-β1 and combination of all 8 cytokines [8-mix] which simulated the mixture of stimuli in the joint) for 24 hours. Whole transcriptome data was obtained by RNA-sequencing using HiSeq 2500 (Illumina) and subsequently analyzed by edgeR and Weighted Gene Co-expression Network Analysis (WGCNA) package. Chromatin immunoprecipitation (ChIP)-sequencing of H3K4me3, H3K4me1, and H3K27ac enrichment was performed and analyzed by HOMER. The effect of EP300 inhibition was assessed by collagen-inducer arthritis (CIA) model. **[Results]** The presence of inflammation amplifier was suggested by remarkable expression of key genes contribute to RA pathogenesis (i.e, IL-6) under the 8-mix. Whole transcriptome analysis by WGCNA suggested that some epigenetic modulators are crucial for that phenomenon. In integration with epigenome analysis, EP300 was assumed to bind the particular enhancers those are specifically activated under the 8-mix. Moreover, some transcription factors were suspected to form a complex with EP300. In in vitro assay, the inhibition of EP300 reduced IL-6 expression in both mRNA and protein level, proliferation, migration and invasion activity of RA-FLS. Furthermore, in in vivo assay, EP300 inhibitor significantly ameliorated arthritis in CIA mice. **[Conclusions]** Through the comprehensive analysis, a characteristic transcriptional organization of RA-FLS has been elucidated. The efficacy of EP300 inhibition suggested the potential usefulness of the epigenome targeting in FLS as RA treatment.

ICW8-4

Long noncoding RNAs expression levels, genes single nucleotide polymorphisms in rheumatoid arthritis

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Conflict of interest: None

[Object] The aim of our study was to evaluate two lncRNAs (linc00654, linc5150) expression levels and genes polymorphisms in rheumatoid arthritis (RA) patients. [Methods] In this study, we evaluated the expression levels of linc00654, linc5150 in peripheral blood mononuclear cells (PBMCs) from 65 RA patients and 54 normal controls. Simul-

taneously, we genotyped three SNPs (rs13039216, rs6085189, rs6085190) of *linc00654,* three SNPs (rs1590666, rs141561256, rs144047453) of *linc5150 in* 627 RA patients and 590 normal controls recruited from Chinese population. [Results] When compared to normal controls, the linc00654 level in PBMCs from RA patients was significantly increased ($P = 0.001$), whereas the linc5150 level in RA patients was significantly reduced ($P < 0.001$). Moreover, there were statistically significant associations of linc00654, linc5150 levels with CRP in RA patients ($P = 0.011$, $P = 0.014$, respectively), while linc5150 level was associated with ESH in RA patients ($P = 0.022$). Six SNPs were analyzed, and the results demonstrated that the TT genotype of rs13039216 in *linc00654* gene was statistically associated with a reduced risk of RA (TT vs. CC, $P = 0.046$), and a decreased risk of rs13039216 variant was observed under the recessive model (TT vs. TC+CC, $P = 0.038$). In addition, the G allele frequency of rs141561256 polymorphism in *linc5150* gene was significantly associated with RF in RA patients ($p = 0.034$). However, there were no associations between linc00654 level with *linc00654* genotype frequency, linc5150 level with *linc5150* genotype frequency in RA patients, respectively. [Conclusions] In summary, our results imply that linc00654, linc5150 maybe involved in the development of RA. Nevertheless, functional studies on different races, larger samples are still required to further explore the exact roles of these lncRNAs in RA.

ICW8-5

Role of Folypoly Glutamate synthase gene in methotrexate pharmacokinetic pathway with efficacy and adverse effects

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Conflict of interest: None

Objective: Folypoly Glutamate synthase (FPGS) is a key enzyme responsible for polyglutamation of Methotrexate inside the cells. The main aim of this study was to check the response, adverse effects and methotrexate polyglutamate (MTXPG) levels of methotrexate drug in relation to polymorphism and gene expression at transcriptional levels in rheumatoid arthritis patients. Methods: This study enrolled 117 RA patients who were treated prospectively with MTX for 24 weeks. Patients were categorized on the EULAR criteria into responders (good and moderate) and non-responders. Adverse effects were ascertained using a questionnaire. FPGS polymorphism were ascertained using hydrolysis probes rs10106 (FPGS 1994A>G) and rs1544105 (FPGS G>A). Gene Expression was studied using taq man chemistry. RBC MTXPG1-5 levels were determined using HPLC at 4,8,16 and 24 weeks. Results: FPGS 1994A>G GG genotype was associated with a significantly lower risk of adverse effects to MTX (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%. The other polymorphisms were not associated with response or adverse effects. FPGS expression level was found to be up regulated in responder group. None of the polymorphisms were associated with change in MTXPG levels. Conclusion: FPGS (1994A>G) GG Genotype is associated with a lower risk of adverse effects in response to MTX. FPGS expression level is also responsible for efficacy of drug.

ICW8-6

Pathophysiological research of systemic lupus erythematosus (SLE) using SLE patient-derived iPS cells with genome editing approach

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Conflict of interest: None

[Object] Systemic lupus erythematosus (SLE) is an autoimmune disease that develops on the basis of the certain genetic and environmental factors. Dendritic cells (DC) play pivotal roles in the pathogenesis of SLE by production of inflammatory cytokines and antigen presentation. 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] SLE and healthy donor-iPS (H-iPS) cell were differentiated into DCs using our original protocols, and DCs were analyzed by FACS, qPCR, mixed lymphoid reaction (MLR) test and ELISA. Whole exosome analysis of two SLE sisters-derived iPS cells were performed. SLE risk SNP at IFIH1 (G>A), which is reported to cause upregulation of Type 1 IFN signaling, was introduced into SLE-iPS cells using CRISPR/Cas9 systems. [Results] Our protocol induced differentiation of CD123+ pDC-like cells which were characterized by high expression of TLR7 and TCF4, promoting allo-T cell proliferation, and IFN-α secretion. Notably, SLE-iPS cell-derived CD123+pDCs secreted higher concentration of IFN-α by dsRNA stimulation than H-iPS-derived pDCs. CD123+DCs derived from SLE-G/G, SLE-G/A and SLE-A/A iPS cells showed decreased frequencies at culture day 25 in a risk-SNP dose-dependent manner with increasing Annexin and PI-positive cells. IFN-α secretion from CD123+DCs was also increased in a risk-SNP dose-dependent manner. These apoptosis and IFN-α secretion from CD123+DCs were partially regulated by anti-IFNR antibody. Furthermore, whole exome analyses and ingenuity variant analysis revealed 34 variants that were common to two SLE-iPS cells. [Conclusions] We established iPS-derived CD123+pDC differentiation protocol, which could work as a SLE pathophysiological model. IFIH1 played a pivotal role in the phenotypes and fate of CD123+ pDCs. This SLE-iPS cell-derived in vitro system could be a promising technique in the investigation and new drug discovery of SLE.

ICW9-1

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

[Object] 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 was 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] We identified Cathepsin E (*Ctse*), in which 13 methyl-CpGs within 583 bp region of intron 1 were hypomethylated, and mRNA upregulated in MRL compared with B6 mice. One of methyl-CpGs, mCGCG was hypomethylated and mutated to CGGG in MRL mice. Kaiso is known to bind to mCGCG and we hypothesized that it represses expression of *Ctse*. The binding of Kaiso to mCGCG site in B6 was reduced in MRL mice revealed by ChIP-PCR. EL4 cells treated with 5-azaC and/or TSA showed the suppression of the binding of Kaiso to mCGCG motif by ChIP-PCR and the overexpression of *Ctse* was demonstrated by qPCR. *Ctse* gene silencing by siRNA in EL4 cells resulted in reduction of IL-10 secretion. Accordingly, *IL10* and *CTSE* mRNAs up-regulated in CD4+ T cells both in MRL mice and the patients with SLE. [Conclusions] The hypomethylation of mCGCG motif, reduced recruitment of Kaiso, and increased expression of *Ctse* and *Il-10* in CD4+ cells may be involved in the pathogenesis of SLE.

ICW9-2

Peptidylarginine deiminase 4 deficiency ameliorated imiquimod-induced lupus mice model

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Conflict of interest: None

[Object] Peptidylarginine deiminase 4 (PADI4) is known to play several roles, such as neutrophil extracellular trap (NET) formation, epigenetic regulation, and apoptosis. Although PAD inhibitors are reported to suppress MRL/lpr mice, the precise roles of PADI4 in SLE remain elusive. *Padi4* knock out (KO) mice was used to elucidate them. [Methods] Mouse model for imiquimod (IMQ)-induced lupus was analyzed. IMQ was administered topically in the ear of B6 wild-type (WT) and *Padi4* KO mice. Spleen weight, proteinuria, NETosis, serum anti-dsDNA levels, frequencies of renal immune cells, MMP9 amounts in kidney, and histopathological findings of ear and kidney were assessed. [Results] Compared with control, IMQ-administered WT (WT-IMQ) mice showed increased spleen weight and proteinuria, elevated serum anti-dsDNA levels, enhancement of NETosis, increased kidney MMP9 amount and exacerbation of dermatitis. There was a positive correlation between the degree of proteinuria and kidney neutrophils and conventional dendritic cells (cDCs) infiltration. In contrast, *Padi4* KO-IMQ mice showed decreases of spleen weight and kidney MMP9 amount. Moreover, proteinuria and dermatitis were not exacerbated, and NETosis was totally suppressed in *Padi4* KO-IMQ mice. Significant decreases in kidney neutrophils and cDCs were noted in *Padi4* KO-IMQ mice. Notably, the serum anti-dsDNA levels, frequency of splenic germinal center B cells, and the degree of immune complex deposition showed no significant difference between the WT and *Padi4* KO-IMQ mice. [Conclusions] Although B cell autoimmunity was unsuppressed, nephritis was ameliorated in *Padi4* KO mice. As the infiltrated neutrophils and cDCs were reduced in *Padi4* KO mice, *Padi4* could regulate the migratory functions of these cells. We analyzed the transcriptome of *Padi4* KO neutrophils to clarify this point. Our study shed light on the importance of neutrophils in the pathogenesis of SLE, and the PADI4 inhibition will be a unique therapeutic strategy for SLE.

ICW9-3

SH3BP2 gain-of-function mutation alleviates lupus phenotypes in B6.MRL-Faslpr mice

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Conflict of interest: Yes

[Object] SH3BP2 (Src homology domain 3 binding protein 2) 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 gain-of-function mutation exacerbates arthritis in a murine autoimmune arthritis model (Mukai T, et al. PLoS One 2014). To further investigate the role of SH3BP2 in other autoimmune diseases, we here tested a murine lupus model using SH3BP2 mutant mice. We hypothesized that the SH3BP2 gain-of-function mutation aggravates autoantibody production and organ damage in lupus-prone mice. [Methods] SH3BP2 gain-of-function mutant (P416R knockin; Sh3bp2$^{KI/+}$) mice and lupus-prone; B6. MRL-Fas^{lpr} mice were crossed to yield the double mutant (KI/+ Fas^{lpr}) mice. Serum anti-dsDNA antibody levels and histopathological scores of glomerulosclerosis were assessed at 48 weeks of age. B cell and T cell subsets in the lymph nodes were analyzed by flow cytometry. Purified splenic B cell and T cell proliferation was compared between wild-type (WT) and Sh3bp2$^{KI/+}$mice. [Results] SH3BP2 gain-of-function mutation alleviates lupus in Fas^{lpr} mice, as shown with an enhanced survival rate, a reduction of proteinuria, and a reduced glomerulosclerotic score. Serum anti-dsDNA antibody levels were significantly reduced in KI/+ Fas^{lpr} mice (90.5% decrease compared to those in control Fas^{lpr} mice). Lymph nodes B220^{+}CD4^{-}CD8^{-} double-negative T cell population typically seen in Fas^{lpr} mice were decreased by the SH3BP2 gain-of-function mutation. Purified splenic B cell and T cell proliferation was comparable between WT and Sh3bp2$^{KI/+}$ cells, suggesting that the genetic SH3BP2 mutation may not directly affect B cell and T cell function. [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 immunoregulatory role of SH3BP2 in SLE.

ICW9-4

Lgals9 deficiency attenuates nephritis and arthritis in Pristane induced mice model of SLE

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Conflict of interest: None

Object: In systemic lupus erythematosus (SLE), an autoimmune disease associated with multiple organ involvements, lupus nephritis determines prognosis and arthritis impairs quality of life of the patients. Galectin-9 (Gal-9, *Lgals9*) is a β-galactoside binding lectin and the attempts for its clinical application have been made in autoimmune disease, since recombinant Gal-9 as a ligand for Tim-3 induces apoptosis in activated CD4^{+}Tim-3^{+}Th1 cell. We investigated wethere the deficiency of *Lgals9* is beneficial or deleterious in pristane mice model of SLE **Methods:** Arthritis, proteinuria, and autoantibody production were assessed in Gal-9 +/+ and Gal-9 -/- pristane-injected (PI) BALB/c female mice, renal pathology, joints inflammation, lipogranuloma formation were evaluated at 7 months after PI. The subsets of inflammatory cells in spleen and peritoneal lavage, and expression of cytokines from peritoneal macrophages were also analyzed. **Results:** *Lgals9* deficiency protects pristane-induced lupus model of BALB/c mice from immune-complex glomerulonephritis, arthritis, and peritoneal lipogranuloma formation. The population of T cell subsets and B cells in spleen and peritoneum was not altered by *Lgals9* deficiency in pristane-injected BALB/c mice. *Lgals9* deficiency protected mice from pristane induced lupus without altering TLR7-IFN-I pathway **Conclusion:** Galectin-9 is required for the induction and development of lupus nephritis and arthritis in pristane-induced mice model of SLE. The current investigation provided a new strategy, in which the antagonism of Galectin-9 is beneficial for the treatment of nephritis and arthritis in SLE by targeting activated macrophages.

ICW9-5

Next generation sequencing identifies miRNA-based biomarker panel for Lupus nephritis

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Conflict of interest: None

[Object] The symptomatology of lupus nephritis (LN) consists of foamy urine, lower leg edema, and other systemic manifestations, such as oral ulcers, arthralgia/arthritis, and lymphadenopathy. However, these symptoms can appear mild and non-specific. If these symptoms are unrecognized and treatment is delayed, approximately 10% of LN patients may develop permanent kidney damage and end-stage kidney disease. Therefore, the aim of this study is to identify a surrogate biomarker for the early detection of LN. [Methods] In this study, we first adopted next generation sequencing (NGS) in order to screen differential expression levels of microRNA (miRNA) between SLE patients with and without LN. According to results from the NGS and literature review, 15 miRNA were confirmed through real-time qPCR. We also considered clinical laboratory data for additional analysis. [Results] A total of 41 microRNAs demonstrated significant differences through the NGS screening. We then verified eight microRNAs from NGS and seven microRNAs from the literature review using the real-time qPCR method in peripheral mononuclear cells. mir-125a-5p, miR-146a-5p, and mir-221-3p were found to be statistically significant in both the screening study and the real-time qPCR verification studies. Finally, miR-146a-5p showed significant cor-

relation with clinical biochemistry markers and was observed to be a surrogate biomarker for early detection of lupus nephritis. [Conclusions] This report is the first to show that the intracellular biomarker miR-146a-5p could function as a useful specific biomarker for detection of lupus nephritis among lupus patients, regardless of serum albumin levels and spot urine protein/creatinine ratio, in the future.

ICW9-6

Multi-omics analysis of immune cell subsets for revealing the pathogenesis of systemic lupus erythematosus

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Conflict of interest: Yes

[Object] SLE is a systemic autoimmune disease. As the precise etiology remains unknown, we are trying to take multi-omics approaches to explore the etiology of SLE. [Methods] We picked up 49 SLE patients and 30 healthy controls (HCs). Each immune cell subset in PBMCs was sorted by flow cytometry and followed by RNA-seq. Plasma samples were collected from 21 SLE patients and 15 HCs and analyzed by mass spectrometry. We also performed ATAC-seq analysis to get epigenetic data from 8 SLE patients and 8 HCs. [Results] We revealed the importance of mitochondrial dysfunction in SLE memory B cells through the analysis of DEGs. Weighted gene co-expression network analysis in memory B cell subsets confirmed specific correlation between mitochondria-related modules and disease activity. As mitochondria produce substantial amount of ATP through oxidative phosphorylation (OXPHOS), we examined the correlation between IFN signature and OXPHOS signature and found strong correlation in B cells. The elevated mitochondrial mass proven by the transmission electron microscopy in SLE memory B cells combined with the metabolic assay data by the Flux Analyzer supported our hypothesis that mitochondrial dysfunction is a key player in SLE B cells. Next, we performed network analysis to identify the significant metabolic modules by using the metabolome data and found some modules were correlated with some gene-expression modules in SLE B cells. [Conclusions] Interestingly, metabolome data had some relation to transcriptome data in SLE patients. Because mitochondria regulate metabolic status of cells, it is consistent with our finding that mitochondrial dysregulation in memory B cells can be a major factor for SLE pathogenesis. Moreover, ATAC-seq data provided us the information of open chromatin status in each immune cell subset, showing that some B cell-specific epigenetic changes related to mitochondria/OXPHOS exist in SLE. Such a multi-omics analysis can shed new light on SLE pathogenesis.

ICW10-1

Abnormal B cell receptor repertoire maturation in SLE unveiled by RNA sequencing of various B cell subsets

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Conflict of interest: Yes

[Object] Systemic lupus erythematosus (SLE) is characterized by emergence of various autoantibodies. Among autoantibody structure, complementarity determining region 3 (CDR3) is especially important for antigen recognition. For elucidating B cell receptor (BCR) repertoire maturation process in SLE, we utilized RNA sequencing technology, which can determine BCR sequences along with transcriptome signatures. [Methods] We performed RNA sequencing of peripheral blood immune cells including five B cell subsets ($CD27^-IGD^+$, $CD27^+IGD^+$, $CD27^+IGD^-$, $CD27^-IGD^-$, $IgD^-CD27^{++}CD38^{++}$) from 49 SLE patients, 30 rheumatoid arthritis (RA) patients and 36 healthy controls (HC). Reads were mapped to BCR reference sequences to determine CDR3 sequence and isotype. Whole transcriptome profiling was also performed. [Results] Interferon signature was strikingly upregulated in SLE patient B cells. The diversity of plasmablasts was significantly increased in SLE, which showed positive correlation with the strength of interferon signature. V gene usage was strikingly skewed in SLE compared with HC or RA. The number of somatic hyper mutations in plasmablasts was significantly decreased in SLE and negatively associated with interferon signature. Isotype ratio was skewed in SLE memory B cells and pasmablasts. Some CDR3 sequences were shared among SLE patients exclusively, and CDR3 sequence pattern could clearly differentiate SLE patients from HC or RA. These public CDR3 sequences showed decreased load of somatic hyper mutations compared with others, and showed signs of defects in negative selection process. [Conclusions] Low load of somatic hyper mutations and defected negative selection in SLE suggested the abnormal B cell maturation process outside the germinal center. This abnormal maturation was strongly associated with natural immunity signals including interferon signature. Abnormal repertoire maturation in SLE might result in characteristic shared BCR sequences and contribute to SLE pathogenesis.

ICW10-2

Decreased expression of Serine/arginine-rich splicing factor 1 in T cells from patients with active systemic lupus erythematosus contributes to reduced expression of RasGRP1

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Conflict of interest: None

[Object] Serine/arginine-rich splicing factor 1 (SRSF1) binds pre-mRNA to regulate alternative splicing of many genes including T cell receptor associated CD3ζ. Reduced SRSF1 levels are known to be responsible for alternative splicing of CD3ζ and correlate with CD3ζ expression in T cells from systemic lupus erythematosus (SLE) patients. RasGRP1 is highly expressed in T cells and activates small GTPase Ras followed by Mitogen-activated protein kinase (MAPK) pathway activation. Recent genome association study identified RasGRP1 as one of SLE susceptibility loci. Our previous study revealed SLE T cells expressed an alternatively spliced (AS) form of RasGRP1 mRNA lacking exon 11 with reduced RasGRP1 protein levels. The purpose of this study was to determine if SRSF1 controls alternative splicing of RasGRP1. [Methods] T cells were collected from 45 SLE patients, 11 RA patients and 18 healthy subjects. Expression levels of SRSF1, wild type (WT) RasGRP1 and DNA methyltransferase (DNMT) 1, which is suggested to be downstream of MAPK pathway were assessed by quantitative PCR. Direct binding between SRSF1 and RasGRP1-exon11 mRNA was evaluated by oligonucleotide-protein pulldown assay. Human T cells were transiently transfected with SRSF1 specific siRNA to evaluate the effect on RasGRP1 expression. [Results] Expression levels of SRSF1 were significantly lower in SLE patients compared with healthy subjects. In SLE T cells, SRSF1 transcript levels correlated inversely with SLE disease activity, and positively with those of RasGRP1-WT and DNMT1. SRSF1 directly bound to RasGRP1-exon11 mRNA. Silencing of SRSF1 in human T cells led to increased ratio of RasGRP1-AS to WT and decreased RasGRP1 protein. [Conclusions] SRSF1 controls normal splicing of RasGRP1 and subsequent protein expression, and thereby downstream DNMT1 expression. We propose that SRSF1 regulates the splicing of important genes in SLE T cells including RasGRP1 and CD3ζ.

ICW10-3

Calcium/calmodulin-dependent protein kinase 4 promotes GLUT1-dependent glycolysis in systemic lupus erythematosus

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Conflict of interest: None

[Object] We sought to clarify the significance of immunometabolism in the pathological contidion of systemic lupus erythematosus and to determine the effect of Calcium/calmodulin-dependent protein kinase 4 on T cell metabolisms. [Methods] To elucidate the contribution of CaMK4 to cellular metabolic activities in T cells, we performed metabolomic profiling using capillary electrophoresis mass spectrometry in naive cells from MRL/lpr mice treated with anti-CD3/28 antibodies in the absence or presence of a CaMK4 inhibitor (KN-93). We examined the expression of GLUT1 and CaMK4 in CD4+ T cells from healthy controls (HC: n=34), and patients with inactive SLE (n=18), and with active SLE (n=24) by flowcytometry and quantitative PCR. We performed in vitro experiments by using human and murine T cells the effect of KN-93 on the expression of GLUT1. [Results] CaMK4 inhibition significantly decreased the levels of glycolytic intermediates, such as G6P, F6P, DHAP, pyruvate, and lactate whereas it did not affect the levels of the pentose phosphate pathway intermediates such as 6-PG, Ru5P, R5P and S7P. The expression of GLUT1 and CaMK4 in effector memory CD4 T cells displayed significantly higher in active SLE patients than HC and inactive SLE patients. Functional analysis revealed that CaMK4 inhibition decreased the expression of GLUT1 during T cell activation followed by the reduction of IL-17 production. [Conclusions] Our results indicate that the activity of CaMK4 has been suggested to be responsible for glycolysis and that CaMK4 may contribute to an aberrant expression of GLUT1 in T cells from active SLE patients.

ICW10-4

Activation signal transduction by IL-12-STAT1/4 in Tfh-Th1-like cell epigenetic modulation in patients with systemic lupus erythematosus

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Conflict of interest: None

[Object] T follicular helper (Tfh) cells play a pivotal role in the pathogenesis of systemic lupus erythematosus (SLE). To assess the characteristics and mechanisms of differentiation of Tfh cells, we investigated cytokine-induced signal transducer and activators of transcription (STAT) family factors and phenotype of T helper cells in SLE patients. [Methods] Peripheral blood mononuclear cells and serum from patients with SLE and healthy donors were analyzed by flow cytometry and cytometric bead array. $CD4^+$ T cells were isolated and stimulated by T cell receptor and various cytokines. Expression of Tfh-Th1 markers and phosphorylation of STATs were analyzed by flow cytometry and qPCR. Histone modifications were performed by ChIP-PCR. [Results] Differentiation of $CD4^+CXCR5^+CXCR3^+Bcl\text{-}6^+T\text{-}bet^+IL\text{-}21^+IFN\text{-}\gamma^+$ Tfh-Th1-like cells was induced by IL-12-induced activation of STAT1 and STAT4. IFN-γ responded to expression of IL-12 receptors as a trigger device. After IL-12-stimulation, STAT1 and STAT4 directly bound on Bcl-6 and T-bet gene loci accompanied by suppression of repressive histone mark trimethylated histone 3 lysine 27. Levels of IL-12 and IFN-γ in serum, expression of IL-12 receptor, responsiveness of activation of STAT1 and STAT4 followed by IL-12 in $CD4^+$ T cells were up-regulated and proportion of $CXCR5^+CXCR3^+CCR6^-$ activated Tfh-Th1-like cells were increased in patients with SLE compared with healthy donors. [Conclusions] Our findings suggest that IL-12-mediated activation of STAT1 and STAT4 alters histone modification and induces differentiation of Tfh-Th1-like cells. These findings could be one of underlying mechanisms responsible for expansion of Tfh-Th1-like cells and potentially helpful towards development of cell-specific treatment for SLE.

ICW10-5

MircroRNA MiR-326 regulates the B cells activity and the autoantibody production in systemic lupus erythematosus

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Conflict of interest: Yes

[Object] The aim of this study was to investigate the effect of miR-326 expression on autoantibody production and the differentiation of B cells in MRL/lpr mice. [Methods] 4 groups of female MRL/lpr mice were injected with lentivirus-miR-326 (LV-326), LV-sponge, LV-ctrl and the same amount of PBS through the tail vein respectively. The percentage of plasmablasts in spleen B cells were detected by flow cytometry. The titer of anti-dsDNA antibody in serum was determined by ELISA. Immunohistochemistry labeled kidney IgG expression. Differences between groups were analyzed by SPSS software. [Results] Results of flow cytometry demonstrated that the percentage of plasmablasts in spleen B cells were significantly higher in mice injected with LV-326 compared to mice with LV-sponge (P=0.0001) and LV-ctrl mice (P=0.0016). The results showed that levels of anti-dsDNA increased in mice injected with LV-326 than in mice with LV-sponge (P=0.005) and LV-ctrl (P= 0.03), there was no significant difference between LV-ctrl and PBS mice (P=0.90). The deposition of IgG in kidney of LV-326 mice was more than that in LV-sponge (P<0.0001) and LV-ctrl mice (P=0.0017). [Conclusions] These findings suggest that miR-326 may play a catalytic role in the development of lupus-like changes in lupus model mouse by promoting B cell differentiation and autoantibody production. These implied that miR-326 might be a candidate in SLE pathogenesis.

ICW10-6

Resveratrol inhibits plasma B cells differentiation and immune globulin production of CD19+ B lymphocytes in systemic lupus erythematosus patients through increasing the expression of Sirt1

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Conflict of interest: None

[Object] Systemic lupus erythematosus (SLE) is a systemic autoimmune disease that characterized by B cell activation and autoantibodies synthesis. Sirt1 deficiency results in the development of lupus-like disease in mice and resveratrol, the agonist of Sirt1, could inhibit the antibody production and proliferation of B cells in the lupus-mice. However, whether the Sirt1 is dysregulated in SLE patients and how it plays its role in the SLE pathogenesis is unclear. Therefore, this study was conducted to determine the expression of Sirt1 in SLE and explore its role in plasma B cell differentiation and immune globulin production. [Methods] Expression levels of Sirt1 were measured by both flow cytometry and real-time PCR (RT-PCR). Frequencies of B cell subsets were determined by flow cytometry. CD19+ B cells were stimulated with IL-21, anti-IgM and CD40L, followed by culture with resveratrol. Changes in mRNA levels of Sirt1, PRDM1, BCL-6, AID and T-bet were measured by RT-PCR. Plasma cell differentiation was assessed by flow cytometry; antibody production was analyzed by ELISA. [Results] The expression of Sirt1 were significantly decreased in CD19+ B cells of SLE patients when compared to HDs. The expression of Sirt1 in the SLE patients with high disease activity (SLEDAI scores >= 10) was lower than the patients without. The expression of Sirt1 is negatively correlated with the frequencies of CD19+ B cell and immature B cells (defined as CD19+IgD+CD38hi). After cultured with resveratrol, Sirt1 was increased in a dose-dependent manner. Resveratrol inhibited CDl38+ plasma cell differentiation and IgG

production. In addition, resveratrol suppressed the expression of PRDM1, AID, T-bet mRNA, but increased BCL-6 mRNA of B lymphocytes. [Conclusions] Sirt1 is downregulated in SLE patients. Resveratrol, the agonist of Sirt1, may present as a novel approach for the treatment of SLE by targeting Sirt1 and inhibiting plasma cells differentiation and immune globulin production.

ICW11-1

Serum MicroRNA-1 is a Novel Biomarker for Predicting Therapeutic Responses of Polymyositis/dermatomyositis-associated Interstitial Lung Disease

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Conflict of interest: None

[Object] Although intensive immunosuppressive treatment is necessary for the severe cases of polymyositis (PM)/dermatomyositis (DM), the predicting factor for therapeutic response is still unclear. MicroRNA-1 (miR-1) has been shown to be associated with myocyte differentiation and decreased in muscle biopsy sample from patients with inflammatory myopathies. Here we investigated the association between serum miR-1 level and clinical course of PM/DM patients. [Methods] We retrospectively analyzed clinical data, therapeutic regimens, and outcomes of PM/DM patients who had received initial treatment at Yokohama City University Hospital from 2008 to 2017. The serum samples from PM/DM and healthy controls (HC) were recruited. We measured serum miR-1 levels by quantitative real-time PCR and calculated the cut-off value as the mean plus two standard deviations in HC. [Results] Twenty-two patients (PM 4, DM 11, clinically amyopathic DM (CADM) 7) were recruited. The mean age was 63.5 ± 8.5 years, 13 (59%) were female, and 14 (64%) had interstitial lung disease (ILD). The serum miR-1 level was significantly higher in the PM /DM patients as compared to HC (p = 0.0085) and was decreased by treatment (p = 0.032). We divided the PM/DM patients with ILD into two groups, high miR-1 group and normal miR-1 group, by the serum miR-1 level at baseline. Although there were no significant differences in the clinical data and the initial prednisolone (PSL) dose between the high miR-1 group and the normal miR-1 group, PSL dose at 16 weeks and cumulative PSL dose until 16 weeks were significantly higher in the high miR-1 group than the normal miR-1 group (p = 0.025 and p = 0.036, respectively). We also found that serious infections were significantly more frequent in the high miR-1 group than the normal miR-1 group (p = 0.026). [Conclusions] This study demonstrates that miR-1 is a novel biomarker for predicting therapeutic responses and risk of infections in PM/DM patients with ILD.

ICW11-2

Circulating Endothelial Cells and Endothelial Activation Markers Correlate with Disease Activity in Juvenile Dermatomyositis

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Conflict of interest: Yes

[Objectives] Circulating endothelial cells (CEC), von Willebrand Factor antigen (VWF:Ag), P-selectin (PSEL) and thrombomodulin (TM) are released from damaged endothelium. In addition, endothelial progenitor cells (EPC) have been associated with poor vascular outcomes in systemic autoimmune diseases. We hypothesized that these endothelial markers may be indicators of disease activity in juvenile dermatomyositis (JDM). [Methods] In 20 patients (pts) with probable or definite JDM and matched healthy controls, peripheral blood CEC and EPC were quantitated by flow cytometry; EPC markers included CD34+/133+, KDR+/133+, and CXCR4+/133+. VWF:Ag was measured by immunoassay, and VWF activity by Ristocetin cofactor assay. TM and PSEL were measured by ELISA. Myositis disease activity and damage measures were assessed and nailfold capillary (NFC) morphology was quantified. Wilcoxon-rank sum and Spearman's rank correlations assessed relationships between variables. [Results] Among endothelial markers, CEC (median 0.85 vs. 0.18 cells/uL, VWF:Ag (141 vs. 96 IU/mL), and TM (7.0 vs. 1.9 ng/mL), but not EPC subsets or PSEL, were significantly elevated in JDM pts. CEC correlated with pulmonary activity (rs 0.56). CXCR4+/133+ EPC negatively correlated with extramuscluar and parent global activity (rs -0.65- -0.70). KDR+/133+ EPC correlated with NFC tortuosity (rs 0.63) and negatively correlated with LDL and total cholesterol (rs -0.68 - -0.71). VWF:Ag correlated with physician and parent global activity, cutaneous and extramuscluar activity, and NFC avascularity (rs 0.45-0.52). TM only correlated with NFC avascularity (rs 0.52). None of the markers correlated with Myositis Damage. [Conclusion] Markers of endothelial damage, including CEC, VWF and TM, were increased in JDM pts and correlated with extramuscular disease activity. EPC inversely correlated with myositis activity measures, suggesting decreased blood vessel regeneration during active disease.

ICW11-3

Association of myositis antibodies profile with clinical manifestations and outcome in patients with polymyositis / dermatomyositis: experience from a tertiary referral center

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Conflict of interest: None

[Object] To assess the profile of myositis antibodies in Chinese patients with polymyositis (PM)/dermatomyositis (DM) and explore its association with clinical features and prognosis. [Methods] 16 serum myositis-specific and associated antibodies (mi-2α, mi-2β, TIF1γ, MDA5, NXP2, SAE1, Ku, PM-Scl100, PM-Scl75, Jo-1, SRP, PL-7, PL-12, EJ, OJ, Ro-52) were measured by immunoblotting. Associations between antibody profile and clinical manifestations, laboratory data and outcome were determined. [Results] The study population comprised 19 PM, 49 DM and 12 clinically amyopathic dermatomyositis (CADM) patients. Overall, the most common antibody was anti-Ro-52 (71.3%), followed by anti-ARS (Jo-1/PL-7/PL-12/EJ/OJ, 51.4%), anti-MDA5 (31.3%), anti-SRP (17.5%), anti-TIF1γ (12.5%), anti-NXP2 (7.5%), anti-SAE1 (7.5%), anti-Ku (7.5%), anti-PM-Scl75 (6.3%), anti-mi-2α (3.8%), anti-mi-2β (3.8%) and anti-PM-Scl100 (3.8%). Anti-MDA5 antibody was exclusively seen in DM and CADM patients and the prevalence was higher in CADM than in DM (83.3% vs 30.6%, P=0.003). Anti-MDA5 positive patients have more rapidly progressive ILD and Gottron sign (92.0% vs 61.8%, P=0.006; 92.0% vs 41.8%, P<0.001), as well as lower creatine kinase concentrations (71 vs 992 IU/L, P<0.001). Anti-ARS positive patients demonstrated significantly higher prevalence of mechanic's hands (16.1% vs 0.0%, P=0.007). In addition, anti-TIF1γ antibody was associated with more frequent tumor prevalence (20% vs 0%, P=0.014). During the follow-up period (median 13 months), 9 patients died, among which 7 were anti-MDA5 positive. The survival time of anti-MDA5-positive patients was significantly less than those who were negative (6.9 vs 16.0 months, P=0.001). [Conclusions] Anti-ARS are the most common MSA in Chinese PM/DM patients. Anti-MDA5 is predominantly seen in patients with CADM and closely associated with rapidly progressive ILD and high mortality. Anti-TIF1γ positive patients should be routinely screened for tumors.

ICW11-4

Elevated serum Krebs von den Lungen-6 predicts relapse of myositis associated interstitial lung disease

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Conflict of interest: None

[Object] Interstitial lung disease (ILD) associated with polymyositis (PM), dermatomyositis (DM), and clinically amyopathic DM (CADM) often relapse after the remission. The aim of this study was to elucidate predictors of relapse in PM/DM/CADM associated ILD. [Methods] PM/DM/CADM-ILD patients who have ever visited our institution between 2002-2017 and achieved remission once were enrolled. We retrospectively collected clinical data from medical records and compared patient characteristics between relapse group and non-relapse group. Relapse was defined as exacerbation of radiological findings of which doctor-in-charge decided to intensify therapy. Then, using each characteristics which showed significant difference, we conducted proportional hazard analysis. [Results] Among 72 patients, 24 experienced relapse (relapse group) and 48 did not (non-relapse group). At the time of diagnosis, mean levels of serum Krebs von den Lungen-6 (KL-6), the rate of patients who had upper lung field lesion by CT, and anti-aminoacyl tRNA synthetase (anti-ARS) antibody prevalence were significantly higher in relapse group than in non-relapse group (1870 vs 935 mg/dl, p=0.003; 62 vs 27%, p=0.01; 88 vs 60%, p=0.03, respectively). Mean levels of %vital capacity (%VC) was significantly lower in relapse group than in non-relapse group (65.7 vs 81.2%, p=0.02). We set cut-off levels of KL-6 as 1359 mg/dl and that of %VC as 70.5% for predicting relapse by using receiver operating characteristic curve. Multivariate analysis revealed only serum KL-6>1359 mg/dl was an independent risk factor for relapse (hazard ratio: 4.9 (95%CI 1.0-24.0), p<0.05) among these 4 characteristics. [Conclusions] Elevated serum KL-6 predicted relapse of PM/DM/CADM associated ILD.

ICW11-5

Distinguishing Features of Clinically Hypomyopathic and Amyopathic Juvenile Dermatomyositis (CAJDM) from Juvenile Dermatomyositis (JDM)

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Conflict of interest: None

Objective: Clinically amyopathic juvenile dermatomyositis (CAJDM) has characteristic JDM rashes with little to no evidence of muscle involvement. The study purpose was to examine if CAJDM is a distinctive phenotype from JDM. **Methods:** Demographic, clinical, and treatment data of 12 (9 hypo- and 3 amyopathic) pts meeting Sontheimer criteria and 60 myositis Ab (MSA)-matched probable or definite JDM pts were examined. Differences were evaluated by Fisher's exact and Mann-Whitney tests. MSAs were tested by immunoprecipitation and IP-immunoblotting. **Results:** Nine (75%) pts with CAJDM had anti-TIF1, 1 had anti-MDA5 Abs and 2 were MSA negative. CAJDM were younger at diagnosis (median 4.1 vs. 7.3 yrs) with more frequent mild disease severity at onset (75 vs 12%) vs. Ab-matched JDM. Gottron's papules tend to be most frequent first rash in CAJDM (50 vs 20%). CAJDM less frequently had myalgias (8 vs 62%), arthralgias (17 vs 55%), arthritis (0 vs 48%), mucous membrane changes (9 vs 40%), calcinosis (0 vs 33%), dysphagia (0 vs 32%), abdominal pain (0 vs 37%), and fatigue (33 vs 82%) than JDM. The median muscle (0 vs. 0.3), skeletal (0 vs. 0.5) and overall total clinical system scores (0.06 vs. 0.2) were lower in CAJDM than JDM. CAJDM did not have ILD or malignancy. The total treatment duration did not differ between CAJDM and JDM. CAJDM used fewer medications compared to JDM. Only 50% of CAJDM used oral prednisone vs. 100% of JDM, but the maximum dose did not differ. None of the CAJDM pts received other DMARDs or biologics. There was no difference between CAJDM and JDM in the proportion of pts with a flare requiring an increase in therapy, who discontinued corticosteroid therapy, or who achieved remission. At a median f/up of 2.9 yrs, all CAJDM had normal function, none developed clinical weakness or calcinosis. **Conclusion:** CAJDM may be distinguished from JDM in that they more likely have TIF1 Abs, fewer clinical manifestations, receive less therapy and more favorable outcomes.

ICW11-6

Predictors of Clinical Outcomes in Patients with Juvenile Dermatomyositis

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Conflict of interest: Yes

[Object] We examined a large JDM registry for predictors of excellent treatment (Rx) responses, including discontinuation of corticosteroid therapy (CS-DC), complete clinical response (CCR, clinically inactive disease for ≧6 continuous mths on Rx), and remission (inactive disease for ≧6 continuous mths off all Rx). [Methods] We evaluated the probability of achieving CS-DC, CCR, and remission by Weibull time-to-event modeling in 305 JDM pts. Significant univariable predictors were examined in multivariable time-to-event analysis using Markov chain Monte Carlo Weibull extension models. The conditional probability of each outcome was also evaluated using Bayesian network models. [Results] Median Rx duration was 30 mths and follow-up duration was 43 mths. Fifty-two percent (159 pts) experienced CS-DC and the probability of achieving CS-DC was 57% at 5 years after initial Rx. Thirty-three percent (99 pts) and 26% (80 pts) achieved CCR and remission, respectively. The probability of CCR and remission at 5 years after Rx start were 44% and 31%, respectively. The absence of calcinosis, gastrointestinal, pulmonary or cardiac symptoms, and infection before illness onset were associated with shorter times to achieve these 3 outcomes. Anti-MDA5 autoantibodies (Abs) and absence of anti-p155/140 Abs were associated with CS-DC, but anti-MJ Abs and lack of early flare were associated with shorter time to CCR. Achievement of CCR strongly predicted shorter time to remission, with CS-DC, absence of lipodystrophy and younger age at first Rx as other predictors. The probability of CCR or remission was conditional on CS-DC and/or CCR. [Conclusion] A large proportion of JDM patients achieve positive Rx responses, including CS-DC, CCR, and remission, although timelines for these important outcomes are relatively long. Factors associated with shorter times to achieve these outcomes include selected clinical features, myositis Abs, and environmental factors.

ICW12-1

Th22 cells are a potent inducer of osteoclastogenesis in rheumatoid arthritis

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Conflict of interest: None

[Object] T helper (Th) cells can differentiate into functionally distinct subsets and play a pivotal role in rheumatoid arthritis (RA). Although elevated levels of IL-22 in the synovial fluids of patients with RA were reported, the relevance of Th22 cells to RA pathology remains unknown. [Methods] Human Th subsets such as Th1, Th17, and Th22 cells were sorted from the peripheral blood. We analyzed the influences of inflammatory cytokines on Th22 cell differentiation. $CD3^+CD4^+IL\text{-}22^+IL\text{-}17^-IFN\text{-}\gamma^-$Th22 cells and ligands of Th22-cell chemokine receptors (CCL17, CCL20, CCL28) in synovial tissues in patients with RA and osteoarthritis

(OA) were evaluated by immunohistochemistry. Th1, Th17 or Th22 cells were co-cultured with monocytes in the presence of M-CSF and RANKL and osteoclast formation was assessed. [Results] $CD3^+CD4^+CCR4^+CCR6^+CCR10^+$cells produced IL-22 alone, and that their ability to produce IL-22 exceeded that of other Th subsets. The stimulation with tumor necrosis factor-α, IL-6, and IL-1β induced differentiation of Th22 cells. Th22 cells were markedly infiltrated in synovial tissue in patients with RA, but not in patients with OA. CCL17, CCL20, and CCL28 were highly expressed in the synovial tissues of patients with high RA disease activity. Addition of IL-22 to the culture of monocytes increased numbers of tartrate resistant acid phosphatase positive osteoclasts formation. Co-culture of Th22 cells with monocytes induced osteoclasts formation more efficiently than that of either Th1 or Th17 cells. IL-22 neutralizing antibody inhibited osteoclast formation in co-culture of Th22 cells with monocytes. [Conclusions] The results indicated that Th22 cells possess strong potency of tissue migration and accumulate into inflamed synovial tissues. Th22 cells have the capacity to promote osteoclast differentiation through production of IL-22 and thus play a pivotal role in bone destruction in RA. Th22 cells might represent a new target for the treatment and control of RA-related joint destruction.

ICW12-2

Repression of the E3-Ubiquitin Ligase RNF146 by RANKL Integrates Multiple Pathways Controlling Osteoclastogenesis

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Conflict of interest: None

[Object] Bone undergoes continuous remodeling equally regulated by osteoblast-mediated bone formation and osteoclast-mediated bone resorption. RANKL, a member of the TNF cytokine family, is critically required for osteoclast differentiation. In addition to the induction of the osteoclastogenic master transcription factor NFATc1 by RANKL signaling, osteoclast development requires modulation of two additional signaling pathways: the coordinated activation of the SRC tyrosine kinase with the simultaneous inhibition of the Wnt/β-catenin pathway. However, the molecular mechanism by which these three independent pathways are integrated during osteoclastogenesis remains unclear. [Methods] We generated *Rnf146* conditional knockout mice (*Rnf146$^{fl/fl}$ LysM-Cre*) to examine the *in vivo* bone phenotype in the absence of RNF146 in macrophages. Micro-CT, histomorphometric analysis, Co-IP, ChIP, promoter assay, BrdU assay, ubiquitin assay, cell growth assay, differentiation assay, bone resorption assay, LPS challenge and ELISA were performed to investigate the molecular mechanism in this study. [Results] We found that RANKL simultaneously coordinates the activation of SRC and the suppression of β-catenin in addition to activation of its canonical NFATc1 pathway. RANKL represses the expression of the E3-ubiquitin ligase RNF146, which results in the stabilization of 3BP2, an obligate upstream regulator of SRC, and AXIN1, a component of the β-catenin destruction complex. Further, we identify the mechanism by which RANKL suppresses *RNF146* transcription through an inhibitory element in the *RNF146* promoter regulated by NF-κB. Lastly, depletion of RNF146 causes osteoporosis and hyper-sensitivity to LPS-induced TNF-α production *in vivo*. [Conclusions] We have unveiled a new pathway downstream of RANKL showing that RNF146 acts as an inhibitory switch controlling osteoclastogenesis and cytokine production that may be a control point underlying the pathogenesis of chronic inflammatory diseases.

ICW12-3

Bone destruction by RANKL-expressing T cells in chronic gouty arthritis

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Conflict of interest: Yes

[Object] To analyze the cellular expressions of pro-resorptive cytokines in gouty tophus tissues, to determine the capacity of monosodium urate monohydrate (MSU) crystals to induce these cytokines, and to understand the mechanisms of bone destruction in chronic gout. [Methods] Fourteen fixed, paraffin-embedded, uninfected tophus samples were analyzed immunohistochemically. Peripheral blood mononuclear cells (PBMCs) were cultured *in vitro* with MSU crystals, and gene expression was assessed by reverse transcription-polymerase chain reaction. *In vitro* osteoclastogenesis was performed using PBMCs and synovial fluid mononuclear cells (SFMCs). [Results] CD4+ T cells, CD8+ T cells, CD20+ B cells, and mast cells infiltrated tophus tissues. Tartrate-resistant acid phosphatase (TRAP)+ osteoclasts were present around tophi and in osteolytic lesions. Interleukin (IL)-1, IL-6 and tumor necrosis factor (TNF)-alpha were produced from infiltrated mononuclear cells, whereas receptor activator of nuclear factor κB ligand (RANKL) was strongly expressed in T cells. However, osteoprotegerin (OPG) was not or weakly expressed in tophus tissues. MSU crystals induced the expressions of IL-1, IL-6, TNF-alpha and RANKL in PBMCs, but inhibited OPG expression. In addition, the pro-resorptive cytokines were highly expressed in SFMCs of gouty arthritis patients. Furthermore, *in vitro* osteoclastogenesis was enhanced in SFMC cultures, but inhibited in T cell-depleted SFMC cultures. [Conclusions] Our study demonstrates that RANKL-expressing T cells and TRAP+ osteoclasts are present within gouty tophus tissues, and that infiltrating cells express pro-resorptive cytokines. Furthermore, our data show that MSU crystals have the potential to induce pro-resorptive cytokines, and T cells are involved in osteoclastogenesis in chronic gout.

ICW12-4

Myostatin inhibition reduces bone loss in an unloading osteoporosis model

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Conflict of interest: Yes

[Object] Myostatin, a secreted member of TGF-β superfamily, is a negative regulator of skeletal muscle mass as shown by increased muscle mass in myostatin-deficient mice. Myostatin has been reported to directly promote osteoclastogenesis (Nat Med 2015). However, it is still controversial whether myostatin inhibition could regulate bone mass in vivo. Here, we examined the effect of genetic inhibition of myostatin on bone loss in murine osteoporosis models. [Methods] Bone marrow-derived macrophages were treated with RANKL and myostatin, and osteoclast differentiation and function were analyzed in vitro. For in vivo experiments, we used mutant myostatin transgenic ($Mstn^{Pro}$) mice, in which myostatin prodomain, an endogenous myostatin suppressor, is excessively expressed and subsequently inhibits myostatin activity. We applied two different types of bone loss models, tail-suspension and RANKL-injection. For tail-suspension unloading model, the tails of mice were suspended for 2 weeks. For RANKL-injected model, RANKL (1 mg/kg) was injected intraperitoneally at day 0 and 1, and the bones were collected at day 2. Bone properties were determined by micro-CT. [Results] Myostatin stimulation enhanced RANKL-induced osteoclast formation and resorption activity in vitro. $Mstn^{Pro}$ mice exhibited increased muscle mass similarly to the previously reported myostatin-null mice. Bone volume was reduced by 45.2 ± 10.6% in WT mice after the tail-suspension, whereas the reduction was significantly improved in $Mstn^{Pro}$ mice (13.7 ± 11.2 %). On the other hand, RANKL-injection induced bone loss in both WT and $Mstn^{Pro}$ mice to the similar extent. [Conclusions] Myostatin inhibition by excessive prodomain alleviated bone loss in the unloading osteoporosis model but not in RANKL-injected model. The effect of myostatin inhibition might vary in different pathological conditions. Further research is required to clarify the clinical implications of myostatin inhibition in various disease settings.

ICW12-5

Pharmacological inhibition of tankyrase induces bone loss in mice by increasing osteoclastogenesis

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Conflict of interest: Yes

[Object] Tankyrase is a poly (ADP-ribose) polymerase that leads to ubiquitination and degradation of target proteins. Since tankyrase inhibitors work as Wnt inhibitors, they are being investigated as drug candidates for cancer. Tankyrase is reported to degrade the adaptor protein SH-3BP2. We have previously shown that SH3BP2 gain-of-function mutation enhances RANKL-induced osteoclastogenesis in murine bone marrow-derived macrophages (BMMs). Although the interaction between tankyrase and SH3BP2 has been reported, it is not clear whether the inhibition of tankyrase affects bone cells and bone mass. In this study, we investigated the effect of tankyrase inhibition in bone metabolism in vitro and in vivo. [Methods] To examine in vitro effects of tankyrase inhibitor, primary murine BMMs and primary calvarial osteoblasts from wild-type (WT) mice were treated with tankyrase inhibitors (IWR-1 or G007-LK). We evaluated osteoclast and osteoblast differentiation, respectively. To examine in vivo effects, 7-week-old WT male mice were treated with G007-LK for 4 weeks, and then tibias were analyzed by micro-CT and histology. [Results] In murine BMMs, both tankyrase inhibitors enhanced RANKL-induced osteoclast formation and function through the accumulation of SH3BP2, subsequent activation of Syk and NFATc1. Next, in primary calvarial osteoblasts, tankyrase inhibitors enhanced osteoblast differentiation, accompanying enhanced nuclear translocation of ABL, TAZ, and Runx2. Finally, in vivo experiment, the administration of G007-LK significantly decreased trabecular bone volume of tibias in association with increased numbers of osteoclasts. [Conclusions] Tankyrase inhibition upregulates both osteoclast and osteoblast differentiation. Also, we demonstrated that in vivo administration of the tankyrase inhibitor induces bone loss. Our findings uncover the role of tankyrase inhibition in bone cells and highlight the potential adverse effects of the inhibitor on bone.

ICW12-6

Retrospective evaluation of non responder for denosumab in osteoporosis treatment of rheumatoid arthritis patient

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Conflict of interest: None

(Object) We have evaluated non-responder (NR) for denosumab (d-mab) in during osteoporosis (OP) treatment of rheumatoid arthritis patient (RA) retrospectively. (Methods) 86 patients who were treated with d-mab for osteoporosis from June 2013 to September 2017 continuously for more than 2 years, were enrolled. Their bone mineral density (BMD) was measured with dual energy X-ray absorptiometry method. Patient's BMD in lumbar spine (LS), femoral neck (FN) were measured at the start of d-mab administration, and at every 6 months when administrated. Change of BMD from the baseline of each part was calculated for every measurement. Patients were classified as NR in according to change of BMD in every part, whereas last observation demonstrated lower than the first BMD. Parameters such as patient's background and disease control indices, bone metabolism markers such as tartrate-resistant acid phosphatase 5b (TRACP-5b) and type-1 pro-collagen -N- pro-peptide (TP1NP), and BMD at baseline and their change, were statistically evaluated for each part with Binary Regression Analysis. Statistically significant level was set within 5%. (Results) In LS, lower extremities compartment of modified Health Assessment Questionnaire and its change, and TRACP-5b and TP1NP at the baseline demonstrated significant correlation with NR, while administration and dosage of methotrexate thrown, and change of TRACP-5b demonstrated in FN. The other parameters demonstrated no statistical correlation. (Conclusions) As d-mab is antibody drug, existence of non-responder is predictable. Our results supported that it is also indicative in RA.

ICW13-1

Summary of Incidence Rates for Serious Infection, Herpes Zoster and Malignancies in Japanese Patients with Rheumatoid Arthritis Treated with Tofacitinib or Biologic Disease Modifying Antirheumatic Drugs Across Clinical Trial and Real-World Data Sources

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Conflict of interest: Yes

Objectives: Tofacitinib is an oral JAK inhibitor for the treatment of rheumatoid arthritis (RA). We summarized the incidence of serious infection (SI), herpes zoster (HZ) and malignancies with tofacitinib in Japanese and global clinical trials, and with biologic disease-modifying antirheumatic drugs (bDMARDs) from Japanese clinical trials, post-marketing surveillance (PMS) and registries of Japanese patients (pts) with RA. **Methods:** Incidence rates (IRs; pts with event/100 pt-years) for SI, HZ and malignancies were summarized for tofacitinib in Japanese and global pts with RA based on data pooled from Phase 1, 2 and 3 and long-term extension (LTE) clinical trials (1 LTE study ongoing at time of analysis; March 2015 data cut) and for bDMARDs (adalimumab, tocilizumab, infliximab, certolizumab, etanercept and golimumab) in Japanese pts with RA, within separate clinical trial, PMS and RA registry databases. **Results:** The IR for SI with tofacitinib was 3.39 and 2.70 in Japanese and global clinical trials, respectively; SI IRs reported for Japanese pts who received bDMARDs ranged from 1.69-8.36 in clinical trials, 2.50-8.95 in PMS and 3.03-10.68 in registries. The IR for HZ with tofacitinib was 8.00 and 3.90 for Japanese and global clinical trials, respectively; HZ IRs reported for Japanese pts who received bDMARDs ranged from 2.29-2.90 in clinical trials and 1.67-2.24 in PMS, and was 1.21 in registries. The IR for malignancies with tofacitinib was 1.29 and 0.90 in Japanese and global clinical trials, respectively; malignancy IRs reported for Japanese pts who received bDMARDs ranged from 0.53-1.25 in clinical trials, 0.64-1.13 in PMS and 0.47-1.85 in registries. **Conclusion:** In Japanese pts with RA who received tofacitinib in clinical trials, IRs for SI and malignancy were within the range reported for Japanese pts who received bDMARDs. The IR for HZ was higher for Japanese pts who received tofacitinib vs bDMARDs and for Japanese vs global pts in tofacitinib clinical trials.

ICW13-2

Efficacy and Safety of Tofacitinib with and without Methotrexate and Adalimumab with Methotrexate in Patients with Rheumatoid Arthritis Stratified by Baseline Methotrexate Dose

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Conflict of interest: Yes

Objectives: Tofacitinib is an oral JAK inhibitor for the treatment of rheumatoid arthritis (RA). ORAL Strategy, a global Phase 3b/4 study (NCT02187055; not conducted in Japan), compared tofacitinib 5 mg twice daily (BID) monotherapy, tofacitinib 5 mg BID + methotrexate (MTX), and adalimumab 40 mg once every 2 weeks + MTX in patients (pts) with RA and inadequate response to MTX (MTX-IR). This post-hoc analysis assessed efficacy and safety in ORAL Strategy by baseline (BL) MTX dose. **Methods:** Data were stratified by mean BL MTX dose (before randomization): low (≦15 mg/wk; N=720); high (>15 mg/wk; N=426). Efficacy outcomes at Month (M) 6 included ACR20, ACR50 (primary endpoint) and ACR70 responses, and rates of DAS28-4 (CRP) and DAS28-4 (ESR) scores <2.6. Safety was reported over the full study du-

ration. **Results:** Across treatment arms, mean BL body mass index was 27.5-27.8 and 28.0-29.3 kg/m² in the low and high BL MTX groups, respectively. At M6 in the tofacitinib monotherapy, tofacitinib+MTX, and adalimumab+MTX groups, respectively: ACR50 responses were 38%, 49% and 44% with low BL MTX, and 39%, 41% and 43% with high BL MTX; ACR20 responses were 65%, 74% and 72% with low BL MTX, and 64%, 71% and 69% with high BL MTX; ACR70 responses were 19%, 25% and 20% with low BL MTX, and 17%, 25% and 22% with high BL MTX; rates of DAS28-4 (CRP) <2.6 were 21%, 30% and 25% with low BL MTX, and 22%, 32% and 33% with high BL MTX; rates of DAS28-4 (ESR) <2.6 were 9%, 11% and 10% with low BL MTX, and 13%, 14% and 17% with high BL MTX. AEs (serious AEs) occurred in 56% (10%), 59% (9%) and 61% (5%) with low BL MTX, and in 64% (9%), 66% (5%) and 74% (9%) with high BL MTX. **Conclusion:** In ORAL Strategy, efficacy within each treatment arm was generally similar regardless of BL MTX dose; pts were MTX-IR and their response was likely due to the active medication. Fewer AEs were reported in the low vs the high BL MTX group for all treatment arms; frequency of serious AEs was similar between groups.

ICW13-3

Rapid and sustained effect of filgotinib, an oral JAK1 selective inhibitor, on patient-reported outcomes: Results from a Phase 2B dose-ranging study in active RA patients

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Conflict of interest: Yes

Background: Filgotinib is an oral, selective JAK1 inhibitor that has shown efficacy and safety both as add-on to methotrexate (MTX) and as monotherapy in two 24-week (wk) placebo-controlled Phase 2B studies in patients with active rheumatoid arthritis (RA) and inadequate response to MTX. **Objective:** To investigate the effect on patient-reported outcomes (PROs) of filgotinib as add-on to MTX in patients with active RA. **Methods:** Patients with active RA on a stable dose of MTX were randomized in a double-blinded manner to placebo (PBO) or one of three total daily doses of filgotinib (50mg, 100mg, 200mg) and two regimens (qd and bid) for 24 wks. PROs measured were patient's global disease assessment and pain, physical function (HAQ-DI), fatigue (FACIT) and HRQoL-SF36 mental/physical component scores (MCS/PCS). Results are presented from patients dosed with filgotinib 100mg or 200mg qd (selected Phase 3 doses) or PBO. **Results:** 594 patients were randomized and dosed. Baseline mean DAS28 (CRP) was 6.1 and mean HAQ-DI was 1.7, indicating significant disease burden. Both doses of filgotinib showed rapid statistically significant improvement in PROs compared to PBO: 200mg qd showed statistically significant effects as early as wk 1 for patient global disease assessment, wk 2 for patient pain and HAQ-DI, and wk 4 (earliest timepoint measured) for FACIT and SF-36 PCS. With 100mg qd, patient global disease assessment, patient pain and HAQ-DI significantly improved as of wk 2; and FACIT and SF-36 (PCS and MCS) as of wk 4. At wk 12, in both the 100mg qd and 200mg qd dosing groups, a higher proportion of patients showed normalized values for HAQ-DI, FACIT and SF-36 PCS and MCS compared to PBO. Responses were maintained or continued to improve throughout 24 wks dosing. **Conclusion:** Filgotinib 100mg and 200mg qd as add-on treatment to MTX, led to rapid decrease in RA disease burden as demonstrated by significant improvement in PROs as of the first timepoints measured.

ICW13-5

Efficacy of tacrolimus based on dosage and trough in systemic lupus erythematosus: a cross-sectional study

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Conflict of interest: None

[Object] To evaluate the relations among efficacy, dosage and serum trough level of tacrolimus (TAC) in systemic lupus erythematosus (SLE). [Methods] Patients with SLE who visited our hospital from April, 2016 to September, 2017 were included in the study. We collected the patient's demographic, clinical and laboratory parameters including SLE disease activity index (SLEDAI) at observation point of time (October, 2017) and just before starting TAC. We investigated the relation among the parameters cross-sectionally by univariate analyses. [Results] Two hundred twenty-three SLE patients were included in the study, and 49 received TAC at observation point of time. The mean age and disease duration were 42.2 ± 14.4 years and 16.4 ± 11.1 years, respectively. The mean dosage and trough level of TAC was 2.5 ± 0.9 mg/day and 5.4 ± 3.7 ng/ml, respectively. The trough level of TAC exceeded 5 ng/ml in 17 (44.7%) patients. The dose of prednisolone (PSL) was significantly reduced at observation point as compared to that before starting TAC (19.7 ± 14.6 vs 6.4 ± 4.7 mg/day, $p < 0.01$). SLEDAI score was also significantly decreased (7.1 ± 6.0 vs 3.7 ± 4.7, $p < 0.01$). Among the components of SLEDAI, hypocomplementemia ($p < 0.01$), leukopenia ($p = 0.04$) and new rash ($p = 0.04$) were improved, although there was no significant difference in scores of arthritis, proteinuria and thrombocytopenia. Patients who reached 5 ng/ml of TAC trough level showed significantly larger reduction in SLEDAI score as compared to those who showed under 5 ng/ml of trough level (6.4 ± 3.5 vs 1.1 ± 4.2, $p = 0.0005$), although there was no significant difference in reduction of PSL dose (17.5 ± 18.5 vs 11.8 ± 10.3 mg/day, $p = 0.28$). TAC dosage was not correlated with reduction of PSL dose ($r = -0.19$, $p = 0.20$) and SLEDAI score ($r = -0.07$, $p = 0.65$). [Conclusions] TAC is effective for decreasing SLE disease activity and steroid dose sparing. The trough level of TAC is important for controlling disease activity.

ICW13-6

The efficacy and safety of mycophenolate mofetil for the patients with lupus nephritis

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Conflict of interest: None

Objectives; We examined the efficacy and safety of mycophenolate mofetil (MMF) for 47 consecutive patients with lupus nephritis (LN). **Methods;** 47 eligible study subjects since August 2015 until May 2017 were over 16 ages men and women, who met the American College of Rheumatology criteria in 1987 or SLICC2012 for the classification of SLE and had lupus nephritis at a single center (LOOPS registry). MMF was started from 1g/day and weekly increased to 2-3g/day. Differences at screening and at 6 months were examined by paired t test. **Results;** Baseline characteristics were males:females=6:41, age 42.3 years and disease duration 199.7 months. The 46/47 patients were trailable at 6 months. The primary endpoint; the rate of major clinical response (MCR) was 27/46 (58.7%) while the partial clinical response (PCR) was 6/46 (13.0%) at 6 months (LOCF). Secondary endpoint; disease activity scores were significantly improved (SLEDAI 11.3→3.9, p<0.0001, total BAILAG 11.0→3.5, p<0.0001). Dose of corticosteroid was decreased from 25.9 to 10.9 mg/day (p<0.0001). Next, we examined the efficacy of MMF further focused in active LN. LN was classified as active (BILAG A or B) in 28 of the 46 patients at baseline. Two patients were lost to follow-up at 6 months. Of the 26 patients (WHO I:1, II:4, III:3, IV:9, V:4, III+V:3, IV+V:2), 20 (76.9%) improved in assessment of renal BILAG. In the same patients, serum creatinine decreased 0.91→0.86mg/dl (p=0.305) and UPCR (urine protein to creatinine ratio) significantly decreased 2.48→1.03 g/gCr (p=0.017). The persistence rate at 6 months was 71.7% (33/46). Thirteen patients were discontinued until 6 months because of diarrhea:3, cytopenia:3, no effect:2, exacerbation:1, self-judgement:1, edema:1, herpes zoster:1 and hair loss:1. **Conclusion;** MMF treatment

was effective in decreasing disease activity, taper of corticosteroid and well tolerated in patients with LN. However, further investigation for longitudinal efficacy and safety is needed.

ICW14-2

Relationship between RA disease activity and periodontal disease or smoking

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Conflict of interest: None

[Background and Object] Periodontal disease and smoking are thought to correlate with the onset of RA and treatment responsibility. The aim of this study was to validate the relationship between RA disease activity and periodontal disease and smoking. [Patients and Methods] The subjects are RA patients who visited Obihiro Kousei Hospital from 25 May to 24 Oct 2017. We asked the patients to answer the situation of oral health in 3 ways: having untreated cavity or periodontal disease, no cavity or periodontal disease, or toothless using a questionnaire. Patient also answered the smoking habit in 3 ways: current smoker, never smoked or ex-smoker. RA disease activity was also evaluated. [Results] Of 790 questionnaires collected, valid responses and complete dataset were obtained from 646 patients (81.2%). 102 (15.6%) were current smokers. 258 (34.0%) answered that they have self-reported untreated cavity or periodontal disease. Positive rate of anti-CCP antibody in current smokers, never-smoked patients and ex-smoker were 77.5%, 74.2% and 80.4%, respectively (not significant: NS, χ-square test). Positive rate of anti-CCP antibody in those who have cavity or periodontal disease, those who have no cavity or periodontal disease, those who are toothless were 77.6%, 75.8% and 78.4%, respectively (NS). Ratio of the patients in remission or low disease activity in current smokers, non-smokers and ex-smoker were 85.3%, 75.7% and 77.6%, respectively (NS). Ratio of the patients in remission or low disease activity in in those who have cavity or periodontal disease, those who have no cavity or periodontal disease, those who are toothless were 75.9%, 79.7% and 76.1%, respectively (NS). [Conclusions] In our patients, we couldn't find significant impact of having periodontal disease or smoking on anti-CCP positivity and RA disease activity. Under the treat-to-target strategy, it could be negligible.

ICW14-3

Characteristics of elderly-onset rheumatoid arthritis

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Conflict of interest: None

Objectives: To elucidate recent characteristics of elderly-onset rheumatoid arthritis (EORA). **Methods:** Patients who were diagnosed with rheumatoid arthritis in our institution from November 2015 until May 2017 were enrolled. They were divided into two groups EORA and younger-onset RA (YORA) according to the age at onset above or below 65 years old. Clinical data were collected from their clinical records and statistically analyzed. **Results:** 176 patients with RA were enrolled; EORA 37% and YORA 63%. The mean age was 74.0±1.5 and 46.3±2.4 years old, and female was 73.9% and 84.7%, respectively. The duration from onset to first visit was significantly shorter in EORA compared to YORA (4.7±3.0 to 13.9±5.9 months; p=0.038). Inflammatory biomarkers at the first visit were significantly higher in EORA than in YORA; CRP (2.6±0.7 vs 1.2±0.5 mg/dl, p<0.001), ESR (68±9 vs 38±6 mm/hr, p<0.001), ferritin (173.3±36.7 vs 102.3±18.8 ng/ml, p<0.001). Disease activity was also higher in EORA; DAS28-CRP (4.47±0.35 vs 3.49±0.27, p<0.001), CDAI (20.5±3.6 vs 15.1±2.2, p=0.009), SDAI (23.2±4.0 vs 16.1±2.3, p=0.001). EORA was more functionally impaired; HAQ-DI (1.26±0.22 vs 0.75±0.12, p<0.001). RF and anti-CCP antibody were less positive in EORA than in YORA (RF 55.4 vs 72.1%, p=0.024; anti-CCP 40.0 vs 63.1%, p=0.003). Large joints were more involved in EORA, but small joint involvement was not different between EORA and YORA. **Conclusions:** EORA developed more rapidly and showed severer inflammatory signs with more large joint involved.

ICW14-4

Prevalence of frailty increased with disease activity in patients with rheumatoid arthritis from the CHIKARA study

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Conflict of interest: None

[Object] Frailty is defined as the degradation of physical and cognitive function in elderly adults. The relationship between frailty and rheumatoid arthritis (RA) is unclear. We investigated factors related to frailty in RA patients from a prospective observational study. [Methods] Ninety-five of 100 patients entered in the CHIKARA study (UMIN000023744) were investigated using a frailty checklist. According to the reported article, frailty was defined as a score of 8-25, pre-frailty as 4-7, and normal as 0-3. We investigated relationships to disease activity in three groups, and analyzed factors influencing frailty. [Results] The frailty group was the oldest of the three groups (age: frailty 72.5, pre-frailty 68.6, normal 60.7; P=0.004). Disease activity score 28 ESR (DAS28E) and matrix metalloproteinase 3 (MMP3) concentration were higher in the frailty group than in the pre-frailty and normal groups (DAS28E: frailty 3.62, pre-frailty 3.27, normal 2.83, P=0.015; MMP3: frailty 143.7 ng/dl, pre-frailty 95.9 ng/dl, normal 88.6 ng/dl, P=0.033). Conversely, modified health assessment questionnaire (mHAQ) score was higher in the frailty group than in the pre-frailty and normal groups (frailty 0.9, pre-frailty 0.4, normal 0.1, P<0.001). Remission of RA was seen in 66.6% in the normal group and 6.7% in the frailty group. However, moderate or high disease activity was seen in 13.3% of the normal group and 46.7% of the frailty group. Prevalence of frailty increased with disease activity. Factors influencing frailty were age, locomotive syndrome, leg muscle score, grip strength, DAS28E, mHAQ, and Steinbroker class according to univariate analysis. Steinbroker class (odds ratio 3.25, P=0.031) and mHAQ (odds ratio 1.29, P<0.001) were independent factors according to multivariate analysis. [Conclusions] Frailty involved disease activity and physical function in RA patients. Control of disease activity is important to prevent not only disease progression, but also frailty.

ICW14-5

Comparison of the effects of forefoot joint-preserving arthroplasty and resection-replacement arthroplasty on walking plantar pressure distribution and patient-based outcomes in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] The purpose of this study is to clarify the difference in plantar pressure distribution during walking and related patient-based outcomes between forefoot joint-preserving arthroplasty and resection-replacement arthroplasty in patients with rheumatoid arthritis (RA). [Methods] Four groups of patients were recruited. Group1 included 22 feet of 11 healthy controls (age 48.6 years), Group2 included 36 feet of 28 RA patients with deformed non-operated feet (age 64.8 years, Disease activity score assessing 28 joints with CRP [DAS28-CRP] 2.3), Group3 included 27 feet of 20 RA patients with metatarsal head resection-replacement arthroplasty (age 60.7 years, post-operative duration 5.6 years, DAS28-CRP 2.4), and Group4 included 34 feet of 29 RA patients with metatarsophalangeal (MTP) joint-preserving arthroplasty (age 64.6 years, post-operative duration 3.2 years, DAS28-CRP 2.3). Patients were cross-sectionally examined by F-SCAN II to evaluate walking plantar pressure, and the self-administered foot evaluation questionnaire (SAFE-Q). Twen-

ty joint-preserving arthroplasty feet were longitudinally examined at both pre- and post-operation. [Results] In the 1st MTP joint, Group4 showed higher pressure distribution (13.7%) than Group2 (8.0%) and Group3 (6.7%) (P<0.001). In the 2nd-3rd MTP joint, Group4 showed lower pressure distribution (9.0%) than Group2 (14.5%) (P<0.001) and Group3 (11.5%) (P<0.05). On longitudinal analysis, Group4 showed increased 1st MTP joint pressure (8.5% vs. 14.7%; P<0.001) and decreased 2nd-3rd MTP joint pressure (15.2% vs. 10.7%; P<0.01) distribution. In the SAFE-Q subscale scores, Group4 showed higher scores than Group3 in pain and pain-related scores (84.1 vs. 71.7; P<0.01) and in shoe-related scores (62.5 vs. 43.1; P<0.01). [Conclusions] Joint-preserving arthroplasty resulted in higher 1st MTP joint and lower 2nd-3rd MTP joint pressures than resection-replacement arthroplasty, which were associated with better patient-based outcomes.

ICW14-6

Modified Scarf osteotomy with medial capsule interposition for hallux valgus deformity in rheumatoid arthritis cases including severe 1st metatarsophalangeal joint destruction

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Conflict of interest: None

[Object] For severe hallux valgus (HV) deformity in rheumatoid arthritis (RA) cases, joint preservation surgery has recently been performed with the progress of medical treatment of RA. This study aimed to investigate outcomes of modified Scarf osteotomy for RA cases, including severe 1st MTP joint destruction, and to evaluate risk factors for recurrence. [Methods] A retrospective observational study of 76 cases (60 patients) [mean follow-up period: 35 months (24-56 months)] that underwent the modified Scarf osteotomy with medial capsule interposition was performed. Japanese Society for Surgery of the Foot (JSSF) RA foot ankle scores and hallux scores were evaluated, along with preoperative and postoperative radiographic parameters. [Results] The mean JSSF RA foot ankle score and hallux score improved significantly (RA: preoperative: 52, final follow-up: 77, hallux: preoperative: 38, final follow-up: 75). Recurrence (hallux valgus angle [HVA] >20°) occurred in 12 feet (16%). Preoperative DAS28-CRP (Disease activity score evaluated on 28 joints-C-reactive protein), intermetatarsal angle between the first and second metatarsal bone (M1M2A), and M1M5A, as well as HVA, M1M2A, M1M5A, and Hardy grade at 3 months after surgery, were significantly greater in the recurrence group. There was a significant negative correlation between preoperative DAS28-CRP and JSSF RA foot and ankle scores at final follow-up (β=-0.39: p=0.02), while there was a significantly positive correlation between preoperative DAS28-CRP and HVA at the final follow-up (β=0.44: p=0.001). [Conclusions] The modified Scarf osteotomy for HV deformity improved outcomes in RA cases with severe 1st MTP joint destruction. Increased preoperative M1M2A and M1M5A, incomplete reduction of the sesamoid bone, HVA, M1M2A, and M1M5A at 3 months after surgery should be kept in mind for recurrence. The preoperative DAS28-CRP score was associated with clinical and radiographic outcomes after surgery.

ICW15-1

Autophagy Promotes Citrullination of Vimentin in Synovial Fibroblasts

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Conflict of interest: None

Objective: Our previous studies have indicated a critical role of autophagy in stress-induced cell death in synovial fibroblasts (SF). Given the relationship between autophagy and citrullination, we aimed to clarify the role of SF and autophagy in the autoimmunity in patients with rheumatoid arthritis (RA). **Methods:** Anti-cyclic citrullinated peptide antibodies and anti-citrullinated vimentin antibodies were measured in RA patients' sera using ELISA. The amounts of vimentin, citrullinated proteins, LC3, and βactin were quantified in SF by western blotting. To activate autophagy, SF were incubated in serum-free medium or treated with a proteasome inhibitor MG132. To inhibit autophagy, SF were treated with 3-methyladenin. To evaluate antigen presenting capacity of SF, the expression of HLA-DR and B7 molecules, including CD80, CD86, B7-H1, B7-H2, B7-H3, B7-H4, and B7-DC, was analyzed by flow cytometry after 72h treatment of IFNγ. **Results:** Anti-cyclic citrullinated peptide positive sera strongly bound to a 54 kDa protein in SF lysates, indicating the presence of antigen in SF. By immunoprecipitation with anti-vimentin and-citrulline antibodies, the 54 kDa protein was revealed to be citrullinated vimentin. Serum-free starvation (2h) or treatment with MG132 (10 mM, 24h) activated autophagy, evaluated by the conversion of LC3-I to LC3-II (p =0.04, n =4. p =0.03, n =6. respectively) and the increase of citrullinated vimentin (p =0.04, n =4. p =0.006, n =6. respectively). These effects were cancelled by 3-methyladenin, in SF. HLA-DR, B7-H1, and B7-DC were expressed on SF following treatment with IFNγ (100 U/mL, 72h), while B7-H3 was expressed on SF regardless the presence of IFNγ. **Conclusions:** Our current data indicates that SF may contribute to the autoimmunity of RA through the citrullination of vimentin promoted by autophagy.

ICW15-2

Both systemic administration of angiotensin II and its type 1 receptor gene deletion exacerbates erosive bone destruction in hTNF-transgenic arthritis mice

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Conflict of interest: Yes

[Object] Recent studies have demonstrated that angiotensin II (Ang II) functions on various organs including the skeletal system through its specific receptors, Ang II type I receptor (AT1R), type II receptor and Mas receptor. The receptors for Ang II and angiotensin-converting enzyme were shown to be up-regulated in the synovial tissue in patients with rheumatoid arthritis, suggesting the potential involvement of Ang II in the disease process. The purpose of this study was to investigate whether the renin-angiotensin system affects TNF-induced bone destruction using a murine arthritis model. [Methods] Ang II was infused by osmotic pumps from 12 to 16 weeks of age in human TNF-transgenic (hTNF-tg) mice. Bone erosion on the talus was analyzed by micro-CT. Inflammation, bone erosion, and osteoclast formation were evaluated by histological analysis. Serum TRAP5b levels were measured by ELISA. To examine the role of endogenous AT1R, AT1R-deficient mice were crossed with the hTNF-tg mice, and the yielded double mutant mice were evaluated as described above. [Results] Systemic administration of Ang II significantly augmented bone erosion on the talus associated with a 2.1-fold increased number of osteoclasts in the hTNFtg mice. Serum TRAP5b levels were also increased by 1.6-fold in the Ang II-infused hTNFtg mice. The swelling of the paws and histological inflammatory cell infiltration was not affected by Ang II infusion. Of interest, the gene deletion of AT1R in hTNFtg mice also resulted in more severe bone destruction compared to AT1R-sufficient control mice. [Conclusions] Both systemic Ang II administration and AT1R gene deletion exacerbated bone destruction in hTNF-tg mice without affecting the severity of arthritis. These results suggest that Ang II is involved in the TNF-induced bone destruction, and that the effect of Ang II is likely to be mediated by the receptors other than AT1R.

ICW15-3

Gene expression profiling of synovial fibroblast subsets revealed novel transcription factors to regulate IL-6

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Conflict of interest: Yes

[Object] Synovial fibroblasts play a crucial role in the pathogenesis of rheumatoid arthritis (RA). They secrete a variety of inflammatory cytokines including interleukin (IL)-6. We reported that synovial fibroblasts consist of three major subsets with distinct functions, and that one subset, which is defined as CD45-CD31-CD34+PDPN+ cells, is a dominant producer of IL-6. The present study was conducted to identify transcription factors to regulate the expression of IL-6 in the synovial fibroblasts, using gene expression profiling data of the synovial fibroblast subsets in the RA synovial tissues. [Methods] Global gene expression profiling data of freshly isolated synovial fibroblast subsets, which derived from the RA synovial tissues, were used to select transcription factors, differentially expressed across the fibroblast subsets. RA synovial fibroblast cell lines were transfected with siRNA against the selected transcription factor or control using the RNAiMax reagent. Cells were then cultured in the presence of 1ng/ml TNFa for 24 hours. IL-6 in the supernatant were quantified with ELISA. [Results] We identified ten transcription factors that were highly expressed in the CD45-CD31-CD34+PDPN+ fibroblast subset compared to the others. We silenced the ten transcription factors with siRNA specific to the individual factor genes, and found that silencing of AHR, EBF1, OSR2 or NFIA suppressed the IL-6 expression. Of note, AHR and EBF1 were involved reportedly in the regulation of IL-6 in synovial fibroblasts and adipocytes respectively. [Conclusions] We identified new transcription factors to regulate the expression of IL-6 in RA synovial fibroblasts. Identification of the synovial fibroblast subsets enabled us to clarify the mechanisms to regulate IL-6 production in the RA synovial tissues.

ICW15-4

Optimal application of a novel delivery system with mesenchymal stem cells (MSCs) treated with IL-6R seeded on PLGA nano-fiber in the repair of articular cartilage in RA

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Conflict of interest: None

[Object] Mesenchymal stem cells (MSCs) differentiate into several types of cells, including chondrocytes. MSCs are considered as an ideal tool for joint repair of rheumatoid arthritis (RA). Although local delivery system of MSCs is prerequisite to aim tissue repair, the methodology of local delivery remain unclear. Aim of this study is to establish how to implant poly-lactic-co-glycolic acid (PLGA) nano-fiber with MSCs into joint tissues in order to regenerate articular cartilages efficiently and safely. [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 implantation on articular cartilage repair were assessed by X-ray image, Safranin O (S-O) staining, or immunohistochemistry to detect human Aggrecan (ACAN) or human leukocyte antigen (HLA). [Results] X-ray images revealed that joint image of knees from AIA rats implanted with PLGA+ (MSCs+IL-6R), but not PLGA alone or PLGA+MSCs, were comparable with those of wild-type (WT) rats. S-O staining revealed that knee's joints from AIA rats implanted with PLGA+ (MSCs+IL-6R), but not PLGA+MSCs, showed similar positive image to those of WT ones. Human ACAN was exclusively detected in knee's joints from AIA rats implanted with PLGA+ (MSCs+IL-6R). No human HLA was detected in knee's cartilage tissues from AIA rats implanted with all cell-based tools. [Conclusions] After co-implantation of PLGA+ (MSCs+IL-6R) into AIA rat's joint space, MSCs efficiently differentiate into chondrocytes, and reside at damaged articular cartilages. The chondrocytes produce cartilage matrix, efficiently provide the repair of cartilage tissue, and further exhibit high safety. These results suggest a potential clinical application of MSC-based treatment by utilizing PLGA for the repair of articular cartilage in patients with RA.

ICW15-5

MicroRNA profiling of MTX-treated fibroblast-like synocvial cells in Rheumatoid arthritis revealed a possibility of microRNA-887-3p as novel therapeutic target of RA

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Conflict of interest: None

Background The hallmarks of RA is the expansive of FLS, therefore inhibition of FLS proliferation might be potent therapeutic strategy of RA. Recently, several studies reported drugs modulated microRNA expression and that have been considered as one of important mechanism of cellular action to drug. **Objective** To investigate the effect of MTX in microRNA modulation in RA-FLS. **Methods** RA-FLS was treated with MTX with 1uM for 48 hours. To investigate differentially expressed miRNAs, we performed miRNA array analysis. Expression of miRNA-887-3p (miR-887) was analyzed by quantitative real-time PCR. To investigate the functional role of miR-887, RA-FLS was transfected with synthetic precursor miRNA / inhibitors of miRNA of miR-887 using Lipofectamine. The cytokine/ chemokine production were screened by multiplex cytokine/chemokine bead assays and confirmed by ELISA. Finally, migratory activities of RA-FLS was analyzed by scratch assay. **Results** After 48 h of treatment with MTX, the expression of 13 miRNAs were changed. Among them, quantitative real-time PCR with additional samples confirmed that miR-887 was up-regulated in response to MTX (1.79 ± 0.46 -fold, $p<0.05$, $n=7$). Microarray analysis with gene ontology analysis revealed that several genes correlated with cell signalling was modulated by miR-887. Overexpression of miR-887 decreased cytokine/ chemokine production of RA-FLS such as TNF-a, GM-CSF, CXCL10. Among these candidates, the secretion of GM-CSF was consistently and strongly decreased from RA-FLS transfected with pre-miR-887. Furthermore overexpression of miR-887 reduced migratory activity in scratch assay. **Conclusion** Our result showed that MTX altered micro RNA expression profiles in RA-FLS. MiR-887 might be downstream effector of MTX in suppression of its cytokine production and invasive phenotype. This knowledge may also be useful for the development of novel therapeutic strategies based on other treatments able to boost the cellular reservoir of miR-877.

ICW15-6

Bioactive compounds in Gundelia tournefortii L. inhibit TNF-a-mediated matrix metalloproteinase-13 induction in articular chondrocytes by downregulation of MAP kinases, AP-1 and NF-kB transcription factors

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Conflict of interest: None

[Object] Currently, traditional medicinal plants are targeted for phytochemicals capable of affording cytoprotective activity against arthritic inflammation and cartilage resorption. Prospective cytoprotective mechanisms were investigated by pretreating chondrocytes (ATCC© CRL-2846™) with *Gundelia tournefortii* L. dichloromethane (DCM) extract followed by stimulation with TNF-α and expression profile assessment of genes mediating MMP-13 induction. [Methods] Chondrocytes were initially tested for biocompatibility with *G. tournefortii* DCM extract via resazurin-based viability assay. Cells were later passaged in 96-well plates prior to pretreatment with DCM extract 30 min before exposure to TNF-α. Set-ups pretreated with celecoxib and ibuprofen were utilized as

anti-inflammatory controls. Total RNA was later extracted and subjected to qRT-PCR using primers specific for MMP-13, MAP kinase, AP-1 and NF-κB genes, respectively. A second setup was performed for western immunoblot analysis. All assays were performed in triplicate. LC-MS was performed to determine the phytochemical profile of the plant extract. [Results] The extract showed biocompatibility and provided cytoprotection against TNF-α-activated chondrocytic inflammation as shown by significant downregulation of MMP-13, MAP kinase, AP-1 and NF-kB transcripts at an effective concentration of 3.1 μg/mL. Equivocally, western blot analysis revealed significant decrease in MMP-13, MAP kinase, AP-1 and NF-kB protein products. The anti-inflammatory activity of *G. tournefortii* was observed to have no significant difference with celecoxib and ibuprofen. LC-MS afforded β-sitosterol, stigmasterol, β-amyrin, linoleic and oleic acids. [Conclusions] The cytoprotective activity of *G. tournefortii* against arthritic inflammation may be attributed to the presence of bioactive compounds. Results show the promising pharmacognostic application and may therefore potentially be a source of natural chemotherapeutic compounds against arthritis.

ICW16-1

The risk of obstructive sleep apnea in 52994 patients with systemic autoimmune diseases in taiwan: a nationwide population-based study

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Conflict of interest: None

Background: Several pathological mechanisms may underlie an association between obstructive sleep apnea (OSA) and autoimmune diseases. There is few evidence of increasing risk of OSA in patients with rheumatoid arthritis, ankylosing spondylitis. The association between systemic autoimmune disease and OSA were not clear in Asian. We hypothesized that autoimmune diseases would predispose patients to the occurrence of OSA. **Objectives:** To explore the association between the OSA and autoimmune diseases **Methods:** 52994 adult patients with systemic autoimmune diseases diagnoses recorded in the Taiwan National Health Insurance Research Database between 2002 and 2011, after excluding those with antecedent OSA. A comparison cohort of 211976 participants was formed by age-, gender-matched controls. Multivariable Cox regression was performed on the two cohorts to compute the risk of OSA during follow-up period. **Results:** In patients with systemic autoimmune diseases, the overall risk for incident OSA was significantly higher than in controls (adjusted hazard ratio [HR] = 1.58, 95% confidence interval [CI] = 1.38-1.82). Risk of OSA in individual autoimmune diseases, including rheumatoid arthritis (RA), Sjögren's syndrome (SS) and Behçet disease, was also significantly higher than in controls (HR [95% CI] for RA, primary SS, secondary SS and Behçet disease were 1.36[1.12-1.63], 2.28 [1.68-3.10], 2.88 [2.14-3.87] and 2.39[1.43-4.01], respectively). Increased risk for systemic lupus erythematosus did not reach statistical significance (HR: 0.79 [0.49-1.28]). **Conclusions:** Patients with systemic autoimmune diseases including of RA, primary or secondary SS and Behçet disease were associated with a higher risk for developing OSA.

ICW16-2

Evaluation of right ventricular function and prediction of prognosis by combining cardiac magnetic resonance with right heart catheterization in pulmonary hypertension associated with connective tissue diseases

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Conflict of interest: None

Object: Pulmonary hypertension (PH) is an increased blood pressure in pulmonary arteries, and affects the right side of the heart, ultimately leading to heart failure and death. Accurate evaluation of right ventricular (RV) function is thus critical to predict the prognosis of PH patients. This study aimed to evaluate RV function of patients with PH associated with connective tissue diseases (CTD) by combining cardiac magnetic resonance (CMR) with right heart catheterization (RHC) and to predict the prognosis of those patients. **Methods:** This is a single center retrospective analysis comprising 77 consecutive CTD patients who underwent both CMR and RHC from January 2008 to October 2017. End-systolic elastance (Ees, mPAP/RV end-systolic volume index), pulmonary arterial elastance (Ea, (mPAP-PAWP)/stroke volume index), Ees/Ea, and RV end-diastolic dimension index (RVEDDI) were calculated as parameters of load-independent RV systolic function, RV afterload, RV systolic function, and RV diastolic function, respectively. **Results:** Of 77 patients, 52 had pulmonary arterial hypertension (PAH), 10 had PH without PAH, and 15 did not have PH. Ten patients died during a median follow-up period of 26 months. The 2-year overall survival rate was significantly lower in patients with Ees/Ea of < 0.4 or RVEDDI of > 31 mm/m^2 compared to other patients (56% vs 98%, p<0.001). The 2-year survival of patients with both Ees/Ea of < 0.4 and RVEDDI of > 31 mm/m^2 was only 40%. RVEDDI of > 31 mm/m^2 strongly predicted the mortality of CTD-PH patients with a sensitivity of 75%, a specificity of 99%, and an AUC of 0.85. In patients with PAH associated with systemic sclerosis (SSc), survival rate was significantly lower (p = 0.026) and RVEDDI was significantly higher (p = 0.004) compared to other PAH patients. **Conclusions:** Our data indicated that combining CMR with RHC accurately evaluate RV systolic and diastolic function, strongly predicting the prognosis of patients with CTD-PH, including SSc-PAH.

ICW16-3

Biologic Use and Incident Chronic Kidney Disease in Rheumatoid Arthritis

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Conflict of interest: None

[Object] Rheumatoid arthritis (RA) is associated with reduced kidney function, possibly due to chronic inflammation or the use of nephrotoxic therapies. However, little is known about the effects of RA therapy using novel non-nephrotoxic biologic agents on the risk of incident chronic kidney disease (CKD). We aimed to investigate the association of biologic treatment with incident CKD and change in estimated glomerular filtration rate (eGFR). [Methods] The overall cohort included 20,757 U.S. veterans with an eGFR ≧60 mL/min/1.73m^2 who were diagnosed with RA from 2004-2006, with follow-up through 2013. We examined the associations of biologic use with incident CKD (eGFR <60 with a decrease of at least 25% from baseline, and eGFR <45 mL/min/1.73m^2) and change in eGFR (<-3, -3 to <0 [reference], and ≧0 mL/min/1.73m^2/year) in propensity-matched patients based on their likelihood to initiate biologic treatment, using Cox models and multinomial logistic regression models, respectively. [Results] Among 20,757 patients, 4,617 (22.2%) started biologic therapy. In the propensity-matched cohort, patients treated (versus not treated) with biologic agents had a lower risk of incident CKD (hazard ratios [95% CI], 0.95 [0.82-1.10] and 0.71 [0.53-0.94] for decrease in eGFR <60 and <45 mL/min/1.73m^2, respectively) and progressive eGFR decline (multinomial odds ratios [95% CI] for eGFR slopes <-3 and ≧0 [versus -3 to <0] mL/min/1.73m^2/year, 0.67 [0.58-0.79] and 0.76 [0.69-0.83], respectively). A significant deceleration of eGFR decline was also observed after biologic administration in patients treated with biologics (-1.0±1.9 versus -0.4±2.2 [mL/min/1.73m^2/year] before and after biologic use, respectively, *P* <0.001). [Conclusions] Biologic agent administration was independently associated with lower risk of incident CKD and progressive eGFR decline. Clinical trials are warranted to test whether active biologic interventions can prevent adverse renal outcomes associated with RA.

ICW16-4

Maternal and neonatal outcomes in women with autoimmune disease using biologics in pregnancy: A systematic review and meta-analysis of observational studies

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Conflict of interest: None

Objectives: Existing studies on the impact of biologics on pregnancy outcomes have small sample sizes and report conflicting results. Our objective was to conduct a systematic review and meta-analysis of existing literature on this important question. **Methods:** A systematic review and meta-analysis was conducted in Cochrane Database of Systematic Reviews, Embase, and MEDLINE to identify literature in English, French, German or Spanish published from 1995 to 2017 related to perinatal use of biologics among women with autoimmune disease and risk of adverse maternal and neonatal outcomes. Studies were included if they were observational studies of women exposed to biologics before or during pregnancy, with a comparator group of unexposed disease-matched pregnant women, and reported at least one pregnancy outcome of interest (i.e., preterm delivery, congenital malformations [CM]). For respective outcomes, we pooled findings across included studies with random-effects models using RevMan5. **Results:** 16 studies were included of which 13 studies reported only crude rates of outcomes. Pooled crude rates of outcomes in biologics users vs. disease matched pregnant non-users showed that biologics users were at increased risks of preterm deliveries (odds ratio [OR] 1.61, 95% confidence interval [CI] 1.36-1.90) and low birth weight births (OR 1.67, 95% CI 1.21-2.31); but not CM (OR 1.27, 95% CI 0.99-1.62) or stillbirths (OR 0.89, 95%CI 0.54-1.47). Only 3/16 studies reported adjusted risk estimates. Pooled adjusted risk estimates did not show any statistically significant associations with biologics use and preterm delivery (aOR 1.15, 95%CI 0.80-1.64) or CM (aOR 1.27, 95%CI 0.93-1.74). No other outcomes were reported in these studies. **Conclusion:** Studies reporting adjusted risk estimates showed no increased risk of preterm delivery or CM associated with biologics use, suggesting that increased rates of adverse outcomes may be due to disease activity itself or other confounders.

ICW16-5

Our experience of methotrexate-related lymphoproliferative disease (MTX-LPD) in RA treatment

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Conflict of interest: None

[Objective] To investigate cases of MTX-LPD that occurred during use of MTX against RA in our department. [Patients and Methods] Nine patients that MTX-LPD occurred during use of MTX against RA in our department were included in this study. The average age at onset of RA was 48.3-year-old. The average age at onset of MTX-LPD, MTX dose at the onset, a time duration from onset of RA to the onset, a time duration to MTX administration until the onset, a site of lymphoma development, clinical symptoms, values of LDH and IL-2R at the onset, EB virus morbidity, clinical course and RA treatment after the onset were examined. [Results] The average age at onset of MTX-LPD was 68.4-year-old. The MTX dose at the onset was 6.7 mg/week. The time duration from onset of RA to the onset was 20.1 years. The time duration to MTX administration until the onset was 12.8 years. Lymphomas occurred mainly in cervical lymph node swelling, while swelling of the inguinal lymph node and the thyroid lymph node was also observed. In addition, extranodal lesions also showed in parotid glands, liver, tonsils and as retroperitoneal tumors, palate swelling, and showed various generation sites. LDH value at the onset was high in 5 cases. IL-2R value was high in all cases at the onset. EB virus was positive in 4 of 7 cases that could be confirmed. In 3 of 9 cases, the lymphadenopathy was relieved only with follow-up observation with MTX discontinuation. Six cases underwent biopsy, and all cases were diagnosed diffuse large cell B cell lymphoma. One of them was relieved only MTX discontinuation. In 5 cases, the R-CHOP chemotherapy was administered up to 6 courses. In one of 5 cases, peripheral blood stem cell transplantation was performed in combination. All cases survived in the mean period of 3.1-year after the onset. [Conclusion] Although all cases of MTX-LPD cases in our department are alive at the present time, careful follow-up is necessary for lymphoma and RA together in the future.

ICW16-6

Clinicopathological features of clinical methotrexate-induced lymphoproliferative disorders (c-MTX-LPD)

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Conflict of interest: None

[Object] Although methotrexate (MTX) withdrawal is accepted as the first step in managing patients who develop MTX-induced lymphoproliferative disorders (MTX-LPD), other etiologies, such as viral infection and the worsening of AD activity cause the similar LPD symptoms. In the clinical practice, MTX withdrawal often induces prompt regression of LPD (suggestive LPD; s-LPD), making tissue biopsy futile. In this study, we aimed to analyze patients with clinical MTX-LPD (c-MTX-LPD), being defined as patients with s-LPD manifestations but did not undergo biopsy because of the prompt LPD regression after MTX withdrawal. [Methods] Data were collected from 28 patients with autoimmune diseases (ADs) who had s-LPD with a retrospectively analysis. [Results] A total of 28 cases of c-MTX-LPD were recorded among patients with ADs at our institutions Nine men and 19 women were recored, with a median age of 65.0 years at the time of s-LPD development. The ADs were 27 patients had rheumatoid arthritis (RA). The main initial manifestations of s-LPD were lymphoadenopathy (N = 14) and fever (N = 9). The median duration from the time of s-LPD development to the time of MTX withdrawal was 23 days. After MTX withdrawal, 7 of the 28 patients (25%) developed definite LPD (d-LPD). The median duration from the time of MTX withdrawal to the time of d-LPD development was 11 months. A total of 6 of the 7 patients with d-LPD had Hodgkin lymphoma,. A total of 24 among the 28 patients with c-MTX-LPD were alive. The 5-year OS rate was 82.4%. Death was caused by progressive disease (N = 3) and secondary acute myeloid leukemia (N = 1). The markers of CRP > 5 mg/dl ($p = 0.00297$) and sIL-2R > 4000 U/L ($p = 0.0135$) were detected d-LPD development in comparison between patients with and without d-LPD. [Conclusions] In the clinical practice, the c-MTX-LPD is one of the most important concerning in terms of the clinical management. To further understanding, the accumulated analyses should be required.

ICW17-1

Plasmablast Proliferation is Associated with Toll Like Receptor 7 Polymorphisms and Upregulation of Type I Interferon, Contributing to the Antibody Production in Antiphospholipid Syndrome

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Conflict of interest: None

[Object] Antiphospholipid antibodies (aPL) are pathogenic autoantibodies in systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS). This study aimed to clarify the mechanism of aPL production. [Methods] A total of 19 subsets of B and T cells were evaluated in peripheral blood mononuclear cells (PBMC) of 26 primary APS (PAPS), 18 SLE-associated APS (SLE/APS) patients and 10 healthy controls by flow cytometry. Twenty-one single nucleotide polymorphisms (SNP), which were shown to be associated with autoimmune or thrombotic diseases, were analyzed in genomic DNA of those patients. Interferon (IFN) score was calculated based on the mRNA expression of Ly6e, Mx1, IFIT1 and IFIT3 in PBMC. PBMC obtained from APS patients were cultured ex vivo following depletion of CD19+CD20+ or CD19+CD20- cells and the

culture supernatants were applied to aPL measurements. [Results] In PAPS and SLE/APS patients, plasmablasts, Th2 cells and Th17 cells were increased while pre- and post- switched memory B cells, regulatory B cells and regulatory T cells were decreased compared to healthy controls. Genomic analysis revealed that the increase of plasmablasts and the decrease of memory B cells were more pronounced in patients with a risk allele of SNP in toll like receptor 7 (TLR7) gene (rs3853839). IFN score was significantly higher in the TLR7 SNP risk allele carriers, confirming the altered downstream signaling of TLR7. Ex vivo experiments showed that aPL, including anti-cardiolipin/β2-glycoprotein I-IgG and -IgM, were present in the culture supernatant of CD19+CD20+ depleted PBMC from APS patients, but not in that of CD19+CD20- depleted cells. [Conclusions] Our data indicate a crucial role of plasmablasts in the production of aPL. Furthermore, plsmablast proliferation was associated with TLR 7 and type I IFN, suggesting a common pathophysiology in SLE and APS. Targeting plasmablasts might be a novel, immunological therapeutic approach in the treatment of APS.

ICW17-2

Risk factors for heart valve disease in patients with antiphospholipid syndrome

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Conflict of interest: None

Objectives: Antiphospholipid syndrome (APS) is well known to be a risk of heart valve diseases (HVDs). The purpose of this study is to elucidate risk factors for HVDs in patients with APS. **Methods:** We reviewed consecutive APS patients diagnosed according to the Sydney criteria in 2006 who had been followed in Keio University Hospital in October 2017. The presence of HVDs was identified by the latest transthoracic and/or transesophageal echocardiography. Antiphospholipid antibodies (aPLs) included lupus anticoagulant [LA], anticardiolipin antibodies [aCL], anticardiolipin β2-glycoprotein I complex antibody [aCL-β2GPI]). We divided the patients into two groups by the presence of HVDs, and compared the groups. **Results:** Fifty-five APS patients were identified. Among them, 43 patients underwent echocardiography and enrolled in the analysis. Six patients were primary APS, 36 were secondary APS with systemic lupus erythematosus, and one with Sjögren syndrome. HVDs were detected in 26 (60.5%) patients including 20 patients with mitral regurgitation (MR) and a patient with Libman-Sacks endocarditis. The use of prednisolone, miscarriage episodes and the presence of arterial or venous thrombosis in patients with HVDs did not differ from those without HVDs. While the positivity of aCL or aCL-β2GPI was not different between patients with HVDs and those without, positive LA was much higher in patients with HVD and in patients with MR than those without (88.5% vs 35.3%, $p<0.01$; 85.0% vs 52.2%, $p=0.027$, respectively). In addition, patients with HVDs had double and triple positive tests of aPLs significantly frequently than those without HVDs ($p=0.010$ and $p=0.023$, respectively). **Conclusion:** Positive LA test and positivity for 2 or more tests of aPLs are a risk factor for LVD in patients with APS, which suggests regular monitoring cardiac ultrasonography is needed in such patients.

ICW17-3

Morbidity and mortality in patients with antiphospholipid syndrome during a 10-year period: a longitudinal cohort study of 157 Japanese patients

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Conflict of interest: None

[Objectives] The objective of this study is to clarify the morbidity and mortality in patients with antiphospholipid syndrome (APS). [Methods] This study is a longitudinal cohort study of Japanese APS patients, conducted in our clinic between April 1990 and March 2017. Patients who were followed-up for less than 2 years were excluded. Events were defined as the recurrence of thrombosis, severe bleeding, and mortality. Kaplan-Meier curves were applied to estimate the events survival rate. [Results] A total of 157 APS patients (137 females, median age 39 years [range 30.0 - 54.0 years], 59 primary APS) were included and followed-up for a median of 7.0 years [range 4.0 - 14.0 years]. At the start of observation, a history of thrombosis was observed in 132 patients (84.1%) and any obstetric manifestation was found in 50 patients (31.8%). The main clinical manifestations were strokes, deep vein thrombosis, pulmonary embolism and early pregnancy loss. During the observation, mortality occurred in 13 patients (8.3%) and the survival probability at 10 years was 92.4%. Recurrence of thrombotic events was observed in 45 patients (28.7%, recurrence rate 3.3 per 100 patient-years). Thirty five out of 36 patients with a history arterial thrombosis (97.2%) had recurrent arterial thrombotic events, while recurrent venous thrombosis occurred in 6 out of 9 patients (66.7%) with a history of venous thrombosis. Serious bleeding events were observed in 8 patients (5.1%, 0.59 per 100 patient-years) and event free survival rate in 10 years was 65.6%. In Kaplan-Meier analysis, patients with a history of arterial thrombosis and diabetes mellitus experienced significantly more frequent event occurrences (Log-rank $p=0.001$, 0.03). [Conclusion] Patients with APS develop recurrent thrombosis and serious bleeding with high mortality despite current treatment. Diabetes mellitus is a risk factor of the recurrent thrombosis, severe bleeding, and mortality.

ICW17-4

Efficacy and safety of possible therapeutic regimens in the management of antiphospholipid antibody associated thrombocytopenia: a systematic review and meta-analysis

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Conflict of interest: None

Background: Despite the pro-thrombotic nature of antiphospholipid antibodies (aPL), thrombocytopenia is frequently observed in patients with antiphospholipid syndrome (APS) or in non-APS patients with aPL. The management of the thrombocytopenia in aPL positive patients (aPL associated thrombocytopenia; APAT) is often deductive, due to the paradoxical risks of thrombosis and hemorrhage: Antiplatelet agents (APs) are frequently used as prophylaxis for thrombosis; and glucocorticoid therapy (GC) or splenectomy are often applied for cases with severe thrombocytopenia. **Object:** To evaluate the efficacy of therapeutic regimens in APAT through a systematic review (SR) of the literature. **Methods:** Four representative therapeutic approaches for APAT (APs, GC, splenectomy and thrombopoietin receptor agonist) were selected as the evaluations for SR and redefined using the PICO format and prioritized. SR was performed by Cochrane Japan Centre using three major databases; MEDLINE, EMBASE and CENTRAL. **Results:** We identified 9 case-controlled trial citations: 1 for APs; and 4 for GC and splenectomy, respectively. APs reduced thrombotic events compared with the control group (3/75 vs 4/28, $p < 0.03$), but no effect was found on platelet counts or hemorrhagic complications. Complete remission rates were higher in patients with GC or splenectomy compared with the patients without them (7/19 vs. 0/7, $p < 0.05$ and 49/55 vs. 4/48, $p < 0.001$, respectively). Meta-analysis of splenectomy on intractable cases revealed the positive effect on platelet counts (mean difference 22.6×10^4 /μL, $p = 0.007$). There were no thrombotic complications due to GC or splenectomy. However, the risk of bias of literature was high, especially for GC related citations. **Conclusions:** The APs as prophylaxis for thrombosis and GC or splenectomy for treatment of severe cases seem suitable therapeutic approach for APAT. Further clinical trials are required to establish substantial agreements on therapeutic recommendations.

ICW17-5

The effect of intensive immunosuppressive therapy on the long-term prognosis of SLE-associated pulmonary arterial hypertension: A Prospective cohort study

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Conflict of interest: None

Objective: PAH targeted therapy is traditionally recommended as the first line medication in the treatment of PAH. As immune and inflammatory mechanisms are involved in the genesis and progression of SLE-associated pulmonary arterial hypertension (PAH), immunosuppressive therapy may play a significant role in the management of SLE-associated PAH. This study aimed to investigate the effect of intensive immunosuppressive therapy on the long-term prognosis of SLE-associated PAH. **Methods:** This single-center cohort study enrolled 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. The clinical endpoint was death from any cause. Kaplan-Meier curves and Cox proportional hazards regression analysis were used to evaluate the effect of intensive immunosuppressive therapy. **Results:** 110 patients with SLE-associated PAH were enrolled in this study. Among them, 80 patients received intensive immunosuppressive therapy (IST), which is a combination of high-dose glucocorticosteroids and cyclophosphamide, mycophenolate or acetazolamide. 71 patients received PAH target therapy at baseline. The 1, 2 and 3-year survival rates were 96.3%, 92.5% and 88.8% in patients with IST, and were 90.0%, 86.7% and 74.8% in patients without IST. Further cox regression analysis showed that the long term survival of patients with IST was significantly better than those without IST (HR 2.59, p=0.043, 95% CI [1.03, 6.54]). The same result was shown in patients with PAH target medication at baseline (p=0.041), while not shown in patients without PAH target medication (p=0.838). **Conclusion:** Intensive immunosuppressive therapy was significantly associated with better long-term outcome of patients with SLE-associated PAH, especially when combing with PAH target medication.

ICW17-6

Primary Sjogren's syndrome-associated Pulmonary Arterial Hypertension-a multicenter study in China

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Conflict of interest: None

[Object] To explore primary Sjogren's syndrome-associated pulmonary arterial hypertension (pSS-PAH) with its clinical characteristics, risk factors, and prognosis. [Methods] pSS patients from nine academic centers in China were recruited. PAH was diagnosed by right heart catheterization (RHC). Case-control study between pSS-PAH and pSS-non PAH was conducted to identify the risk factors. Cohort study was conducted to identify the prognosis. [Results] 105 patients with pSS-PAH were enrolled. The onset of PAH was at the age of 41.1 with 46.7% presented as initial manifestation. The mPAP was 48.1mmHg and the Cardiac Index was 2.6L/(min×m^2). The primary therapy was the combination of immunosuppressive agents and PAH targeted drugs (68.6%). (1) Risk factor. 526 pSS-non PAH were as controls. Anti-SSB (p<0.001, OR=4.095) and anti-U1RNP antibody (p<0.001, OR=29.518), the age of pSS onset (p<0.001, OR=0.651) and positivity of corneal staining (p=0.003, OR=0.409) were identified as related factors of PAH. (2) Survival analysis. The 1, 3, 5-year survival rate were 94.0%, 88.8% and 79.0%. CI<2.5L/(min×m^2) (p=0.044, HR=8.393) and SSDDI (p=0.031, HR=1.446) were identified as the independent survival predictors. (3) Goal-achieving analysis. The 1, 3, 5-year rate of goal-achieving were 40.6%, 67.4% and 73.9%. The anteroposterior diameter of right ventricle larger than 32mm (p=0.017, HR=0.345) and the use of immunosuppressant (p=0.032, HR=3.746) were identified as independent predictors of goal achieving. [Conclusions] This study established the pSS-PAH cohort based on RHC diagnosis. The regular screening of PAH is recommended in pSS patients with risk factors and those with poor prognostic factors should receive intensive therapy which based on immunosuppressant.

ICW18-1

Clinical and serological characteristics of lupus enteritis and its prognostic factors in patients with systemic lupus erythematosus

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Conflict of interest: None

[Object] Mesenteric vasculitis (MV) and protein-losing enteropathy (PLE) are rare complications of systemic lupus erythematosus (SLE). The aim of this study is to clarify their clinical characteristics and associated factors for the prognosis. [Methods] Consecutive SLE patients in our hospital between 2009 and 2017 were retrospectively reviewed, and those who were newly diagnosed as lupus enteritis complicated by MV or PLE were enrolled. Poor prognosis was defined as any surgical treatment or recurrence. The patients were divided into 2 groups according to the prognosis and analyzed. [Results] Among 556 SLE patients, 23 patients were identified as developing lupus enteritis, and enrolled. Eighteen (78%) were MV and 5 (22%) were PLE. Eighteen (78%) were female, the mean age at SLE onset was 31.5 years, and the mean duration between the onset of SLE and MV or PLE was 10.6 years. The mean SLE disease activity index at the onset of lupus enteritis was 9.6. All patients were treated with glucocorticoid (mean initial predonisolon dose was 40.4 mg/day), and 4 patients (17%) were in combination with cyclophosphamide. Among the MV patients, 4 patients required surgical treatment and 4 patients experienced recurrence. In univariate analysis, patients in the poor prognosis group had a higher ratio of multiple ulcer type than ischemic colitis type (43% vs. 0%, p=0.043), colon lesions (83% vs. 17%, p=0.008), higher serum IgA (391 mg/dl vs. 247 mg/dl, p=0.008), and lower serum total cholesterol (152 mg/dl vs. 191 mg/dl, p=0.012). No difference was found in anti-dsDNA antibodies and complement levels, initial predonisolone dose, and the concomitant cyclophosphamide use between the two groups. [Conclusions] The higher level of serum IgA and lower level of serum total cholesterol are associated with surgical treatment or recurrence and are potential predictive biomarkers for poor prognosis.

ICW18-2

Osteopontin in cerebrospinal fluid as a diagnostic marker of NPSLE

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Conflict of interest: Yes

[Object] Osteopontin (OPN) is a component of bone matrix protein and is a glycoprotein having physiological function such as migration of leukocytes to inflammatory site. It has been reported that OPN is highly expressed in the blood and urine of patient with systemic lupus erythematosus (SLE) and correlates with disease activity suggesting the involvement of OPN in pathophysiology of SLE. Full length of OPN (OPN full) is cleaved by proteases including thrombin and matrix metalloproteinase-3, and the N-terminal fragment of the cleaved OPN (OPN N-half) attracts immune cells. Neuropsychiatric SLE (NPSLE) is a refractory organ involvement of SLE. Clinical markers for early diagnosis and disease status are needed. We measured OPN full / N-half in CSF of NPSLE and investigated their clinical utility. [Methods] We collected CSF from 18 randomly selected patients with SLE who had neurological symptoms and

were hospitalized in our hospital. Eleven patients were diagnosed as NPSLE, while 7 patients were diagnosed as other disorders unrelated with SLE (Non NPSLE). OPN full / N-half in CSF were measured by ELISA. Inflammatory cytokines in CSF were measured by multiplex. [Results] The OPN N-half concentration in CSF was not significantly different between NPSLE and Non NPSLE (p=0.97), whereas the OPN full concentration in CSF was significantly higher in NPSLE (NPSLE: 1507±1318 ng/ml vs Non NPSLE: 538.4±230.7 ng/ml; p=0.004). OPN full in CSF was correlated with PAI-1 and IL-8 (r=0.49 and 0.91, respectively) which have been reported to be highly expressed in NPSLE. Furthermore, cluster analysis of cytokines in CSF suggested that the pathophysiology of NPSLE could be classified into two groups, OPN full group and IL-6 group. When the cutoff value of OPN full in CSF was set to 631.4 ng/ml, the sensitivity was 90.0% and the specificity was 81.8% to diagnose NPSLE. [Conclusions] OPN full in CSF could be a novel diagnostic marker of NPSLE.

ICW18-3

Clinical significance of anti-DNA/N-methyl-D-aspartate receptor 2 antibodies in de novo and post-steroid neuropsychiatric systemic lupus erythematosus

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Conflict of interest: None

[Object] Anti-DNA/ N-methyl-D-aspartate receptor 2 (NR2) antibodies (anti-DNA/NR2 antibodies) are a subset of anti DNA autoantibodies that cross-react with the extracellular domain of the GluN2A/GluN2B subunits of NR2. These antibodies induce apoptosis of hippocampus neurons and psychiatric disorder in mice and humans. Neuropsychiatric SLE (NPSLE) can develop after initiation of corticosteroids (post-steroid neuropsychiatric manifestation: PSNP) or before treatment (*de novo* NPSLE), however, pathophysiological differences between these subtypes remain unclear. The objective of this study was to clarify the prevalence of anti-DNA/NR2 antibodies in patients with NPSLE. [Methods] This study involved a cohort of patients with NPSLE who were admitted to Hokkaido University Hospital. NPSLE patients were classified into two groups, *de novo* NPSLE and PSNP-SLE. Serum anti-DNA antibodies and anti-DNA/NR2 antibodies were measured using in-house ELISAs. [Results] Serum samples were obtained from 24 patients with *de novo* NPSLE, 25 with PSNP-SLE and 76 healthy controls (HC). The level of anti-DNA antibodies in patients with *de novo* NPSLE and PSNP-SLE were significantly higher than those in healthy controls. The level of anti-DNA/NR2 antibodies in patients with *de novo* NPSLE and PSNP-SLE were also higher than those in HC. Positive correlation between anti-DNA antibodies and anti-DNA/NR2 antibodies were found in PSNP-SLE (R^2=0.50, P<0.0001), but not significant in *de novo* NPSLE. [Conclusions] The levels of anti-DNA/NR2 antibodies in PSNP-SLE were similar to those in *de novo* NPSLE. Anti-DNA/NR2 antibodies in PSNP-SLE were suggested as dominant subset of anti-DNA antibodies, indicating that anti-DNA/NR2 antibodies may be a predictive factor in PSNP-SLE.

ICW18-4

Association between pathological characteristics and clinical outcome in 254 SLE patients performed kidney biopsy

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Conflict of interest: None

[Object] Lupus nephritis (LN) is one of the most serious manifestation of systemic lupus erythematosus (SLE), associated with poor prognosis. The aim of this study is to elucidate the association of pathological characteristics and clinical outcome at 52 week (w). [Methods] SLE cases performed kidney biopsy sinse 1995 to 2015 were enrolled in this study. Clinical data, renal pathology, clinical outcome at 52 w were examined. [Results] 254 patients were studied. 224 were female, and the mean age at biopsy was 40.7 years old. Renal pathology was classified based on the INS-RPS classification, I: 1 case, II: 54 cases, III 71 cases, IV: 69 cases, V: 16 cases, III/IV+V; 23 cases, non-LN: 20 cases. The mean prednisolone (PSL) dosage is 41.3 ± 23.3mg/day. CH50 (unit /ml) II: 33.0, III: 29.1, IV: 21.5, V: 39.5, III/IV+V: 39.5, ds-DNA II: 76.7, III: 127.2, IV: 246.2, V: 29.3, III/IV+V: 44.6, U-prot (g/day): II: 0.28, III: 0.81, IV: 1.38, V: 1.68, III/IV+V: It was 2.3. As for the disease activity, SLEDAI (baseline, at 52w) are II: 12.8, 3.5, III: 14.0, 2.1, IV: 19.3, 2.3, V: 12.6, 5.3, III/IV+V: 14.6, 3.6, BILAG (baseline, at 52w) are II: 14.1, 2.2, III 15.8,1.3, IV: 18.1,1.9, V: 12.9, 0.9, III/IV+V: 12.7, 3.4. The SRI-4 remission achievement rate at 52w are II: 92.6%, III: 86.1%, IV: 97.7%, V: 90.9%, III/IV+V: 83.3%. SRI4 non-remission cases were all women, have low SLEDAI score at baseline (16.4±6.8 vs 8.22±3.76, p=0.0004), low BILAG score at baseline (16.9±9.9 vs 8.9±6.7, p=0.0075), high serum Hb at baseline (10.5±1.8 vs11.9±1.9, p=0.03), no cellular/fibrocellular crescent (p=0.03), low PSL dose (45.7±22.1 vs. 26.5±23.5, p=0.01), no ARB administration (p=0.01), serum high IgG at 52 w (1330.5±444.7 vs 1892.2±944.3, p=0.03). [Conclusions] Adequate quantity of PSL administration and combination with ARB may improve LN remission at 52 w.

ICW18-5

Delayed lupus nephritis in the course of Systemic Lupus Erythematosus predicts a poorer renal response to induction therapy and renal flares: A multicenter, retrospective observational study

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Conflict of interest: None

[Object] Some prognostic factors for lupus nephritis (LN) have been mentioned such as male, nephrotic syndrome, class 4 and chronicity on histology. We previously reported a potentially poorer renal outcome in LN that developed later after SLE onset (delayed, D-LN) compared with LN manifesting at SLE onset (early, E-LN). This multicenter study investigated whether D-LN was a predictor of poor response to induction therapy and renal flares in addition to the established prognostic factors. [Methods] We retrospectively examined 215 biopsy-proven LN patients (136 E-LN, 79 D-LN) who attended 3 hospitals above between 1997 and 2014. We compared baseline clinical, serological, pathological features and treatment options at LN onset between E-LN and D-LN. We compared the cumulative complete response (CR) and relapse rates between the two groups and evaluated predictors of the response and flares with univariate and multivariate analysis. [Results] Anti-Sm/RNP antibodies and mixed proliferative and membranous nephritis (class 3+5 or 4+5) were significantly more prevalent in D-LN than E-LN patients (49.4*vs.*30.9%, 67.1*vs.*39.0%, 38.0*vs.*22.1%, respectively). Log-rank test showed significantly lower cumulative CR rates over 3 years and significantly higher relapse rates over 20 years in D-LN. We performed multivariate Cox regression analysis for the response as well as for renal flare, including significant variables on univariate analysis such as class 4+5, chronicity index on histology and positive anti-RNP antibodies, respectively. As independent predictors of non-CR, D-LN [HR 2.09, $p<0.01$] and nephrotic syndrome were identified. As those of renal flares, D-LN [HR 1.77, $p=0.04$] and non-CR at 1 year after induction therapy were detected. [Conclusions] D-LN might be a novel predictor of a poorer treatment response and renal flares independent of renal histology and severity of nephritis. D-LN patients might reflect a refractory SLE subset with specific immunological profiles.

ICW18-6

Comparison of the disease control and the treatment of systemic lupus erythematosus between recent 5 years and 15 years ago

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Conflict of interest: None

[Object] To compare the disease control of systemic lupus erythematosus (SLE) and the treatment of SLE between recent 5 years and 15 years ago. [Methods] We enrolled 45 patients with SLE during 1999-2003 (Group A) and 71 patients during Oct. 2012 to Sep. 2017 (Group B) excluding those enrolled in Group A. We examined retrospectively patient backgrounds, the dose of glucocorticoids and the use of immunosuppressive drugs. BILAG-2004 A and B were applied for the definition of SLE flare. [Results] The median age of patients at entry was significantly higher (p=0.01) in Group B (44 years) than Group A (39 years), although the median age of onset was comparable (32 years and 34 years, respectively, in Group A and Group B). The average number of flare per person-year was significantly reduced in Group B than Group A (0.2 versus 0.4, respectively, p<0.01). There was no difference in oral dose of glucocorticoids at the start of observation (6 and 5 mg/day of prednisolone equivalent in Group A and Group B, respectively), as well as that upon SLE flare (5 mg/day for both groups). On the contrary, significantly reduced dose of glucocorticoids was used in Group B (10 mg/day of prednisolone equivalent) than Group A (20 mg/day) for the treatment of disease flare. In addition, the rate of introduction or alteration of immunosuppressive drugs was more frequent in Group B (71.2%) than in Group A (20.1%, p<0.01). [Conclusions] A better disease control of SLE has been achieved by aggressive use of immunosuppressive agents with reduced glucocorticoids dose during last 2 decades.

ICW19-1

Antibody against commensal streptoccocal L7/L12 ribosomal protein in diagnosis and prognosis of systemic lupus erythematosus (SLE) and other systemic autoimmune diseases

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Conflict of interest: None

[Object] Streptoccocal infection have well known to cause rheumatic fever with various presentations similar to SLE. Whether oral commensal bacteria could induce pathogenic antibodies remained unknown. So we aimed to search for novel biomarkers in SLE through antibody repertoire screening, and investigated to find specific antibodies presented in the serum of lupus patients. [Methods] The L7/L12 ribosomal protein (RP-L7/L12) was identified through LC-MS and and by a proteomics survey. RNase treatment slightly diminished the immunoblotting. We already purified the target protein in streptococci with expression vector, and antibody level will be detected quantitatively. We recruited patients with SLE, other systemic autoimmune diseases (AIDs), healthy control and bactermia patients to elucidate the performance of this biomarker. Multiple blood samplings were conducted and the response of Rituximab (RTX) and other treatment in SLE were evaluated in this prospective observational study. [Results] 51 lupus patients and 54 patients with primary Sjogren's syndrome, primary antiphospholipid syndrome, rheumatoid arthritis, spondyloarthrapathy and other systemic autoimmune disease were enrolled. Nine matched healthy control and five hospitalized patients with various kinds of bacteremia were also enrolled too. The value of the anti-RP-L7/L12 was 0.28+/-0.70 unit in healthy control, while those titers were 0.73+/-0.24 unit in SLE, 1.32+/-2.34 unit in other autoimmune diseases (AIDs). The bacteremia patients' values were 0.28+/-0.44 unit. An average 76.0% decrease of anti-RP-L7/L12 after a 24-week interval were detected in SLE (N=5) receiving RTX 1gm in 2 divided dosage. Another one SLE had three-fold increase in anti-RP-L7/L12 after RTX, probably indicative of disease flare. [Conclusions] The novel antibody can differentiate both SLE and other AIDs from healthy controls (p=0.079 and 0.046 respectively), but cannot be diagnostic of lupus (p=0.334.) It may also be prognostic in SLE.

ICW19-2

Invasive Aspergillosis in Patients with Systemic Lupus Erythematosus: A retrospective study focus on clinical characteristics and risk factors of in-hospital mortality

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Conflict of interest: None

Objects To analyze the clinical features and outcomes of patients with invasive aspergillosis (IA), the mortality risk factors and all-cause mortality in patients with systemiclupus erythematosus (SLE) in single center of Taiwan. **Methods** A retrospective study was performed to identify the mortality risk factors associated with IA in patients with SLE. We reviewed the medical records of patients with SLE who were diagnosed with IA between Jan. 2006 and Jun.2017 fromTaipei Veterans General Hospital in Taiwan. **Results** Twenty-one patients diagnosed with proven (n=4; 19.04%) and probable (n=17; 80.95%) IA according to revised definition by EORTC/MSG Consensus Groupwere enrolled in the study and separated into survivors (n=7; 33.33%) and non-survivors (n=14; 66.67%) groups. All patients in invasive aspergillosis demonstrated significantly high incidence of pneumonia (n=19;90.47%), concurrent infections (n=17; 80.95%), and high mortality (n=14; 66.67%). The daily glucocorticoid dose≧20 mg (p=0.007, HR 2.000), rates of recent pulse glucocorticoid therapy (p=0.022, HR 2.800), rates of azathioprine use (p=0.022, HR 2.000), rates of rituximab within 6 months (p=0.022, HR 2.000), plasmapheresis during hospital course (p=0.022, HR 2.000), and acute respiratory distress syndrome (p=0.022, HR 2.000) among non-survivor group were statisticallyhigher than the survivor group. Non-survivors had significantly higher rate ofconcurrent infections (p=0.002, HR 5.667) and CMV viremia (p=0.040, HR 1.750) than survivors. The sensitivity of Galactomannan assay was not good to exclude the diagnosis of invasive aspergillosis. Septic shock (n=7, 50% of non-survivor group) is the most common cause of in-hospital mortality in patients with IA. **Conclusion** The daily glucocorticoid dose≧20 mg, recent pulse glucocorticoid therapy, azathioprine, rituximab within six months, concurrent infections, and CMV viremia are risk factors of in-hospital mortality in invasive aspergillosis patientswith SLE.

ICW19-3

Prevalence and Risk Factors for Cytomegalovirus Antigenemia After High-dose Glucocorticoid Therapy

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Conflict of interest: None

[Object] Cytomegalovirus (CMV) disease is rare but life-threatening complications in immunosuppressive therapy for connective tissue diseases (CTDs), which is the major reason why the preemptive treatment against positive CMV antigenemia has been performed. However, the predictive factors for positive CMV antigenemia is rarely identified. The aim of this study is to evaluate the characteristics of patients with positive CMV antigenemia. [Methods] We enrolled the consecutive patients with CTDs, who underwent high dose glucocorticoid therapy and/or immunosuppressant from January to December 2016, retrospectively. Timing to measure pp65 CMV antigen depended on physician's preference, but cases who were not checked pp65 antigen about 2 weeks and about a month after starting the treatment were excluded. The obtained clinical and laboratorial data were analyzed. [Results] Sixty-four patients were enrolled, and 24 patients (38%) revealed positive CMV antigenemia. No case with positive CMV antigenemia showed CMV disease when they were detect-

ed positive CMV antigenemia for the first time, and 23 patients were treated with antiviral agents. Fourteen patients (58%) repeatedly revealed positive CMV antigenemia, and two patients got CMV disease. A history of positive CMV antigenemia before starting treatment, lymphocytopenia, and hypoalbuminemia were selected as the predictors for CMV antigenemia using univariate analysis. Multivariate analysis demonstrated 3 following predictors: past history of positive CMV antigenemia; lymphocyte before treatment <730 /mm3; albumin <3.3 g/dL. Two patients (8%) who did not have following predictors showed positive CMV antigenemia, though 16 patients (84%) who had 2 or more predictors got positive CMV antigenemia. [Conclusions] Lymphocytopenia and hypoalbuminemia were risk factors of positive CMV antigenemia, as same as that of CMV disease which was previously reported. Regularly measuring of pp65 antigen may be needed for high risk patients.

ICW19-4

Associations with peripheral cell subsets as risk factors for herpes virus infections during induction therapy in patients with active lupus nephritis

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Conflict of interest: Yes

[Object] To elucidate risk factors of herpes virus infections (HVIs) during induction therapies in patients with active lupus nephritis (LNs). [Methods] **Standardized** immunophenotyping of the peripheral blood was performed using flow cytometry in active LNs patients starting an induction therapy between April 2015 to March 2017 in our hospital. [Results] Thirty patients were enrolled and 27 patients were analyzed except for 3 patients (2 died and 1 withdrawn consent). Mean age was 41.7 years, 9 patients (33%) had newly-onset LNs. All patients were treated with prednisolone (mean 51.7 mg/day) and 25 patients were treated with an additional immunosuppressant (cyclophosphamide;13, mycophenolate mofetil;8, tacrolimus;3, rituximab;1). Six patients (22.2%) developed HVIs (5 cytomegalovirus infections and 1 herpes zoster) within 3 months following induction therapy. Univariate analysis revealed that older age, lower proportions of naïve CD8+ T cells, higher proportions of effector CD8+ T cells and HLA-DR+ regulatory T cells at baseline and lower naïve CD8+ T cells at month 3 associated with HVIs ($p=0.011$, $p<0.001$, $p=0.009$, $p=0.024$, $p<0.001$ respectively). Unexpectedly, lymphocyte count, IgG titer, usage of cyclophosphamide at baseline and renal response at month 3 did not associate with HVIs. Multivariate analysis revealed that low proportions of naïve CD8+ T cells and high proportions of HLA-DR+ regulatory T cells at baseline were the only detectable independent risk factor for HVIs ($p=0.014$). [Conclusions] Our results suggest that active LNs patients with low proportion of naïve CD8+ T cells and HLA-DR+ regulatory T cells at the time of induction therapy should be closely monitored for HVIs. Prospective study is desired to confirm our results.

ICW19-5

Difference in therapeutic features of pneumocystis jirovecii between patients with AIDS and rheumatic diseases

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Conflict of interest: None

PURPOSE: Pneumocystis jiroveci pneumonia (PCP), an important opportunistic infection, is treated by Trimethoprim / Sulfamethoxazole (TMP / SMX) as first line drug, and by Pentamidine and / or Atovaquone recently as second drug. Clinical features between Human Immunodeficiency Virus (HIV) -PCP and non-HIV-PCP are quite different. We surveyed PCP therapy in our department. **METHODS:** 31 patients with systemic autoimmune diseases who developed PCP (non HIV-PCP) and 14 with HIV-PCP were reviewed in 5 years from September 2012. PCP was diagnosed with Chest CT findings and PCP-PCR or Grocott staining of sputum or BALF. Treatment was based on The Sanford Guide to Antimicrobial Therapy. **RESULT:** Survival rate of non-HIV-PCP was 74.2% versus HIV-PCP 90%, although there was no significant difference, the prognosis of non-HIV-PCP was poor. Almost patients were treated with TMP / SMX. Because renal function of non-HIV-PCP was significantly lower than HIV-PCP, TMP / SMX was initiated at low dose. Although the efficacy rate of TMP / SMX was high as HIV-PCP 100%, non-HIV-PCP 93.1%, more than 80% occurred in adverse events (renal dysfunction was most common), resulted in reduction of TMP / SMX in half of patients. The efficacy rate / incidence of adverse events of Pentamidine was 40% / 50%, these of Atovaquone was 100% / 25% in HIV-PCP and 80% / 13.3% in HIV-PCP. Only two of eight deaths in non-HIV-PCP died of PCP. The risk factors of death were older, interstitial pneumonia, steroid, drug selection other than TMP / SMX, hypoalbilmia, low number of lymphocyte and anemia. One death of HIV-PCP died of malignant lymphoma one year after onset of PCP. **CONCLUSION:** Non-HIV-PCP requires multidisciplinary therapy as its onset under poor general condition can be lethal. TMP / SMX has high efficacy but high adverse event incidence. As a second-line drug, Atovaquone might be well-tolerated with the same effect as TMP / SMX.

ICW19-6

The effects of trimethoprim-sulfamethoxazole on disease activity in patients with RA - ANSWER longitudinal cohort study -

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Conflict of interest: None

[Objectives] While experimental models suggested bacterial infection, such as periodontal disease and gut microbiota, may be an inciting and aggravating factor in RA, no studies have demonstrated antibiotics resulted in improvement or alleviation of disease activity in patients with RA. In addition, *Pneumocystis jirovecii* pneumonia (PCP) is common among patients with RA and trimethoprim-sulfamethoxazole (ST) is often used for PCP prophylaxis. Therefore, the objective of this multi-center cohort study is to identify the effect of ST on disease activity in RA patients. **[Methods]** RA patients with a sampling interval of less than 1 year were enrolled. Disease activity was assessed using disease activity score 28-CRP (DAS28-CRP) for primary outcome. Linear mixed effect models were used to evaluate the trajectories of disease activity in RA patients. Time from baseline, ST administration, 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 DMARDs were included as covariates. **[Results]** A total of 49939 samples (mean sampling interval: 49 days) from 3255 patients was included. The median age at baseline was 64.0 years (interquartile range, 53.0 to 71.0 years) with 78.2 % of women (ACPA positivity, 79.2%; RF positivity, 70.8 %). The median DAS28-CRP was 2.83 with 33.8 % of patients taking ST at baseline. Patients with taking ST had a significantly better longitudinal trajectory on disease activity

than patients without (-0.0028/month, $P = 0.041$). This result was similar even when patients taking sulfasalazine were excluded from analysis. **[Conclusions]** This result suggested ST was beneficial to improving disease activity besides PCP prophylaxis. This also supports the role of bacterial infection in RA.

ICW20-1

Semaphorins and their involvement in the pathogenesis of autoimmune vasculitis

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Conflict of interest: None

[Object] Semaphorins are intimately associated with the pathogenesis of autoimmune diseases. Recently, we reported a unique function of semaphorin 4D (SEMA4D) in neutrophils and its pathological involvement in ANCA-associated vasculitis (AAV). Based on these findings, we aim to clarify how SEMA4D-mediated inhibitory signaling is regulated *in vitro* and *in vivo*. [Methods] In *in vitro* study, HEK293 cell transfectants are established by introducing a construct expressing full-length SEMA4D or SEMA4D lacking the intracellular C-terminal domain. These transfectants were stimulated with anti-SEMA4D antibody, lysed, and then subjected to western blot assay. In *in vivo* study, we first used BSA-induced small-vessel vasculitis model. As a next step, we are currently developing a passive transfer model of acute AAV, first reported by Xiao *et al*., in which purified antibodies or splenocytes taken from MPO-deficient mice immunized with recombinant mouse MPO are used. [Results] *In vitro* study reveals that SEMA4D is co-expressed with protein X and might be sending inhibitory signals through their coupling. In *in vivo* BSA-induced small-vessel vasculitis model, *sema4d*-deficient mice exhibit severer vasculitis phenotype than wild-type mice, suggesting that SEMA4D functions protectively and is pathologically important in AAV. [Conclusions] Our data suggest that SEMA4D cooperates with another molecule to send intercellular signaling during immune responses. Animal models of AAV are useful in further elucidating the unknown pathological mechanisms and therapeutic potentials of semaphorins.

ICW20-2

CD4+ and CD8+ T Cell Activation in Children with Kawasaki Disease

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Conflict of interest: None

[Object] Kawasaki disease (KD) is an acute systemic vasculitis of unknown etiology. Administration of intravenous immunoglobulin (IVIG) is the standard treatment for KD. However, IVIG is not effective in approximately 20% of patients with KD, and the precise mechanisms are unclear. This study aimed to search the pathophysiology and appropriate treatment for refractory KD, T cell activation was studied in children who suffered from IVIG-resistant KD. [Methods] One hundred pediatric patients who were admitted to our hospital between 2007 and 2016 were enrolled for the study. All patients fulfilled the diagnostic criteria of KD. None of the patients underwent any prior therapy of glucocorticoids or immunosuppressants for KD. Patients who showed defervescence within 48 hrs after the start of the first infusion of IVIG (2 g/kg), and not then required further treatment of KD were defined as the "IVIG-effective group A" (n = 50). The other patients who required further therapy after the first IVIG infusion were defined as the "IVIG-resistant group B" (n = 50). The expression levels of HLA-DR on peripheral blood $CD4^+$ or $CD8^+$ T cells on admission were compared between the 2 groups assessed by flow cytometry. [Results] The percentage of $HLA\text{-}DR^+$ cells among $CD4^+$ T cells, and the absolute number of $HLA\text{-}DR^+ CD4^+$ T cells, in Group B were significantly higher than the percentage and the number of corresponding cells in Group A (both $P < 0.01$). The percentage of $HLA\text{-}DR^+$ cells among the $CD8^+$ T cells, and the absolute number of $HLA\text{-}DR^+$ $CD8^+$ T cells, in Group B were also significantly higher than the variables of these cells in Group A (both $P < 0.01$). [Conclusions] The present results indicated that T cell activation was associated with the IVIG-resistance in KD children. The HLA-DR expression on T cells would be a useful biomarker for predicting IVIG responsiveness during KD pathogenesis. Moreover, the appropriate treatment for IVIG-resistant KD may be to regulate T cell activation.

ICW20-3

Epigenetic hypomethylation and upregulation of inflammasome sensors of NLRC4 and NLRP12 in Kawasaki disease

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Conflict of interest: None

Objects: Kawasaki disease (KD) is a type of childhood febrile coronary vasculitis of unknown etiology. Inflammasomes are multi-proteins complex controlling inflammation-associated signaling and are associated the development of KD. We provided a comprehensive survey of transcripts and global DNA methylation levels of inflammasome sensors of NOD-like receptors, and downstream inflammatory cytokine, interleukin 1β (IL-1β), in KD patients and control subjects. **Materials and methods:** For chips studies, we recruited a total of 18 KD patients, prior to receiving intravenous immunoglobulin (IVIG) and at least 3 weeks after IVIG treatment, as well as 18 healthy and 18 febrile control subjects. We applied Illumina HumanMethylation450 BeadChip and Affymetrix GeneChip Human Transcriptome Array 2.0 to evaluate their CpG markers and expression levels, respectively. Then we used a separate cohort to carry out real-time quantitative PCR validations of mRNA levels. **Results:** The expressions of mRNA levels of NLRC4, NLRP12, and IL-1β were significantly upregulated in KD patients compared to the healthy and febrile controls. Once KD patients underwent IVIG treatment, these genes considerably decreased. In particular, the methylation status of CpG sites of these genes indicated a significant opposite tendency between both stages of not only the KD samples but also the controls. Moreover, the mRNA level of IL-1β represent a positive correlation with NLRC4. We also observed the mRNA level of NLRP12 to be lower in KD patients with coronary arterial lesion formation. **Conclusion:** This study is the first to report epigenetic hypomethylation, increased transcripts, and the upregulation of inflammasome sensors of NLRC4 and NLRP12 as well as inflammatory cytokines of IL-1β in KD patients.

ICW20-4

Reappearance of MPO-ANCA is associated with relapse in ANCA-associated vasculitis; a nationwide nested case-control study

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Conflict of interest: None

[Object] The clinical usefulness of monitoring antineutrophil cytoplasmic antibody (ANCA) level to predict relapse in patients with ANCA-associated vasculitis (AAV) is controversial. The aim of this study was to evaluate clinical links between levels of myeloperoxidase (MPO)-ANCA and relapse in patients with AAV using a data set from two nationwide prospective cohort studies. [Methods] MPO-ANCA positive patients at baseline who achieved remission during 6 months after commencement of remission induction therapy were enrolled from RemIT-JAV and RemIT-JAV-RPGN. MPO-ANCA levels were measured at month 0, 3, 6, 12, 18, 24 and at the time of relapse. The primary outcome was relapse. A nested case-control analysis and multivariable analysis were performed to investigate the relationship between ANCA reappear-

ance and relapse. [Results] Of 477 patients in the two cohort studies, 271 patients were enrolled; 183 was classified as microscopic polyangiitis, 34 as granulomatosis with polyangiitis, 15 as eosinophilic granulomatosis with polyangiitis, and 39 were unclassifiable. The median age was 73 years and 165 (61%) were female. MPO-ANCA levels decreased to the normal levels within 6 months after commencement of treatment in 195 patients (72%, disappearance group) and MPO-ANCA reappeared in 70 (38%) of the 195 patients. Of 182 patients with sufficient follow up data in the disappearance group, 25 (14%) patients experienced relapse during the observation period. For nested case-control analysis, age and gender matched 75 control patients were selected among non-relapsed patients in the disappearance group. Reappearance of MPO-ANCA was more frequent in patients with relapse than in control patients without relapse (odds ratio [95% confidence interval]: 16.1 [5.4 - 54], p<0.0001) after adjusting the confounding factors. [Conclusions] Reappearance of MPO-ANCA could be a useful biomarker for predicting relapse in the remitted MPO-ANCA positive AAV.

ICW20-5

Efficacy of rituximab in association with B cell phenotype in patients with ANCA-associated vasculitis: 1 year results of FLOW study

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Conflict of interest: None

[Object] 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 unclear. [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 45 AAV patients. Based on the analysis, the patients were considered suitable to receive immunosuppressive drugs or RTX. We assessed the phenotype of circulating B cells in active AAV and evaluated the efficacy and safety outcomes at 1 year after treatment. Definition of clinical improvement was a reduction of 50% or more in BVAS. [Results] The proportion of effector or class-switched memory B cells was increased in 17 out of 45 patients.19 out of 21 patients treated with glucocorticoids (GC) and RTX achieved clinical improvement. Among 24 patients received GC and conventional immune suppressants (19 intravenous cyclophosphamide and 5 azathioprine),16 patients achieved clinical improvement. There was no difference in the rate of improvement, relapses, serious adverse events between the 2 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 improvement and GC reduction were significantly higher in RTX group than in conventional immune suppressants group at 6 months after treatment. The rate of survival rate was significantly higher in RTX group than in conventional immune suppressants group. [Conclusions] 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 and higher survival rate 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.

ICW20-6

Long-term outcomes of patients with refractory Takayasu arteritis treated with biologics

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Conflict of interest: None

[Object] Glucocorticoids are effective for Takayasu arteritis (TAK), however relapses occur frequently. The efficacy of biologics in the treatment of refractory TAK has been reported. HLA-B*52 and a SNP in *IL12B* region are genetic risk factors and associated with severity of TAK. To evaluate the efficacy and safety of biologics, we analysed clinical and genetic profiles of the patients treated with biologics. [Methods] We searched for TAK cases treated with biologics in Kyoto University Hospital from 2000 to 2017. Clinical information at 0-24 months after the initiation of biologics was extracted from medical records. [Results] Of 163 cases, 10 cases (6.1%) were treated with infliximab (IFX, N=4), tocilizumab (TCZ, N=3) or ustekinumab (UST, N=3). Gender ratio was 1:9. The age of onset was 29.4±12.2 y.o. (mean±SD). According to Numano's classification, they were grouped into types I (N=3), IIa (2) and V (5). Four patients had aortic regurgitation. The number of immunosuppressive agents used in the past was 1.7±0.8 per patient. HLA-B*52 was positive in 7 (70 %) patients. All the cases had risk-type alleles (A vs. C) of *IL12B* SNP. Dose of prednisolone was significantly decreased from 10.6±1.9 to 7.7±2.4 mg/day after 12 mo. (p=0.018). We could not find significant improvements in imaging modalities. Overall duration of treatments with biologics was 40±23 months. Two cases discontinued IFX due to breast cancer and infusion reaction. Another patient stopped IFX by her will of child-raising, however relapse occurred after the discontinuation. Chronic heart failure was exacerbated in a case treated with TCZ. One of 3 patients treated with UST exhibited steroid-sparing effects without discontinuation for 39 months, however other 2 patients stopped UST due to relapses after the treatment for 34 and 37 months. [Conclusions] Biologics showed steroid-sparing effects in refractory TAK, although about half of the patients discontinued biologics due to relapses or adverse events.

ICW21-1

Prediction of connective tissue disease in an at-risk cohort using a novel interferon stimulated gene expression score

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Conflict of interest: None

Background A period of ANA positivity precedes autoimmune CTDs providing an opportunity for disease prevention. Type I interferons (IFN-I) are important mediators of CTDs but their role in disease initiation is unclear. The objective of this study was to develop biomarkers of progression to CTDs enabling early intervention. **Methods** A prospective observational study was conducted in 150 At-Risk patients: ANA+; ≦1 clinical SLE criteria; symptom duration <12 months; treatment-naïve. Progression was defined by meeting 2012 ACR/SLICC SLE, 2016 ACR/EULAR Primary Sjogren's diagnostic criteria. Expression of 30 IFN-stimulated genes (ISGs) was measured using TaqMan, Factor analysis indicated 2 distinct IFN scores: Score A and Score B. 50 healthy controls (HC) and 150 SLE patients were used as controls. Penalised logistic regression using Lasso method was used to identify baseline predictors of CTD progression. **Results** 118 patients with 1-year follow-up data were included [104 female, median age 48 (20-84) years]. 20 (17%) patients progressed to CTD (SLE=14, Sjogren's=5) in the following 12 months. At baseline in At-Risk vs HC, only Score A was increased (p=0.002). Score B was only increased in SLE. In At-Risk patients, Score B was low in patients who did not progress and increased in those who did progress (p<0.001). ROC indicated that Score B level of >0.126 yielded Area Under the Curve (AUC) of 0.82 with 58% sensitivity, 85% specificity, 46% positive predictive value and 90% negative predictive value. A positive family history of autoimmune rheumatic disease (ARD) [OR 4.22 95% CI (1.07-16.73) and Score B; 2.70 (1.38-5.28)] increased the odds of CTD progression at 12 months in multivariable analysis. **Conclusion** A novel ISG score and family history of ARD predict progression from ANA+ to clinical autoimmune disease. These may allow early intervention to prevent CTD. Analyses of other immunological biomarkers and longitudinal tests are in progress as well as a validation cohort.

ICW21-2

Gene expression of Aryl Hydrocarbon Receptor in immune cells is associated with lung involvement in patients with systemic sclerosis

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Conflict of interest: None

[Object] Genetic and environmental factors are thought to be important for the trigger of development of the systemic sclerosis (SSc). Recent reports suggest that one of environmental factors, environmental toxin such as dioxin, can trigger the process of autoimmunity through aryl hydrocarbon receptor (AhR), and involve in the pathogenesis of SSc. The aim of this study is to investigate the association between expression of AhR in immune cells and the clinical characteristics in patients with SSc. [Methods] Twenty-one patients with SSc who fulfilled 2013 ACR/EULAR classification criteria and 10 healthy controls (HC) were involved. Peripheral blood mononuclear cells were isolated from whole blood and total RNA was extracted. *Ahr* mRNA expression level was examined by quantitative polymerase chain reaction and standardized by mRNA level of *18S* ribosomal RNA in each sample. Expression level of *Ahr* mRNA was compared between SSc and HC and also between SSc patients with and without clinical features. [Results] In 21 SSc patients, mean age was 61 ± 13 years, female was 95% and diffuse cutaneous subset (dcSSc) was 33%. Mean disease duration was 9 ± 9 years. *Ahr* mRNA expression level was tended to be higher in SSc compared to HC (1.7 ± 1.1 versus 1.2 ± 0.6, $p = 0.1$). When SSc patients were stratified into those with and without their clinical characteristics, *Ahr* mRNA was significantly higher in patients with ILD (n = 14) than those without (n = 7) (2.0 ± 1.1 versus 1.0 ± 0.4, $p < 0.05$), while no difference was observed when they are compared between patients with and without other organ involvements, subsets of skin involvement, or SSc-related autoantibodies. [Conclusions] Expression level of Ahr mRNA was higher in patients with SSc, especially those with ILD. These results suggest that AhR expressed in immune cells may play a role in the disease process of ILD in SSc.

ICW21-3

The association between immunophenotype of peripheral blood and nailfold microvascular changes in patients with systemic sclerosis (SSc)

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Conflict of interest: Yes

[Object] Little is known about the relationship between immunological abnormality and microvascular changes in patients with SSc. We stratified SSc patients based on peripheral immunophenotyping and investigated the association between immunophenotyping and vasculopathy in SSc. [Methods] 90 patients with SSc were enrolled in this study. Nailfold videocapillaroscopy was performed for qualitative assessment of morphological microvascular. Peripheral blood mononuclear cells were obtained and the immunophenotype was defined based on flow cytometric analysis for human immune system termed “the Human Immunology Project”. Based on these results, SSc patients were classified into subgroups by cluster analysis. [Results] The proportion of effector T cell was higher in SSc than the healthy control. The proportion of activated Th1 (2.0% vs 1.3%) and activated Th17 (1.2% vs 0.8%), but not Treg and Tfh, was higher in SSc. On the other hand, the abnormalities of B cell differentiation in SSc patients were mild. However, cluster analysis stratified SSc patients into three subgroups: patients who showed almost normal immunophenotype (without abnormality group), patients with high percentage of effector T cell and Th17 cells (T cell-dominant group), and patients with high proportion of plasmablast and effector B cell in addition to T cell abnormality (T/B cell abnormality group). The majority (81%) of SSc patients belonged to the without abnormality group. In contrast, the percentage of patients who had severe microvascular changes was highest among the T cell-dominant group and the T/B cell abnormality group. Meanwhile, the prevalence of anti-RNA polymerase III antibody was often seen in T/B cell abnormality group. [Conclusions] Immune abnormality in peripheral blood was not necessarily found in all cases of SSc. However, our data indicated that there are two types of immunological abnormalities associated with the risk of vasculopathy in patients with SSc.

ICW21-4

Nailfold capillary abnormalities predict organ damage and its progression in patients with systemic sclerosis (SSc)

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Conflict of interest: None

[Objectives] To make clear the significance of microvascular abnormalities in the treatment of SSc. [Methods] 195 SSc patients were enrolled. Nailfold capillary was evaluated using Nailfold videocapillaroscopy (NVC). Based on the findings, NVC stage classification (no abnormality: Normal, initial change: Early, active phase: Active, late period: late pattern) was made. The correlation between capillary findings and organ damage was evaluated. [Results] Mean age was 63.8 years of age, most were female (90.8%), and capillary abnormality was seen in 68.7% of the total. Compare to the cases without microvascular abnormalities, mergers of decreased esophageal peristalsis were seen in that with microvascular abnormalities. Furthermore, in the cases with late pattern showed higher skin score, and the merger rate of pulmonary hypertension, interstitial pneumonia, upper gastrointestinal disorder, and skin ulcer were significantly higher. In patients who evaluated one year later, the progression of microvascular abnormalities were observed in 33.3% (27 out of 81) and the stage advanced in 6.1% (5 out of 81). The positivity of anti-Scl70 antibody was risk factor for its progression. Moreover, in cases already advanced to the active pattern at baseline, microvascular abnormality tended to progress in the following year. [Conclusion] Microvascular abnormalities reflected progression of organ involvement and many complications likely to appear especially in late phase of microvascular abnormality. In addition, microvascular abnormality at the diagnosis is the risk for further progression. NVC may be useful not only for diagnosis but also for judgment of therapeutic intervention.

ICW21-5

The decreased activation status of Ataxia-Telangiectasia Mutated in immune cells is associated with clinical features in systemic sclerosis

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Conflict of interest: None

[Background] Ataxia-telangiectasia mutated protein kinase (ATM), one of key players in a heritable disease with telangiectasia, plays an important role in the process of regulation of oxidative stress. Recent studies show that the inhibition of ATM is associated with enhanced production of reactive oxygen species (ROS), which is known as one of major mediators in pathogenesis of systemic sclerosis (SSc). [Object] To elucidate the expression and activation status of ATM in circulating immune cells in patients with SSc and the association between ATM and its clinical characteristics. [Methods] Seventeen patients with SSc and 5 healthy controls (HC) were involved. The expression levels of ATM and phosphorylated ATM (pATM) were measured in each immune cell subset (neutrophil, monocyte, T cell, B cell and NK cell) by mean fluorescence intensity (MFI) using flow cytometer. Correlation between MFI of ATM

or pATM and the patients' characteristics were also examined. [Results] The expression of pATM was lower in monocyte, neutrophil, and NK cell subsets in SSc when they are compared with HC (1841±177 vs 2623±328, $p < 0.05$; 9859±1145 vs 16616±2112, $p < 0.05$; 1841±191 vs 2706±353, $p < 0.05$; respectively), whereas no difference of total ATM level was observed in each subset. When expression of pATM in each subset was compared between patients with and without clinical characteristics, pATM in monocyte tended to be lower in patients with ILD than those without. Also, there was a tendency of correlation between pATM level in monocyte and parameters of pulmonary function test, such as forced vital capacity. [Conclusions] In SSc, ATM phosphorylation in immune cells was significantly lower. Especially, insufficient ATM activation in monocyte was tended to be associated with ILD. These results suggest that the activation status of ATM might be involved in the disease process of SSc.

ICW21-6

Tacrolimus Following Intravenous Cyclophosphamide Pulse Therapy as a Therapeutic Choice for Systemic Sclerosis Associated Interstitial Lung Disease

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Conflict of interest: None

[Object] Pulmonary involvement in systemic sclerosis (SSc) is one of major cause of death. However, the treatment of interstitial lung disease (ILD) in SSc is limited. Although intravenous cyclophosphamide pulse therapy (IVCY) is effective and widely used, the effect of the therapy does not last for a long time. In this reason, IVCY followed by somewhat immunosuppressants may be needed, but it is uncertain which immunosuppressant is better. In Japan, tacrolimus is frequently used for the treatment of idiopathic interstitial pneumonia. We examined the effect of sequential IVCY followed by tacrolimus for ILD in SSc. [Methods] This retrospective, observational study was performed in a single center in Japan. Twenty consecutive patients with ILD in SSc who received IVCY as first therapy in our hospital from April 2010 to March 2014 were enrolled. The protocol of IVCY is the dose of 400 to 500 mg/body surface area (m^2)/4 weeks and performed 2 to 6 times. In this study, we divided them two groups: treated with tacrolimus and corticosteroids following IVCY (TAC group); only corticosteroids after IVCY (PSL group). We assessed the follow-up for 3 years after IVCY in each group. Disease deterioration of ILD was defined as fulfilling more than 2 following criteria: deterioration of symptoms; expanding lung fibrosis in CT scan; DL_{CO} decreasing more than 5% from baseline in pulmonary function test (PFT). All data were collected from medical record retrospectively. [Results] Ten patients were in TAC group, and other 10 patients PSL group. ILD in TAC group were more severe than that in PSL group according to the PFT result, though they were not reached to significant difference (%VC: 79.5 ± 16.1% vs. 87.4 ± 18.8%). After 3-year follow up, 2 patients revealed disease deterioration, who were PSL group. In TAC group, a case stopped taking tacrolimus due to thrombocytopenia. [Conclusions] Tacrolimus following IVCY may be one of therapeutic choice for ILD in SSc, with good tolerance.

ICW22-1

Finger joint cartilage thickness evaluated by semiquantitative ultrasound score in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] Joint destruction in rheumatoid arthritis (RA) includes both bone and cartilage lesions. By X-ray examination, cartilage destruction is evaluated as the joint space narrowing (JSN). However, JSN is not a direct evaluation of cartilage. Previously we have confirmed the usefulness of the direct imaging of finger joint cartilage thickness (FJCT) by ultrasound (US). Then we aimed to evaluate the FJCT by semiquantitative US score and clarify its clinical significance in patients with RA. [Methods] We enrolled 70 RA patients in low disease activity or clinical remission (DAS28-CRP<2.7) in this study. The FJCT of metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints of 2nd to 5th fingers was bilaterally visualized and measured by US. Furthermore, one US examiner performed the semiquantitative scoring of the recorded cartilage images in a blinded manner on a scale of 0-2 (0=normal, 1=minimal, and 2=severe). In addition, the JSN of fingers was scored by van der Heijde-modified Sharp method with a hand X-ray. The relationship among the total FJCT, the semiquantitative FJCT score and the JSN score were assessed by Spearman's rank correlation coefficient. [Results] FJCT in MCP joints measurement ranged from 0.0 to 1.0mm (median 0.5mm), and FJCT in PIP ranged from 0.0 to 0.6mm (median 0.3mm), respectively. The total FJCT from 8 fingers ranged from 4.0 to 9.4 mm (median 6.8mm), which was significantly correlated with the semiquantitative score (rho=-0.644, p<0.001). And both total FJCT and semiquantitative score were significantly correlated with the total JSN score (rho=-0.604, p<0.001, and rho=0.565, p<0.001, respectively). The semiquantitative score was associated with disease duration (rho=0.372, p=0.011). Age, height and seropositivity were not associated with semiquantitative FJCT score and JSN score. [Conclusions] A simplified and direct evaluation of cartilage damage by semiquantitative US score is valid and useful for finger joints in patients with RA.

ICW22-2

Concordance between ultrasound joint synovitis and clinical joint assessments by patients or physicians in rheumatoid arthritis sorted by disease activity

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Conflict of interest: None

[Object] This study aimed to examine and compare the concordance between joint symptom, tenderness, or swelling and ultrasonography (US) synovitis in different disease activity states. [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. [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 (κ = 0.30) when compared with joint symptoms (κ = 0.39) or swelling (κ = 0.43). In addition, we examined the above concordance sorted by disease activity state defined by DAS28 score. Again, swelling showed the best concordance with US synovitis, (κ = 0.40, 0.41, and 0.35 in patients with remission/low, moderate, and high disease activity, respectively), followed by concordance with patient-reported symptoms (κ = 0.19, 0.39, and 0.33 in patients with remission/low, moderate, and high disease activity, respectively), and concordance with tenderness (κ = -0.03, 0.28, and 0.22 in patients with remission/low, moderate, and high disease activity, respectively). [Conclusions] Joint swelling showed the best concordance with US synovitis, followed by patient-reported joint symptoms and then joint tenderness, irrespective of disease activity. Patient-reported joint symptoms may be a better clinical assessment than the examination for tenderness.

ICW22-3

Concordance rate between inflammation of joints measured with physical examination and MRI does not change after biological treatment

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Conflict of interest: Yes

[Object] Previous studies revealed that subclinical MRI inflammation is frequent among rheumatoid arthritis (RA) patients in clinical remission or low disease activity state. This fact suggests that discrepancy between inflammation of joints measured with physical examination (PE) and MRI may occur after biologic treatment or achieving clinical remission. The aim of this study is to examine whether the concordance inflammation of joints measured with PE and MRI changes after biological treatment. **[Methods]** Thirty-five RA patients treated with intravenous abatacept were studied. MRI of bilateral hands was performed at baseline and Month12. Two readers scored synovitis in MCP (2-5) and wrist at both sides according to OMERACT RA MRI scoring system. We examined the concordance between inflammation detected by PE (swollen and/or tender joint) and synovitis on MRI in 10 joints per patient at baseline and Month12. Subclinical inflammation was defined as the inflammation that is detected by only MRI, not PE. **[Results]** 350 joints of 35 patients at baseline and 310 joints of 31 patients at Month12 were studied, because 4 patients discontinued treatment. MRI detected significantly higher number of joints with inflammation compared to PE at both baseline ($p<0.0001$) and Month 12 ($p<0.0001$). Proportion of joints with subclinical inflammation was 24% at baseline and 26% at Month12 ($p=0.41$). The concordance between PE and MRI was 68% at baseline and 71% at Month12 ($p=0.44$). When we analyzed 11 patients who achieved SDAI remission at Month12, the concordance between PE and MRI was 66% at baseline and 77% at Month12 ($p=0.07$). **[Conclusions]** Concordance rate between inflammation of joints measured with physical examination and MRI does not change after biological treatment, regardless of patient's disease activity state.

ICW22-4

The Corrected QT (QTc) Interval Is Associated with Myocardial Fibrosis in Primary Sjögren Syndrome, Assessed by a Cardiac Magnetic Resonance Approach

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Conflict of interest: None

[Object] The risk of clinically manifested major cardiovascular events in patients with primary Sjögren syndrome (pSS) remain unclear. We hypothesized that myocardial abnormalities were associated with the corrected QT (QTc) interval in pSS. We used cardiac magnetic resonance imaging (CMR) to assess cardiac involvement and determine its association with the QTc interval in pSS patients without cardiac symptoms. [Methods] PSS patients, classified according to the 2012 ACR criteria with no history or clinical findings of hypertension, cardiovascular disease, diabetes, or dyslipidemia underwent contrast-enhanced CMR. Late gadolinium enhancement (LGE) was used to assess myocardial fibrosis. Myocardial inflammation was assessed using a black-blood T2-weighted image (T2-WI). The Sjögren syndrome disease activity index (ESSDAI) was determined. Salivary gland biopsy data were classified by focus score (FS). A QTc interval of 440 ms was considered as prolonged. [Results] Forty-nine female pSS patients (age, 53±10 years) were enrolled. The mean ESSDAI was 2.5±2.7. LGE was seen in 9 (18%), 2 of whom showed T2-WI. T2-WI was seen in 2 patients (4.1%). LGE was significantly associated with Raynaud's phenomenon positive patients ($p=0.003$). FS in LGE (+) patients was significantly higher than that in LGE (-) patients ($p=0.03$). There was significantly higher prevalence of QTc prolongation in LGE (+) than that in LGE (-) ($p=0.014$). Other pSS characteristics, such as disease duration, anti-SS-A/anti-SS-B autoantibodies, ESSDAI, and cardiovascular risk factors, were not significantly associated with myocardial abnormalities and QTc interval. A receiver operating characteristic analysis showed that the QTc interval reliably detected myocardial abnormalities (area under the curve, 0.77). [Conclusions] Subclinical myocardial involvement, as detected by CMR, was frequent in pSS patients without cardiac symptoms. Abnormal CMR findings were associated with a QTc interval.

ICW22-5

Diagnostic and predictive evaluation using salivary gland ultrasonography in primary Sjogren's syndrome

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Conflict of interest: None

[Object] We aimed to assess the diagnostic accuracy of salivary gland ultrasonography (SGUS) as a single test for the detection of primary Sjogren's syndrome (pSS) and examine the prognostic factors for severe structural damage of the salivary glands based on SGUS score. [Methods]: Patients with pSS (n=94) and idiopathic sicca syndrome (n=44) were evaluated using the SGUS 0-48 scoring system, which comprises five parameters: parenchymal echogenicity, homogeneity, hypoechoic areas, hyperechogenic reflections, and clearness of posterior borders. The salivary gland volume and intraglandular power Doppler signal (PDS) were also assessed. A multivariate linear regression analysis was performed to determine the factors associated with SGUS score. [Results] Patients with pSS showed a significant higher SGUS score than controls [median (IQR): 24.5 (13.0) vs 6 (3.75), $p < 0.001$]. An SGUS cut-off of 14 and over had a sensitivity of 80.9% and a specificity of 95.5% for pSS diagnosis. There was no significant difference in the measured volumes and PDS between pSS and controls. The SGUS scores were correlated with unstimulated salivary flow rate (USFR), serum rheumatoid factor and IgG. Double seropositivity of anti Ro/SS-A and La/SS-B (beta = 6.060, $p = 0.001$) and USFR (beta = -1.913, $p < 0.001$) were independently associated with SGUS scores. [Conclusions] The SGUS scoring system is a valuable diagnostic method for pSS. Double seropositivity of anti-Ro/SS-A and La/SS-B is an independent predictive factor for the structural damage of salivary glands.

ICW22-6

RNA Interference Therapy for Rheumatoid Arthritis with Novel Nanopieces Delivery

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Conflict of interest: None

<Object> Our aim was to inhibit the TNF-α gene responsible for the progression of Rheumatoid arthritis (RA) by delivering small interference RNA (siRNA) into RA afflicted mice with novel, biomimetic Nanopieces (NPs). <Method> Collagen induced arthritis (CIA) was generated in 8-week-old DBA/1J mice. ON-TARGETplus siRNA for mouse TNF-α (siTNF) or mouse non-target siRNA (scrRNA) were encapsulated within NPs and administered to CIA mice or non-CIA control mice, respectively, via retro-orbital injections twice per week from 21 days to 49 days after the first induction of arthritis. Von Frey testing was performed to assess the mechanical nociception. TNF-α gene expression was quantified using real-time RT-PCT. X-ray images and high-resolution 3D volume images using a desktop μCT scanner (MicroCT40, Scanco Medical. Tube Settings: 55 kVp and 145 μA. 300 ms integration time) were generated. Mann-Whitney U test, One-way ANOVA and Turkey's post-hoc analysis

were used for statistical analysis. <Results> After twice injections, the NP systemic delivery achieved 96% and 90% knockdown of TNF-α mRNA levels in knee and hind paw joints respectively, indicating NP delivery can achieve highly efficient RNAi in joint tissues. Total arthritis score was significantly reduced in the siTNF treatment group in comparison to the sham treatment group (scrRNA) after CIA induction for 7 and 8 weeks. In addition, siTNF mice had higher mechanical nociception threshold than scrRNA mice. siTNF treatment significantly inhibited bone erosions, and joint destructions and reduction of volumetric density, bone mineral density, and trabecular number and thickness in the CIA mice. <Conclusion> This is the first study to demonstrate that RNAi/NP therapy is highly efficacious in inhibiting cytokine expression in the joint and progression of arthritis in mouse RA model. This systemic siRNA administration technology has great potential to treat RA patients.

Workshop

W1-1

The Boolean remission rate and the annual hospitalization number for serious adverse events for high dose MTX monotherapy in Japanese patients with RA by NinJa 2016 cohort

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Conflict of interest: None

[Object] The purpose of this current study is to review serious adverse event by MTX dose dependent in Japanese patients with RA. [Methods] In 15343 Japanese RA patients registered with NinJa 2016, 4690 patients medicated MTX monotherapy without biological DMARDs and combination synthetic DMARDs were divided 6 groups by MTX dose once a weekly; 1-4mg/week n=660, 6mg/week n=1084, 8mg/week n=1302, 10mg/week n=795, 12mg/week n=599, over14mg/week n=250, respectively. We defined hospitalization for various infectious disease (including opportunistic infections), herpes zoster, interstitial pulmonary disease, pancytopenia, malignant lymphoma as serious adverse event and research annual hospitalization in each groups. Final, we compare the event number for 6 groups by Odds ratio. [Results] The Boolean4 remission rate in each groups were 4mg groups 37.9%, 6mg 34.2%, 8mg 34.7%, 10mg 30.6%, 12mg 29.9%, over14mg 27.6%, respectively. Incidence of serious adverse event of the all NinJa 2015 cohort was 732 patients (4.8%), and the OR with MTX each groups were 0.97, 0.74, 0.55, 0.65, 0.70, 0.48, respectively. [Conclusions] MTX monotherapy within 12mg/week in Japan is safe, but the efficacy was not getting better by dose depending.

W1-2

Study of factors affecting maintenance of disease activity after MTX reduction in rheumatoid arthritis patients with high-dose MTX oral administration

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Conflict of interest: None

[Object] The objective of this study is to investigate maintenance predictive factors of disease activity after MTX reduction in RA patients with high dose (over 14 mg / week) MTX and below low disease activity of SDAI. [Methods] 85 patients with low disease activity or remission of SDAI at the time of MTX reduction in the case of high dose MTX. The outcome was defined as exacerbation after MTX reduction from SDAI disease activity at the time of MTX reduction and the end point was defined as the disease activity maintenance rate at 1 year after MTX reduction. Single COX regression analysis was performed using age, stage, disease duration, presence or absence of biologic drug combination, disease activity maintenance period before MTX reduction, MTX reduced amount: ΔMTX at the time of MTX reduction as a predictor. [Results] The disease activity maintenance rate after one year was 72%. The disease activity maintenance period before MTX reduction was HR: 0.998, 95% CI: 0.997 - 1.000, p = 0.024, and there was a significant difference. The ROC analysis showed a cutoff value of 277 days. [Conclusions] From the results of this study it seems unlikely that disease activity will worsen after MTX reduction if disease activity maintainability of about 9 months with high dose MTX was possible.

W1-3

Prevention for progression of rapid radiographic progression and bone marrow edema in early RA patients with RRP associated with bone marrow edema by treatment with high dose methotrexate

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Conflict of interest: None

(Purpose) To study whether a high dose methotrexate (MTX) treatment prevents the deterioration of bone marrow edema (BE) and rapid radiographic progression (RRP). (Methods) Seventeen early RA patients (male 8, female 9) with extensive BE in hand by MRI test were enrolled. All patients met RRP criteria, and clinical demographics were: average age: 59.7 years old, disease duration: 14.9 months, DAS28-ESR: 4.18, yearly modified total Sharp score (mTSS): 30.7/year. After 24 weeks of treatment with high dose-MTX, changes in DAS28-ESR, mTSS/year, BE in MRI were investigated. (Results) Mean dose of MTX was 10.7mg/week. Six of 17 patients were treated with MTX combined with DMARDs such as SASP (3 patients) BUC (1), LEF (1), and IGU (1). DAS28-ESR was reduced from 4.18 to 2.86 by a short-time treatment with high dose MTX. Importantly, apparent reduction of BE was also determined in 60% of patients. Mean mTSS/y value from all patients was significantly reduced from 30.7 to 5.6, and consequently, RRP rate was decreased from 100% to 35%. None of patients whose BE was improved by treatment were categorized in RRP. (Conclusion) A short-term usage of high dose MTX reduces progression of BE, and consequently prevents the progression of arthritis into RRP category in 60-70 % of early destructive RA.

W1-4

Effect of treatment with methotrexate 16mg in rheumatoid arthritis patients

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Conflict of interest: None

[Object] To examine the efficacy and safety of treatment with methotrexate 16 mg in patients with rheumatoid arthritis (RA). [Methods] Of 40 patients with RA, 36 patients were examined for effectiveness and reason of discontinuation by age, RA duration, body weight, BMI, DAS28, period from MTX 10 mg to 16mg and from14mg to 16mg. [Results] Continuation rate of MTX16mg was 36% at 2 years. 17 patients achieved remission. Eight patients reduced methotrexate for remission or low disease activity. Percentage of remission was 46% in the patients whose BMI under 25, and 22% in BMI>25. Four patients whose BMI was over 30 did not achieve remission. [Conclusions] Higher BMI RA patients might not be easy to achieve remission with MTX 16mg. It may be able to reduce MTX in the patients with remission using MTX 16mg.

W1-5

Dose reduction or withdrawal of prednisolone (PSL) without impaired disease activity by appropriate increase of methotrexate (MTX) in patients with rheumatoid arthritis (RA)

Shintaro Hirata, Takuma Kondo, Kazutoshi Yukawa, Tadahiro Tokunaga, Tatsuomi Kuranobu, Katsuhiro Oi, Yusuke Yoshida, Masamoto Funaki, Keisuke Oda, Takaki Nojima, Eiji Sugiyama
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Conflict of interest: Yes

[Object] To investigate whether PSL could be reduced without impaired disease by increase of MTX in RA patients with stable medication. [Methods] 70 patients with RA who regularly visit our outpatient clinic for ≧ 1yr were enrolled. Clinical characters, disease activity, and medications at present and 1 year before were retrospectively collected. Therapeutic strategy was to increase MTX and to reduce PSL based on patient's consent. Initiating bDMARDs was allowed in case of uncontrollable disease. Wilcoxon test and χ^2 test were used for statistics. [Results] Clinical characters (median [IQR]) were; age 62 [51, 68] yrs; female 69%; disease duration 6.8 [3.4, 13.7] yrs. Rate of MTX was elevated from 57 to 62%, and dose (mean±SD) was increased from 9.8±3.2 to 11.6±3.7mg/w ($p<0.0001$), whereas PSL was suppressed from 56 to 26%, and decreased from 3.6±3.4 to 2.9±2.6mg/d ($p=0.0094$). 16 used bDMARDs, and 2 newly initiated. Median CDAI, SDAI, and DAS28 were decreased from 5.7 to 3.8, 6.2 to 3.9, and 2.92 to 2.77, and remission rate were increased from 24 to 39%, 27 to 41%, and 36 to 41%, respectively. [Conclusions] PSL could be reduced or withdrawn without deterioration of RA. Moreover, disease control was rather improved with appropriately increased MTX.

W1-6

Factors associated with the concentration of methotrexate-polyglutamates in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To identify factors associated with erythrocyte methotrexate-polyglutamate (MTX-PG) concentrations and the efficacy and safety of MTX in patients with rheumatoid arthritis (RA). [Methods] RA patients with stable MTX dose for more than 4 months were enrolled. The concentrations of MTX-PG in erythrocytes were measured using a liquid chromatography and mass spectrometry, and the relevance to each clinical index and adverse events was investigated. [Results] A total of 288 patients were included. 86% of patients were female, the mean age 62 years old, the mean disease duration 8.2 years, and mean DAS28ESR 2.65. The MTX treatment duration was 4.8 years, and the mean MTX dose was 8.6mg/week. Erythrocyte MTX-PG concentrations were significantly affected by MTX dose ($p<0.001$), body mass index ($p=0.009$), and estimated glomerular filtration rate ($p=0.0004$) in the multiple regression analysis. In patients with MTX monotherapy, MTX-PG concentrations were correlated with lymphocyte count (Rho=-0.17, $p=0.04$) and mean corpuscular volume (Rho=0.17, $p=0.04$). MTX-PG long chains (MTX-PG 4,5) was associated with hepatotoxicity. [Conclusions] MTX-PG concentrations in erythrocytes can be a useful biomarker in optimal MTX therapy.

W2-1

Analysis of predictive factors for skeletal muscle index in patients with rheumatoid arthritis (RA)

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Conflict of interest: None

[Object] We aimed to examine the baseline predictive factors for skeletal muscle index (SMI), variables for diagnosis of sarcopenia in patients with RA. [Methods] The mean age and duration of disease in 153 patients including 25 males and 128 females were 68.6 (18-88) years and 14.5 (0.1-45) years, respectively. Skeletal muscle mass was evaluated using Body Composition Analyzer to calculate SMI. Age, disease duration, serum albumin, body mass index (BMI), DAS28-ESR, HAQ were examined to explore the baseline predictive factor for pre-sarcopenia (SMI cutoff values, male: 7.0kg/m^2, female: 5.7kg/m^2). [Results] The pre-sar-

copenia group had significantly longer disease duration, higher age, HAQ, DAS28-ESR and lower BMI, serum albumin than the normal group. Multivariate analyses revealed that long disease duration, high age, high HAQ and low BMI were the factors predictive of pre-sarcopenia. [Conclusions] The results of our study indicated that long disease duration, high age, high HAQ and low BMI might be predictive factors for sarcopenia in patients with RA. The ultimate goals of RA treatment is to delay or halt joint damage, preventing the resultant disability. Also, maintaining the nutritional health and HAQ remission might lead to action being taken to control or prevent sarcopenia.

W2-2

The evaluation of swallowing function for rheumatoid arthritis patient using videofluroscopic examination

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Conflict of interest: None

[Object] In this study we clarified the swallowing function. [Methods] We investigated twenty RA patients (19 females, mean age 58) in order to evaluate physical examination, upper limb exercising function and swallowing difficulties (modified water swallow test MWST, videofluoroscopic swallowing study VFSS). The VFSS (motion analysis of a tongue and cervical, oropharyngeal transit time, distance of hyoid bone displacement, the esophageal transit time) was conducted and analyzed using two dimensional analysis (Move-tr/2). The results of VFSS compared with control. [Results] Larsen grade stage IV18 case, mean DAS28 2.6, Steinbroker grade IV 15 case. The mean pinch was 2.1 (2 finger), MWST (case), wet hoarseness 5. The mean score for swallowing dynamics was 82 points. Sixteen cases were damaged of esophageal. The disorder of upper limb exercising function was correlated with abnormal swallowing posture. The motion of the third cervical and the hyoid bone moved less. The tongue moved slowly. There was little difference in the oropharyngeal transit time but the esophageal transit time was longer. [Conclusions] Our study clarified that RA patients will be taken the exercise It is important for RA patients of the estimation of swallowing and prevention against dysphagia.

W2-3

Overuse syndrome in the patients with rheumatoid arthritis

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Conflict of interest: None

Objectives: We analyzed the clinical characteristics of patients who overused their joints. *Methods:* Patients with rheumatoid arthritis (RA) who satisfied the following criteria were diagnosed with overuse syndrome:(i) had experienced preceding events, which exerted a strain on their joints, and (ii) joint pain and/or swelling of the strained joints. Their clinical parameters were analyzed, and compared them with 123 age- and sex-matched patients. *Results:* Forty-one patients (10 men, and 31 women) were diagnosed with overuse syndrome. The median clinical disease activity index (CDAI) increased from 5.00 to 9.00 due to overuse, and improved to 4.80 at the next visit ($p<0.001$; $p<0.001$, respectively). Logistic regression analysis showed that treatment with biological disease-modifying antirheumatic drugs (bDMARDs), low health assessment questionnaire disability index (HAQ-DI), and Steinbrocker Stage III or IV were important variables for developing overuse syndrome (Odds Ratio 3.28, 95% confidence interval 11.3-8.17; 0.301 (0.107-0.846); 6.89 (2.57-18.5), respectively). *Conclusion:* Patients with lower HAQ-DI, advanced stage of RA, and taking bDMARDs were more likely to suffer from joint overuse syndrome, Patient education including self-control appeared to be important.

W2-4

A study of music therapy for patients with rheumatoid arthritis by using PANAS

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Conflict of interest: None

[Objectives] We previously reported that music therapy improves general health condition and self-efficacy of patients with rheumatoid arthritis (RA) and decrease pain and anxiety. In this study, we investigated the effect of music therapy on both positive and negative emotions by using Positive and Negative Affect Schedule (PANAS). [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 general health visual analogue scare (GH-VAS), face pain rating scale, and PANAS. [Results] Fourteen female patients were participated. mHAQ was 0.50±0.71 (0-2.50). GH-VAS was changed from 3.1 to 1.8 and FS from 6.2 to 1.8 after therapy. Meanwhile, positive emotion score of PANAS changed from 3.1 to 1.8 and negative emotion score did from 17.6 to 16.2. Namely, only the positive emotions were significantly increased, while the negative emotions were not changed. [Conclusion] Music therapy improves positive emotions rather than negative emotions in patients with RA.

W2-5

Multilateral study of pain modifiers in patients with rheumatoid arthritis with disease activity and activity - Analysis of factors affecting psychosocial and emotional problems -

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Conflict of interest: None

[Introduction] We have reported the usefulness of evaluating psychopsychological problems of RA patients. Even if we are in remission, how to respond to patients who complain of complaints from the influence of psychosocial factors is a big problem. In this report, psycho - psychological problem of modifying pain symptoms of RA patients with disease active calories, and factors influencing them are discussed. [Methods] The subjects were 38 female RA patients (mean age 65.08 ± 2.05 years old) who were discharged at our hospital treatment. Evaluation items were age, duration of disease, SDAI as disease activity, VAS as pain intensity, PDAS, HAQ as functional impairment, PCS, HADS as psychophysiological state, addictive helplessness which is a psycho psychological problem And analyzed the relationship of each factor. [Results and Discussion] There were some patients suffering from strong catastrophic thoughts and habitual helplessness even when disease activity subsided and remission. Physical functional problems affected the addictive helplessness of RA patients rather than the main symptoms, which was thought to be influenced by the degree of performance of overall daily behavior. It also suggested that it might be affected by the course of treatment and treatment experience.

W3-1

BAFF and APRIL expression associated with the pathogenesis in ANCA-related hypertrophic pachymeningitis

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Conflict of interest: None

[Object] In the causes of hypertrophic pachymeningitis (HP), anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis is recognized as the most common underlying disease; however, the pathogenesis of ANCA-related HP (ANCA-HP) remains elusive. In this study, we investigated the pathogenic immune mediator associated with ANCA-HP. [Methods] We enrolled 9 patients with ANCA-HP as well as 11 those with multiple sclerosis (MS) and 8 with non-inflammatory neurological disorders (NIND) as the disease controls. The levels of B-cell activation factor of the tumor necrosis factor family (BAFF) and a proliferation-inducing ligand (APRIL) in the cerebrospinal fluid (CSF) and serum were measured using ELISA kit. BAFF and APRIL levels were compared between three groups, and were statistically analyzed with laboratory findings. [Results] BAFF and APRIL levels in the CSF were significantly higher in patients with ANCA-HP than in those with MS and NIND. In addition, a positive correlation between BAFF levels in the CSF and IgG-index was found in patients with ANCA-HP, whereas no correlation was detected between CSF and serum levels of BAFF or APRIL. [Conclusions] Increased levels of BAFF and APRIL produced in the central nervous system may impact on the development of ANCA-HP.

W3-2

The Utility of serum Angiopoietin-1 and Angiopoietin-2 in patients with anti-neutophil cytoplasmic autoantibody-associated vasculitis

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Conflict of interest: None

[Objectives] To examine the serum Angiopoietin-1 (Ang1) and Angiopoietin-2 (Ang2) levels in patients with anti-neutrophil cytoplasmic autoantibody-associated vasculitis (AAV), and investigate the utility as biomarkers. [Methods] Seventy-one patients who had been diagnosed as AAV and referred to Niigata University Medical and Dental Hospital between 2009 and 2017, were participated in this study. Serum Ang1 and Ang2 levels were measured before the initiation of remission-induction therapy. Laboratory findings and disease activity were corrected from patients' clinical records and the correlations between these findings and serum Ang1 and Ang2 were analyzed. [Results] In stepwise multiple regression analysis, estimated glomerular filtration rate (eGFR) was selected as a positive independent variable (beta=0.3769, p=0.0014) for serum Ang1 levels, whereas end-stage renal disease was selected as a positive independent variable (beta=0.5850, p<0.0001) and urinary protein /creatinine ratio (beta=-0.5780, p<0.0001) and eGFR (beta=-0.4311, p=0.0003) were selected as negative independent variables for serum Ang2 levels. [Conclusion] These findings showed the protective effect of kidney functions for Ang1 and the utility of Ang2 as a predictive factor for kidney prognosis.

W3-3

The role of CD93 in the pathogenesis of ANCA-associated vasculitis

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Conflict of interest: None

[Object] We have identified promising biomarkers of disease activity and organ involvement in AAV with a targeted proteomics approach (Arthritis Res Ther 2017;19:218). We examined whether these markers are related to the pathogenesis of AAV. [Methods] $CD14^+$ monocytes from PBMC of healthy donors were differentiated into macrophages in 7-days-culture in M-SFM with M-CSF. After soluble form of CD93 (sCD93) prepared by a wheat germ cell-free synthesis system was added, the concentrations of TNF-α, IL-6 and IL-8 in culture supernatants were determined by ELISA. The same experiments were performed with TIMP1, LRG1, S100A8/A9 or Histone 4 (H4). [Results] The productions of TNF-α, IL-6 and IL-8 were higher from macrophages added with sCD93 than those with TIMP1, LRG1, S100A8/A9 and H4. The productions of TNF-α, IL-6 and IL-8 after stimulation with sCD93 (3μg/mL) significantly increased, compared with control culture (TNF-α, 245 vs 1.6 pg/mL; IL-6, 749 vs 1.3 pg/mL; IL-8, 9.9 vs 0.05 ng/mL, respectively). sCD93 was increased in the culture supernatants of HDMEC and HPMEC. [Conclusions] CD93 is a membrane protein expressed on monocytes and vascular endothelial cells and is shed by inflammatory stimulation. sCD93 induced the productions of TNF-α, IL-6 and IL-8 from local macrophages.

W3-4

Clinical impact of anti-erythropoietin receptor antibodies in patients with anti-neutrophil cytoplasmic antibody-associated vasculitis

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Conflict of interest: None

[Object] We examined the impact of autoantibodies to the erythropoietin receptor (EPOR) in patients with anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV). [Methods] Sixty-three patients with AAV were enrolled in this study. Sera from these patients were screened for anti-EPOR antibodies using the ELISA. [Results] The patients comprised 26 men and 37 women aged 67 (60-73) years. Follow up period was median of 31 months. The survival rate was 54/63 (86 %). Fifteen patients had developed end-stage renal disease (ESRD). Anti-EPOR antibodies were detected in 7 patients. Patients with anti-EPOR antibodies showed higher Birmingham vasculitis activity score (BVAS), especially systemic and skin scores as compared with those without. In addition, antibody titers were correlated with systemic and skin scores of BVAS. Cox regression analysis revealed that male gender, proteinuria and estimated glomerular filtration rate at disease onset, and vasculitis damage index (VDI) at 3 months after treatment were significant risk factors for ESRD. Further, VDI at 3 months after treatment was selected as an independent factor for death. [Conclusions] Anti-EPOR antibodies were associated with disease activity, especially in systemic symptoms and skin lesions in patients with AAV.

W3-5

High dose immunoglobulins can prevent the development of MPO-ANCA-associated vasculitis (MPO-AAV) by inhibiting neutrophil extracellular trap (NET) formation

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Conflict of interest: Yes

[Object] IVIG is effective against some autoimmune diseases. However, its effects on MPO-AAV remain unknown. We examined the effects on MPO-AAV, especially on NET formation related with MPO-ANCA production. [Methods] 1. Human neutrophils were treated by 5mg/mL freeze-dried human sulfo-immunoglobulins (IVIG-S) and then exposed to 100nM PMA. Thereafter, the neutrophils were stained with SYTOX Green followed by flow cytometry (n=6). 2. WKY rats (4 weeks old, male) were given p.o. administration of 10mg/kg/day PTU for 28 days and i.p. injection of 1μg PMA at days 0 and 7. These rats were divided into two groups, namely Group 1 (n=6) with i.p. injection of 400mg/kg IVIG-S at days 8-12 and Group 2 (n=6) with i.p. injection of PBS simi-

larly. Chronological ANCA titers were determined. At day 28, all rats were killed to examine NET formation in the peritoneum and the development of AAV. [Results] 1. IVIG-S significantly inhibited NET formation induced by PMA in vitro. 2. NET amounts in the peritoneum in Group 1 tended to be small compared to Group 2, and ANCA titers in Group 1 were significantly lower than in Group 2. The degree of pulmonary bleeding in Group 1 was also smaller than in Group 2. [Conclusions] High dose immunoglobulins can prevent the development of MPO-AAV by inhibiting NET formation.

W3-6

Preliminary Observation of Serum IL-6 levels in Initial Treatment for Anti-glomerular Basement Membrane Disease (anti-GBM disease)

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Conflict of interest: None

[Objectives] To know whether IL-6 participates in the systemic inflammation of patients with anti-GBM disease [Methods] 5 recent consecutive cases (two females and three males) were enrolled for the current study and serum IL-6 was tested by CLEIA at the beginning of treatment and 2 weeks later along with other inflammatory markers and autoantibodies. The study protocol was admitted by the ethical committee of our hospital. [Results] Anti-GBM disease was diagnosed based on the presence of anti-GBM antibody and rapidly progressive renal failure. MPO-ANCA was positive in 2 females and 1 male. All patients were treated with high dose of corticosteroid, hemodialysis and plasmapheresis. At onset, CRP level was 16.72mg/dl (3.57-27.05), serum Cr 6.08 (4.33-12.52) and IL-6 48pg/ml (11.9-1220) (median (range)). CRP was reduced by 62-90% and IL-6 by 42-98% in MPO-ANCA-positive patients whereas CRP was declined by 93-100% and IL-6 by 90-92% in ANCA-negative. During observation period, serum Cr was kept at high levels in all patients. [Conclusions] Presence of MPO-ANCA may be associated with initial resistance to immunosuppressive therapy for anti-GBM disease.

W4-1

The assessment about the measurements of the disease activity score for Ankylosing Spondylitis (ASDAS) in psoriatic arthritis in the real-life

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Conflict of interest: Yes

The assessment about the measurements of the disease activity score for Ankylosing Spondylitis (ASDAS) in psoriatic arthritis in the real-life [Objective] As there is no gold standard to assess disease activity in Psoriatic arthritis (PsA), but in axial SpA, ASDAS is recommended for a prefferd measure by 2017 update of EULAR. So we evaluated about ASDAS and various measurements in PsA in the real-life. [Methods] Enrolled fifty-six patients with PsA were classified into with (n=27) or without (n=29) biologics. We compared with ASDAS, BASDAI, BASFI, BASMI and MDA. [Results] ASDAS was related with Pt.GAS (ρ0.62), Dr.VAS (0.57), BASFI (0.66), CRP (0.63). But there was no relation between BASMI and ASDAS. A similar pattern was found about BASDAI, except in the case of CRP. There was no difference about background between both groups at 0M. At 12M, ASDAS was a significant decrease in PsA with biologics (P=<0.0001), but there was no change without biologics. Both arms were no change in BASFI and BASMI. At 12M, ASDAS remission accorded closely with MDA (κ0.66). [Conclusions] In the relalife, the ASDAS is a validated, highly correlated various assessment in PsA, and is also very useful in the assessment of treatment efficacy.

W4-2

A phase 3 study of the efficacy and safety of Ixekizumab in patients with active psoriatic arthritis who had previously received tumour necrosis factor inhibitor (s): spirit-p2 (24-week data)

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Conflict of interest: None

[Object] To compare the efficacy and safety of ixekizumab (IXE) vs placebo (PBO) in patients (pts) with active psoriatic arthritis (PsA) who have had an inadequate response (IR) or intolerance to TNF inhibitors. **[Methods]** Data from 24-week (wk), double-blind, PBO-controlled period. Pts were randomised to PBO or IXE 80 mg every 2 (Q2W) or 4 wks (Q4W), after a 160 mg initial dose. ACR20 (Wk24, primary endpoint), ACR50/70, PASI75, DAS28-CRP, HAQ-DI were evaluated. **[Results]** 363 pts were randomized and 314 pts completed Wk24. Significantly more pts achieved ACR20/50/70 and PASI75 in IXE groups vs PBO at Wk24: ACR20 (Q4W, 65 [53.3%]; Q2W, 59 [48%]; PBO, 23 [19.5%]), ACR50 (Q4W, 43 [35.2%]; Q2W, 41 [33.3%]; PBO, 6 [5.1%]), ACR70 (Q4W, 27 [22.1%]; Q2W, 15 [12.2%]; PBO, 0), PASI75 (Q4W, 38/68 [55.9%]; Q2W, 41/68 [60.3%]; PBO, 10/67 [14.9%]). DAS28-CRP and HAQ-DI significantly improved in IXE groups vs PBO at Wk24. No significant differences were observed between either IXE group vs PBO in the incidence of adverse events (AEs) or serious AEs. **[Conclusions]** IXE showed statistically significant efficacy compared with PBO, with no unexpected safety findings in pts with active PsA who have IR or intolerant to TNF inmhibitors. Similar results were seen in pts naive to biologic therapy (SPIRIT-P1).

W4-3

Relationship between severity of skin disease and musculoskeletal symptoms in patients with psoriatic arthritis

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Conflict of interest: None

Purpose: Factors affecting the onset of psoriatic arthritis (PsA) in patients with psoriasis (PsO) are not well understood. In this study we analyze the difference in severity of skin disease between PsA and PsO patients, and the relationship between skin and musculoskeletal symptoms in PsA patients. **Methods:** Among the patients with psoriasis referred from dermatologists for assessment for arthritis between June 2015 and July 2017, those who PASI (Psoriasis area and severity index) was evaluated by dermatologists were enrolled. PsA was diagnosed by CASPAR criteria. **Results:** Between 27 PsA patients and 43 PsO patients without any musculoskeletal manifestations there was no significant difference in PASI (PsA: 7.20, PsO: 8.60; p=0.682). Among 27 patients with PsA, there were no significant differences in sex (p=0.69), enthesitis (p=0.25), inflammatory back pain (p=0.62) and sacroiliac joint pain (p=0.86). And there were significant correlations between PASI and Disease activity score 28-CRP (Pearson's correlation coefficient R=0.46: p=0.04) or MMP-3 (Pearson's correlation coefficient R=0.68: p<0.01).

Conclusions: In PsA patients, there are relationships between severity of skin disease and musculoskeletal symptoms.

W4-4

Clinical features of SAPHO syndrome and treatment with biologics

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Conflict of interest: None

[Object] The synovitis-acne-pustulosis-hyperostosis-oeteitis (SAPHO) syndrome is rare. We reported the clinical features and treatment of our cases. [Methods] Eighty-four cases of SAPHO syndrome were extracted from medical records. [Results] Sixty-four women and 20 men. The age at diagnosis was 51.5 years, the average age at arthritis was 48.0 years, and the average age at skin eruption was 44.2 years old. Palmoplantar pustulosis occurred in 62 cases among 65 cases of skin lesions. The period from eruption to onset of arthritis was 4.3 years. There were 6 cases in which arthritis preceded eruption. Smoking was a high rate in 32 of 59 cases. Among the 20 cases in which HLA was searched, HLA-B 27 positive was one case, but in 9 cases the B7 cross reactive antigen was positive. Treatment was 40 cases of MTX and 25 cases of SASP. In 8 refractory cases, biologics were administrated. In the follow - up period 6 to 62 months, TNFα inhibitor in all cases and CTLA 4Ig in one case were administrated. Biologics were effective in all cases, although there were cases in which the first-line drug was ineffective. Four cases were observed for long-term use. Interruption of biologics resulted in an early relapse. [Conclusions] Biologics may be used to treat refractory SAPHO syndrome.

W4-5

The assessment of efficacy and safety of anti-TNF therapy in SAPHO syndrome

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Conflict of interest: None

[Object] To assess the efficacy of TNF inhibitors (TNFi) in SAPHO syndrome. [Methods] We retrospectively assessed clinical efficacy and safety of TNFi in TNFi-naïve 6 cases of SAPHO syndrome from 2015 to 2017. [Results] Patient characteristics were as followings: male/female 3/3, average age of 59±6 and disease duration of 9±6 years. Cutaneous lesions preceded osteoarticular in 4 cases, and all cases involved axial and peripheral articular disorders. HLA-B27 was negative in all cases. TNFi administrations were as followings: IFX in 3, ADA in 2 and GLM in 1 case. As concomitant drugs, MTX in 5, IGU in 1, NSAIDs in 6, bisphosphonates in 2, and antibiotics in 1 case were used. In all cases, remission of osteoarticular lesions were achieved after initiation of TNFi. A case with remaining cutaneous lesion was required to shorten administration period of TNFi. While, a case with paradoxical reaction (PR) was required to change TNFi. [Conclusions] TNFi possibly has good efficacy especially in osteoarticular lesions and improves QOL in SAPHO syndrome. However, secondary failure and PR are often revealed. Further studies on efficacy of TNFi in Japanese patients with SAPHO syndrome are needed.

W4-6

24 cases of Spondyloarthrits associated with inflammatory bowel disease (IBD) in our department

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Conflict of interest: None

[Object] Spondyloarthrits (SpA) is a common extra-intestinal complication in patients with IBD. We examined the clinical features of them. [Methods] 24 patients with IBD-related arthritis visiting our department were examined on background and treatment. [Results] Age was 48.3 years, 12 cases of men, 17 cases of ulcerative colitis, and 7 cases of Crohn's disease. 4 of them diagnosed as RA, and then developed IBD 8 to 23 years later. They fulfilled RA criteria in ACR1987, and Steinbrocker's stage IV. In the other 20 patients, arthritis developed 10.4 years after onset of IBD, 4 of them were axial SpA, and 16 were peripheral SpA. 2 cases of axial SpA and 4 cases of peripheral SpA were related with the disease activity of IBD. In peripheral SpA, 3 cases were positive for both ACPA and RF. 1 patient was no therapy, 6 were NSAIDs, 4 were SASP, 5 were MTX, and 4 were TNFα inhibitors. In patients with active IBD, arthritis was improved with the treatment of IBD. ACPA/RF positive cases were improved NSAIDs, SASP, MTX, respectively. [Conclusions] The treatment of IBD is effective, however the activity of IBD and arthritis are often unrelated, and treatment as RA, was effective in these patients. Some cases are positive for ACPA, we need to treat considering RA.

W5-1

The risk factors for newly developing/worsening pulmonary abnormalities in RA patients with bDMARDs

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Conflict of interest: None

Object: To identify the risk factors for newly developing/worsening pulmonary abnormalities in RA patients under the bDMARDs (Bio) therapy. **Methods:** Subjects were consecutive 208 RA patients treated with bDMARDs and received HRCT scan before and during the therapy. Pulmonary abnormalities were classified into 20 lesions. **Results:** Subjects were M/F;64/144, mean age;. 59.2 y.o. Pulmonary lesions were found in 70.2% of RA patients before Bio. AD was commonly accompanied with the other lung abnormalities. Newly developing/worsening pulmonary abnormalities were observed in 13.8/100 person years (ILD; 8.5, nodules; 2.2 and AD; 6.5). The risk factors for newly developing/worsening lung abnormalities were older age, older onset, and pre-existing lung lesions, particularly AD. Nine patients died of respiratory failure, the risk factors for which were older age, older onset, and pre-existing lung lesions, particularly ILD (reticular pattern and honeycombing) and AD. **Conclusion:** Newly emerging/worsening lung abnormalities were observed in 13.8/100 person years is under Bio for RA. The risk factors for newly emerging/worsening lung abnormalities were older age and pre-existing lung lesions, particularly AD.

W5-2

Association between severity of respiratory involvement and outcomes of respiratory adverse events in rheumatoid arthritis patients treated with biological therapy

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Conflict of interest: None

[Object] The aim of this study was to assess the association between severity of respiratory involvement based on chest computed tomography (CT) findings and incidence of respiratory adverse events (RAEs), and to detect risk factors of CT findings for RAEs in RA patients receiving biological therapy. [Methods] Clinical and radiological data of 332 RA patients was assessed. According to the CT findings, the patients were categorized to interstitial lung disease (ILD) group (n=32), airway disease (AD) group (n=79), and normal group (n=221). We calculated the incidence of two types of RAEs in each group, and explored risk factors for RAEs among CT findings. [Results] We identified 41 RAEs including respiratory infection events (infection events, n=21), acute onset or exacerbation of ILD (ILD events, n=15), and other events (n=6). The severity of involvement evaluated with CT score was correlated to the incident rates of RAEs. Among CT findings, risk factors for infection events were

bronchiectasis, bronchiolitis, and atelectasis and that of ILD events were reticular changes and honeycomb after age, sex adjustment. [Conclusions] This study suggested that severity of CT score at baseline may associate with risk of RAEs in a course of biological therapy for RA.

W5-3

The relationship between anti-citrullinated peptide antibody titer and interstitial pneumonia in rheumatoid arthritis

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Conflict of interest: None

[Object] We examined the relation of incidence, type, and progression of pulmonary lesion (PL) in rheumatoid arthritis (RA) with anti-cyclic citrullinated peptide antibody (aCCP). [Methods] Of RA who first visited our hospital from 2005 to 2016, 107 patients with PL at the first visit and 360 without PL were tested. We examined the type and frequency of PL and the progression of PL in the 95 patients who underwent chest CT at least twice and analyzed the relation of pulmonary lesions with various parameters including aCCP at the first visit. [Results] Among 107 cases with PL, there were 69 NSIP (64%), 28 UIP (26%), 8 bronchiectasis (7%), and 2 other type. The frequency of positive aCCP in RA with PL was higher than that of RA without PL (93% vs 89%), although not significant. aCCP titer was 587 ± 78 (mean ± SE) U/ml in RA with PL, which was significantly higher than that of RA without PL (240 ± 17). Among 107 with PL, 13 who showed the progression of IP had significantly higher aCCP titer (1056 ± 290) compared PL without progression. On the other hand, RF titer and MMP3 were not different between RA with and withoud PL and between PL with and without progression. [Conclusions] aCCP titer was significantly higher in RA with PL. Higher aCCP in PL may be a risk of PL progression.

W5-4

Abatacept therapy in rheumatoid arthritis with interstitial lung disease

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Conflict of interest: Yes

[Object] The purpose of this study is to evaluate the safety and effectiveness of abatacept (ABT) in rheumatoid arthritis (RA) patients with interstitial lung disease (ILD). [Methods] The RA patients with ABT therapy were retrospectively analyzed. The prevalence of ILD was assessed by high resolution computed tomography (HRCT). HRCT patterns were classified as demonstrating usual interstitial pneumonia (UIP) pattern or nonspecific interstitial pneumonia (NSIP) pattern. ABT therapy survival were analyzed using Kaplan-Meier analyses. [Results] Of 208 RA patients treated with ABT, 66 had RA-ILD. Of the patients with ILD, 33% were men, the mean age was 71.8±8.9 years, and mean disease duration was 8.8±9.0 years. The patients with ILD were significantly older than the patients with no-ILD (71.8 vs 62.6 years, $p<0.0001$). After ABT therapy, 1 and 2 year of retention rates were 90.4% and 71.1% in the patients with ILD, and were 75.6% and 60.3% in the patients with no-ILD. After ABT therapy, KL-6 was significantly improved from 556.4±411.6 U/ml at baseline to 499.8±385.7 U/ml at 6 months ($p=0.005$). [Conclusions] ABT therapy appears to be an acceptable therapy for patients with RA-ILD.

W5-5

Characterization of ten patients with recurrence of rheumatoid arthritis after treatment of lymphoproliferative disorders

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Conflict of interest: None

[Objectives] Lymphoproliferative disorders (LPD) develop in some patients (pts) with rheumatoid arthritis (RA) treated with methotrexate (MTX), which is anchor DMARDs. The efficacy and safety of treatment are unclear in pts with recurrent RA after treatment of LPD. [Methods] We analyzed 10 pts (3 males and 7 females) with recurrent RA after treatment of LPD from January 2010 to October 2017. [Results] The mean age was 48±13, and mean disease duration of RA was 16±10 years at onset of LPD. MTX had been administered to all pts, and 4 pts received biological DMARDs. The mean duration of MTX treatment was 4.9±2.6 years. Five pts were diagnosed to have diffuse large B cell lymphoma. EBV was detected in tumor tissues from 4 of 8 analyzed-pts. Six pts received chemotherapy, while 4 pts discontinued MTX. After treatment of LPD, RA relapsed within mean 16±13 months. All pts had been treated by DMARDs including tacrolimus in 8 pts, and 5 pts received biological DMARDs. LPD relapsed within 21 and 35 months in 2 pts treated with biological DMARDs. The death caused by LPD was not observed. [Conclusion] We analyzed the efficacy and safety of treatment for recurrence RA in pts with a history of MTX-LPD. It is necessary to be careful about recurrence of LPD in pts treated with biological DMARDs.

W5-6

Clinical investigation of RA with MTX-LPD

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Conflict of interest: None

In this study, we aim to clarify the clinical picture from our medical experience of MTX-LPD. Clinicopathological examination was performed retrospectively for 25 cases of RA with MTX-LPD diagnosed in our hospital from 2008 to 2017. The cases include 10 males, 15 females and 4 seronegative RA. The mean onset age of RA was 53.6 years, and MTX-LPD was 68.5 years. Histopathologically, DLBCL was most common and seen in 15 cases (60%), followed by Hodgkin's lymphoma (4 cases). Seven of 15 cases were EBER-positive. MTX therapy at the onset of lymphoma was used for 23 cases, and TOC and INF was in one case respectively. The average follow-up after the onset of lymphoma was 37 mo. Chemotherapy was used in 15 patients, including R-CHOP in 10 patients. DOD was seen in 1 case. After the RA-drug withdrawal, the remission of lymphoma was observed in 8 of 10 patients. The treatment of RA after the onset of lymphoma was SSZ (12 cases), PSL (9 cases), and BUC (5 cases). The cases using multidrug treatment including IGU and TAC became prominent. For resistant cases, biological products such as rituximab (4 cases) and TOC (1 case) were used.

W6-1

Predictor of Relapse in Interstitial Pneumonia Associated with Anti-aminoacyl-tRNA Synthetase Antibodies Positive Dermatomyositis

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Conflict of interest: None

[Object] To identify the clinical features and predictor of relapse in ARS-DMIP. [Methods] This study comprised ARS-DMIP patients who were received first remission induction treatment in our hospitals from April 2012 to September 2015. All patients were divided into relapse and non-relapse group during the 2 years after treatment initiation, and clinical background, characteristics and treatment contents were compared

between the two groups. [Results] Seven cases (26.9 %) out of 26 cases relapse. The relapse median time was 91 weeks after the treatment initiation. There were no significant differences in background and clinical findings between the two group, but serum KL-6 levels of relapse group at treatment initiation was higher than non-relapse group (P=0.046). There were no significant differences in treatment contents at initiation, 1 and 2 years after treatment initiation. Serum KL-6 levels at 6, 12, 18 and 24 months after treatment initiation in relapse group were significantly higher than non-relapse group (P=0.009, 0.029, 0.008, < 0.001, respectively). [Conclusions] This study suggested that in the relapse patients of ARS-DMIP the high level of KL-6 persisted before and after the treatment initiation could be predictors of relapse.

W6-2

Clinical Characteristics of the Patients with Recurrent Myositis in Polymyositis and Dermatomyositis: A Retrospective Study

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Conflict of interest: None

[Object] We aimed to study the characteristics of PM/DM patients with recurrent myositis and to identify its risk factors. **[Methods]** We retrospectively reviewed the medical records of the patients who underwent initial treatment for myositis between 1993 and 2016. All patients satisfied the Bohan and Peter classification criteria for PM/DM. Patients with clinically amyopathic DM were excluded. Recurrent myositis was defined as a sustained elevation in serum CK levels requiring intensification of immunosuppressive treatment. Baseline clinical characteristics were compared between patients with and without recurrent myositis, and logistic regression analyses were performed to identify the risk factors. **[Results]** In the 120 patients included in this study, myositis recurred in 35 patients during the observational periods. Multivariate analysis identified a positive anti-SRP antibody as a positive risk factor (OR 7.7; 95% CI 1.6-38), whereas initial treatment with calcineurin inhibitor as a negative risk factor (OR, 0.2; 95% CI, 0.1-0.7) for myositis recurrence. **[Conclusions]** This study suggested that an anti-SRP antibody is a risk for myositis recurrence and that initial treatment with calcineurin inhibitor might be protective against myositis recurrence in patients with PM/DM.

W6-3

Increase in serum SP-D levels during immunosuppressive therapy predicts poor prognosis in patients with interstitial lung disease in anti-MDA5 antibody-positive dermatomyositis

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Conflict of interest: None

[Object] The purpose of this study is to determine whether the change of serum SP-D levels during immunosuppresive therapy predicts prognosis of patients with interstitial lung disease (ILD) in anti-MDA5 antibody (Ab)-positive dermatomyositis (DM). [Methods] Retrospective analysis was performed on consecutive 20 anti-MDA5 Ab-positive DM patients with rapidly progressive (RP)-ILD who admitted our department from 2009 to 2017. SP-D and KL-6 levels were measured longitudinally. [Results] Twenty patients were included; 8 treated with high-dose glucocorticoid (GC), CsA and IVCY, 7 with high-dose GC and CsA and 5 with high-dose GC, CsA, IVCY and Tofacitinib. Ten (50%) died of respiratory failure. Nineteen patients (95%) showed normal SP-D levels before therapy, while only 5 (25%) revealed normal KL-6 levels. During the therapy, 11 patients (55%) showed increase in SP-D levels, and 9 of them (82%) died of respiratory failure. In contrast, only one patient (11%) was deceased in those whose SP-D levels were within the normal range during the therapy. Levels of KL-6 were increased in all 20 patients. [Conclusions] Increase in serum SP-D levels during therapy predicts poor prognosis in ILD with anti-MDA5 Ab-positive DM.

W6-4

Evaluation of disease activity and prognosis using serum cytokines/chemokine levels in patients with interstitial pneumonia complicated with dermatomyositis or polymyositis

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Conflict of interest: None

[Object] We evaluated the serum cytokine/chemokine levels of patients with interstitial pneumonia (IP) combined with PM/DM and examined their relationships with disease activities and prognosis. [Methods] Forty-two PM/DM-IP patients (PM: 3; DM: 39, including 26 with CADM) were included. [Results] The anti-MDA5-positive patients displayed significantly higher serum IL-10, IL-8, CXCL11, and CCL2 levels than anti-ARS-positive cases. Serum KL-6 levels were correlated with serum IL-18 levels; serum ferritin levels were correlated with serum, IL-18, IL-2, IL-6, IP-10, and M-CSF levels; the $AaDO_2$ was correlated with serum IL-18, IL-2, IL-6, and IL-8 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. Initial serum IL-10, IL-6, IL-8, IP-10, and CCL2 levels were significantly higher in the death group than in the survivor group, and serum IL-6 and IP-10 levels at 2 and 4 weeks after treatment initiation were significantly higher too. [Conclusions] High serum Th1-, monocyte/macrophage-, and neutrophil-associated cytokine/chemokine levels (especially IL-6 levels) were correlated with disease activity and prognosis of PM/DM-IP.

W6-5

Initial predictors for mortality in patients with cancer-associated myositis (CAM)

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Conflict of interest: None

[Object] To identify initial predictors for mortality in patients with CAM **[Methods]** This is a multicenter retrospective study involving consecutive 67 patients diagnosed with CAM in 3 referral centers between 1995 and 2017. Demographic and clinical data at diagnosis as well as treatment regimens and outcomes were collected by review of medical charts. The Cox proportional hazard model was used to identify factors independently associated with mortality. **[Results]** Myositis-specific autoantibodies (MSAs) detected included anti-TIF1-γ in 27, anti-ARS in 6, anti-MDA5 in 5, anti-Mi-2 in 3, anti-NXP2 in 3, anti-SAE in 2, and anti-SRP in one. Univariate analysis identified 3 factors associated with mortality, including breast cancer (OR 0.2; p=0.020), ovarian cancer (OR 4.2; p=0.029), and stage III/IV malignancy (OR 6.8; p=0.001). In multivariate analysis, male (HR 5.2, 95%CI 1.9-14.2; p=0.001) and stage III/IV malignancy (HR 10.9, 95% CI 3.2-36.9; p<0.001) were identified as independent risk factors for mortality. Cumulative survival rates of the patients with 0, 1, or 2 risk factors were 100, 90, and 61% at 1 year, and 94, 51 and 0% at 5 years, respectively. **[Conclusions]** Prognosis of CAM patients is defined by sex and progression of malignancy, rather than myositis phenotype or MSA.

W6-6

A retrospective study of dermatomyositis related interstitial lung disease

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Conflict of interest: None

[Object] The aim of this study is to compare the clinical manifestations of rapid progressive interstitial lung disease (RP-ILD) and non-RP-ILD in dermatomyositis (DM) patients. [Methods] DM patients with IP who visited our hospital from April 2008 to September 2017 were enrolled. The medical records of 64 consecutive patients were reviewed retrospectively. RP-ILD is defined as a progressive ILD within 3 months of the onset of respiratory symptoms. Patients receiving immunosuppressant therapy before first visit to our hospital, as well as those with a history of other connective tissue diseases, malignancy, cirrhosis or chronic infections were excluded. We compared patients' background, laboratory data and prognosis in 18 RP-ILD and 11 non-RP-ILD patients. [Results] There were no differences in age and sex between two groups. The median value of serum KL-6 and ferritin were significantly higher in patients with RP-ILD: 1014 U/ml vs 484 U/ml (p=0.031), 626 ng/ml vs 158.5 ng/ml (p=0.008), respectively. The frequency of the fatal outcome in first admission was 27.8%, 0%, respectively. [Conclusions] Investigation of the serum KL-6 and ferritin on the first treatment is useful for predicting the onset of RP-ILD.

W7-1

The clinical significance of monoclonal gammopathy in patients with rheumatic diseases

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Conflict of interest: None

Background: Monoclonal gammopathy (MG) has been associated with various rheumatic diseases. However, there have been only sparse data as to its clinical significance in rheumatic diseases. Objectives: To investigate the features of patients with concurrent MG and rheumatic diseases. Method: We evaluated 763 patients who underwent serum protein electrophoresis at our department. MG was detected in 46 patients and their clinical data were reviewed. Results: Bone marrow aspirates were obtained in 19 patients, of whom 17 patients were diagnosed as monoclonal gammopathy of undetermined significance (MGUS), one as smoldering multiple myeloma (SMM) and one as multiple myeloma (MM). The other 29 patients were followed up as MGUS based on their low quantity of M protein. Among the 48 patients, 29 patients were diagnosed as rheumatic diseases, and rheumatoid arthritis was the most frequent (16 patients). Among the 29 patients, five patients had previous or concurrent malignancy (MM 1, lymphoma 1, carcinoma 3) and five patients had successive malignancy (MM 1, lymphoma 1, myelodysplastic syndrome 1, carcinoma 2; incidence rate 4.8/100 person-years). Conclusion: MG in rheumatic diseases is associated with substantial risk of malignancy and close follow-up should be considered in such cases.

W7-2

Analysis of clinical and pathological features in methotrexate -related lymphoproliferative disorders with rheumatoid arthritis

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Conflict of interest: None

[Object] Methotrexate (MTX) is key drug treating for rheumatoid arthritis (RA) because MTX has high effectiveness, tolerability and safety. RA patients have high susceptibility to lymphoproliferative disorders (LPD), in particular, for cases of MTX use. However, the risk factors of MTX-LPD are not clarified. [Methods] In our hospital from September 2010 until November 2017, medical records of 23 RA cases complicated with ML treating by MTX were reviewed about age, sex, histology, presence of Epstein-Barr virus (EBV), total duration and amount of taking MTX, and treatment for ML. [Results] The median age of ML diagnosis is 68 years old, 17 patients are female. In histology 10 cases were diffuse large B-cell lymphoma, 6 cases were Hodgkin lymphoma. 10 of 14 cases who analyzed EBV infection were positive. 4 cases regressed spontaneously by MTX withdrawal and all of 4 cases were EBV positive. 13 of 16 cases who treat by chemotherapy and/or radiotherapy were effective. Median total duration of MTX treatment is 8 years, and median total amount of MTX is 2.5 g. [Conclusions] Our reports indicated that the total duration and amount of MTX treatment were inconsistent. Spontaneous regression by MTX withdraw were observed more frequently in EBV-positive cases.

W7-3

Clinical aspects and IL6 receptor expressions associated with lymphoproliferative disorders (LPD) in patients with RA during treatment with methotrexate (MTX)

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Conflict of interest: Yes

[Object] To identify predictive factors for persistent LPD after MTX withdrawal and to determine the optimal choice of treatment for RA after LPD regression. [Methods] Among 3,666 patients with RA given MTX in our department, 24 patients who had LPD that regressed after MTX withdrawal and another 24 patients with persistent LPD were compared with regard to the clinical picture, subsequent treatment for RA, and interleukin-6 receptor (IL6R) expression in LPD tissue. [Results] The serum LDH and sIL-2R levels were significantly higher in persistent-group. In persistent-group, the incidence of DLBCL was higher (79%), and extranodal disease and advanced LPD stages were more common. When we used our persistent-LPD index (PLI) consisting of lower MTX dose and lymphocyte count and higher erythrocyte sedimentation rate (ESR), serum LDH and hemoglobin (Hb), a PLI of 3 points or higher could distinguish persistent LPD with a high specificity (95.8%). Among DMARDs used after LPD regression, tocilizumab was the most effective. The IL6R positive rate was high in both groups (around 70%). [Conclusions] The distinguishability of persistent LPD by means of a combination of patients' background factors and the importance of IL6-IL6R signal in RA-LPD should be well recognized.

W7-4

Extraction of predictive factor on spontaneous regression with MTX associated lymphoproliferative disorders in rheumatoid arthritis patients

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Conflict of interest: None

[Object] It is difficult to predict clinical course of lymphoproliferative disorders (LPD) that develop in rheumatoid arthritis (RA) patients treated with MTX (MTX-LPD). Recently, immune checkpoint molecules have been focus of attention as a mechanism for escape of tumor cells from antitumor immune responses. We investigate the status of immune cells in the biopsy lesion in order to clarify the spontaneous regression of MTX-LPD. [Methods] We enrolled 12 MTX-LPD patients (7 withdrawal and 5 CTx group), and 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 discontinuation (CTx group). We compared the expressed protein (CD4, CD8, PD-1 and PD-L1) in cells at the biopsy lesion by immunohistochemistry (IHC) between the two groups. [Results] In CTx group, the

CD8 positive lymphocyte showed a significant increase. On the other hand, there was no significant difference in CD4, PD-1 and PD-L1 positive cells between the two groups. [Conclusions] Low CD8 positive lymphocyte rate of biopsy lesion tended to spontaneously regress. However, we suggested that PD-1/PD-L1 may not affect the predictive factor of spontaneous regression in MTX-LPD with RA patients.

W7-5

Changes of bone mass and skeletal muscle mass for 7 years in patients with rheumatoid arthritis: TOMORROW study

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Conflict of interest: None

[Objectives] Both osteoporosis and sarcopenia are reported as comorbidities of rheumatoid arthritis (RA). In this study, we evaluated relationship between bone mineral density (BMD) and appendicular skeletal muscle index (ASMI) analyzed by DXA in RA patients for 7 years and compared with healthy volunteer (Vo). [Methods] 202 RA patients and 202 age/sex-matched Vo were enrolled. Between 2010 and 2017, laboratory data as well as baseline characteristics were collected. Firstly, these data were compared between RA and Vo, secondly, only in RA group, relationship between BMD and ASMI were analyzed for 7 years. [Results] Both BMD and ASMI decreased significantly over time for 7 years in both groups. Both BMD and ASMI of RA was always lower, however, there was no interaction between time and RA (p=0.194, 0.089; repeated measure ANOVA). In RA group, change of BMD from baseline (ΔBMD) was correlate positively with change of ASMI from baseline (ΔASMI) (r=0.331, p=0.023). Multiple regression analysis with ΔBMD as outcome variable and 13 factors of BL data as independent revealed that male gender and ASMI were related with ΔBMD independently (p=0.013, p=0.014). Other factors including disease activity were not related to ΔBMD. [Conclusion] BMD and ASMI correlated each other in RA patients.

W7-6

Analysis of dental lesions in rheumatoid arthritis patients with osteoporosis

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Conflict of interest: None

[Object] Dental examination was performed for risk assessment of osteonecrosis of the jaw (ONJ) in rheumatoid arthritis (RA) patients using antiresorptive agents and the relationship between dental lesions and disease activity of RA. [Methods] Thirty patients using antiresorptive agents with some dental complaints or in whom dental lesions had been detected were referred to a dentist. Survey items were dental lesions, X-ray findings, treatment after examination, and relationship between simple disease activity (SDAI) and dental lesions. [Results] Three patients had lost all teeth, nine had caries, and seven had apical lesions. There were 27 cases of periodontitis, which was mild in 12 cases, light to moderate in four cases, moderate in seven cases, and severe in four cases. Treatment after the dental visit consisted of seven cases of periodontal disease treatment, three of tooth extraction, and one of denture preparation. There were no significant relationships between periodontal disease, dental caries, apical lesions, and SDAI. [Conclusions] There are large numbers of untreated patients with symptomatic periodontal disease. Rheumatologists should also pay attention to dental lesions and strengthen collaboration with dentists.

W8-1

Clinical presentations of Behçet's disease depending on sex and age: data from Japanese nationwide survey

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Conflict of interest: Yes

[Object] To investigate effects of sex and onset age on clinical features in Behçet disease (BD). [Methods] We analyzed clinical manifestations of BD in age- and sex- specific subgroups in the database of 7950 BD patients who were newly registered to the Japanese Ministry of Health, Labour and Welfare, from 2003 to 2014. [Results] A total of 6627 patients who met the revised International Criteria for BD were analyzed (male 2651, female 3976m, age 39yo [IQR 31-50], disease duration 1 year [0-4]). Frequencies of ocular involvement and HLA-B51 were lower, and those of intestinal and neurological lesions were higher in this study compared with previous reports. Ocular lesion, arthritis, and vascular lesions were more frequent in elderly-registered patients, whereas genital ulceration, epididymitis, and oral ulceration were more common in younger patients. We found male predominance of ocular lesion except 70 yo or older subgroups and female predominance of genital ulcer during reproductive age. Sensitivity analysis using International Study Group criteria replicated the results. [Conclusions] This study showed that clinical phenotype in early phase of BD was different depending on onset age and sex.

W8-2

Subgrouping of patients with Behcet's disease by principal component analysis (PCA) based on clinical feature

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Conflict of interest: None

[Object] Patients with Behcet's disease (BD) present various clinical symptoms, with different disease outcomes. We performed subgrouping analysis in an attempt to predict treatment and prognosis of BD. [Methods] We performed principal component analysis (PCA) of 691 BD patients, most of them fulfilling the Japanese Ministry of Health, Labor and Welfare criteria (294 males and 397 females) in 7 hospitals from year 1991 to 2017. We analyzed patient's background and clinical symptom (including special type of BD) as a variable. [Results] PCA extracted three significant components; Group A (patients having eye or neurological lesions), group B (patients having vascular or intestinal lesions) and group C (patients without eye and special type of BD). When we compared the three groups, there ware significantly more men in Groups A and B and more women in Group C, more HLA-B51 positive cases in Groups A, more cases with biologics in group A and B by chi-square test. [Conclusions] We identified three distinct subgroups in BD with PCA analysis. To establish "precision medicine" of BD, further examination with larger registry is needed.

W8-3

Clinical features of Behcet's disease patients with joint symptoms

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Conflict of interest: None

[Object] Approximately 60% of Behcet's disease patients have joint symptoms. The present study aimed to clarify the clinical features of patients with Behcet's disease who have joint symptoms. [Methods] 16 cases of Behcet's disease patients with joint symptoms who had been treated at our hospital from 2007 to 2017 were analyzed retrospectively. We investigated clinical characteristics and treatments. [Results] The median age at onset of joint symptoms was 37.4 ± 6.2 years (Mean ± SD). 6 cases are men. Afflicted joints were the most common in knee joints, ankle joints and PIP joints followed. As initial treatment, steroids were administered at 80.0% of the cases, and improvement was confirmed at 80.0% of the cases receiving steroids administration. Improvement ratio was low in the group with dose of PSL less than 10 mg/day. The group using MTX and colchicine in combination prevented the recurrence of joint symptoms as compared with each monotherapy group. [Conclusions] These results indicate that PSL should be administered at a certain dose or higher for treating joint symptoms in acute phase of Behcet's disease. In addition, MTX has the effect of preventing recurrence of joint symptoms of Behcet's disease.

W8-4

A nation-wide survey of haploinsufficiency of A20 reveals the frequent coincidence of autoimmunity in Japan

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Conflict of interest: None

[Object] A20, encoded by the *TNFAIP3* gene, is a negative regulator of the tumor necrosis factor (TNF)-nuclear factor (NF)-kB signaling pathway. Recently, the haploinsufficiency of A20 (HA20) caused by heterozygous mutations in the *TNFAIP3* gene was identified to induce early onset autoinflammatory disease resembling Behçet disease In this study, we performed a multicenter survey investigating HA20 patients found in Japan. [Methods] We summarized the detailed clinical manifestations, genetic analyses and cytokine profiles of Japanese patients with HA20. [Results] A total 30 patients from 9 independent families were enrolled in this study. All identified mutations were evaluated to be functionally pathogenic by several *in vitro* assays. The production levels of proinflammatory cytokines were increased. The excess differentiation of Th17 cells with aging was observed. Intriguingly, not only autoinflammatory phenotypes but also several autoimmune disorders including psoriatic arthritis, Hashimoto's thyroiditis, Graves disease and autoimmune lymphoproliferative syndrome were observed. [Conclusions] Our study revealed unexpected variation in phenotypes of HA20. Therefore, we should be especially cautious of the onset of several autoimmune disorders.

W8-5

Immunophenotyping and gene expression analysis of PBMC subsets in Behcet's disease

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Conflict of interest: None

[Object] Behcet's disease (BD) is a chronic multisystem inflammatory disorder characterized by recurrent oral ulcers, ocular involvement, genital ulcers, and skin lesions, presenting with remissions and exacerbations. The pathogenesis of behcet's disease is largely unknown. We conducted immunophenotyping of peripheral blood mononuclear cells (PBMC) subsets and comprehensive gene expression analysis of each subset in order to elucidate which subsets crucially involved in the pathogenesis of BD. [Methods] Patients of BD (n=15) and healthy controls (HC; n=12) participated in the study. PBMC were isolated from blood samples, then analyzed by flow cytometry and sorted into 20 PBMC subsets. After RNA isolation and cDNA library preparation, RNA sequencing of each PBMC subset was performed. [Results] The frequency of Th17 cells within the population of CD4+ T cells was significantly increased in BD patients. As for gene expression analysis, larger number of differentially expressed genes was detected in Th17 subset than other subsets in BD patients compared to HC. [Conclusions] Findings of our current study indicated that Th17 played an important role in the pathophysiology of BD. Further analysis would enable us to approach the functionality of Th17 and its related subsets in BD.

W8-6

Identification of physical and psychosocial problems associated with patients with Behçet's disease with eye involvement

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Conflict of interest: None

[Object] This study aimed to identify physical and psychosocial problems for the patients with Behçet's disease (BD) having eye involvement by developing a checklist to assess problems in conformity to the International Classification of Functioning, Disability and Health (ICF). [Methods] Thirty patients with BD were interviewed by use of the original ICF Checklist (128 categories), from which they selected 79 categories related to physical and psychosocial aspects. Moreover, 13 categories were added by experts' discussion. Another 100 patients were questioned along these 92 categories. Odds ratios (OR) of the presence of problems were compared between the two groups of BD patients, with and without eye symptoms. [Results] Multivariate logistic regression models revealed that BD patients with eye symptoms found more difficulties in activities of daily living, namely, writing (OR 6.2), understanding nonverbal messages such as gestures and facial expressions (OR 14.0), walking (OR 3.7), moving (OR 4.0), and walking in intense sunlight and bright light (OR 16.0), compared to the latter. Two groups did not find any significant difference on physical problems. [Conclusions] In treatment, it is important to focused on their daily life for patients with BD with eye symptoms.

W9-1

Utility of the Systemic Lupus Activity Questionnaire (SLAQ) in the daily practice: correlation of SLAQ

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Conflict of interest: None

[Object] In the assessment of SLE, laboratory data and clinical findings have been focused but patient-reported outcomes which reflect more QoL are tended to be underestimated. The systemic Lupus Activity Questionnaire (SLAQ) is a multi-dimensional questionnaire and can measure lupus disease activity. Since 9/2017 we started SLAQ and SLEDAI-2K at every visit to assess comprehensively. [Methods] SLE patients were recruited between 9/12/2017 and 10/31/2017. We measured correlation between SLAQ and SLEDAI-2K scores by spearman's correlation. We analyzed the correlation in those who met lupus low disease activity state (LLDAS) or not. [Results] 113 patients were enrolled with 91% of female, average age (SD) of 44 (15) years, steroid user of 93%. SLAQ score were 5 [IQR: 2-7], SLEDAI-2K were 4 [IQR: 2-5] respectively. Among them 48% met LLDAS. The SLAQ score weakly correlated SLEDAI-2K (ρ=0.285, p=0.02). In those who met LLDAS, the good correlation was observed (ρ=0.413, p=0.002), whereas correlation was not shown in those who didn't meet LLDAS (ρ=0.156, p=0.238). [Conclusions] The original paper has not shown even the correlation between SLAQ and SLEDAI. Application of multi-dimensional questionnaire in daily practice may prompt more detection of clinically relevant signs and

symptoms.

W9-2

Association between pregnancy and chronic damage index in systemic lupus erythematosus

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Conflict of interest: None

[Object] 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 309 enrolled patients, median age at registration was 44.1 years, median disease duration was 10.5 years, and median SDI score was 1. The SLE patients experienced pregnancy (n=139; 45.0%) exhibited older age (47.5 vs 37.6 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 139 patients had pregnancy, 36 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.

W9-3

A Prospective cohort study on the short and long-term prognosis, including pregnancy outcomes, of young patients with systemic lupus erythematosus in Japan (Pleasure-J study)

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Conflict of interest: Yes

[Object] Systemic lupus erythematosus occurs in young people. Although the prognosis is improving due to recent progression treatment, the problems of physical and mental cumulative damages or the decreased QOL was remaining. There are few studies that assessed the prognosis of young SLE patients. So, we started the registry of young SLE patients to create the evidence of the long-term prognosis in Japan. [Methods] The participants are new-onset SLE patients ranging in age from 6 to 40 years old. We will follow the patients for 10 years or longer. The main outcomes are death, flare, admission, QOL. Other collection dates are the disease activity (SLEDAI), damage (SLICC-DI), QOL (SF12, Lupus PRO) and blood test. If the patients become pregnant, the patients will register the pregnant cohort. The data will be collected from 60 Certified Educational Facilities of Japan College of Rheumatology. The registry will start from November 2017. [Results] This registry was approved by the ethics board on each working groups facilities. [Conclusions] The long-term young SLE registry start and was expected to create the high-quality evidence from Japan.

W9-4

Association between alcohol, smoking, and disease activity of systematic lupus erythematosus (the second report): cross sectional study

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Conflict of interest: None

[Objectives] We aimed to examine whether alcohol and smoking are associated with the disease activity of SLE. [Methods] The research design was cross-sectional study. 347 SLE patients who satisfied ACR criteria were targeted. They were registered in databases currently being constructed at Showa University Hospital and Okayama University Hospital. Patients divided into 4 groups; group1: smoking (-) alcohol (-), group2: smoking (+) alcohol (-), group3: smoking (-) alcohol (+), group4: smoking (+) alcohol (+). The main outcome was SLEDAI. The sub outcomes were CH50, anti ds-DNA antibody and SDI. The linear regression analysis was performed to analyze the association between smoke, alcohol and the disease activity. Confounding factors were sex, age, present corticosteroid dosage and present immunosuppressant use. [Results] The median age was 43 years old. 89% was female. The median corticosteroids dosage was 5mg. Immunosuppressant use was 62.2%. The median SLEDAI was 4. Group1 was 145/347. Group 2 was 25/347. Group 3 was 122/347. Group4 was 55/347. No significant difference was observed between the 4 groups in Kruskal Wallis test and no significant difference was observed in multiple regression analysis. [Conclusions] We did not show the association between smoking, alcohol and disease activity of SLE.

W9-5

Assessment of Health Related Quality of Life by the EQ-5D in Japanese Patients with Systemic Lupus Erythematosus: A Cross-sectional Study

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Conflict of interest: None

[Object] We aimed to cross-sectionally investigate the health-related quality of life (HRQoL) in Japanese patients with systemic lupus erythematosus (SLE) by EQ-5D, which is a standardized instrument developed as a measure of HRQoL that can be used in a wide range of health conditions and treatments and often used for cost-effectiveness analyses. **[Methods]** Japanese patients with SLE (n = 382) completed the EQ-5D and other related demographic questionnaires, and physicians simultaneously completed the SLE Disease Activity Index 2000 (SLEDAI-2K) and the Systemic Lupus International Collaborating Clinics Damage Index (SDI). **[Results]** The mean age, SLEDAI-2K score, and SDI score were 44.7 years, 2.4, and 0.6, respectively. The mean EQ-5D index score of the SLE patients was 0.855, which was significantly lower than the age- and sex-matched national norm score, 0.922. EQ-5D index scores were collated with the physical, mental, and role component summary scores of the SF-36 (r = 0.68, 0.24, and 0.40, respectively). EQ-5D index scores were inversely collated with age and the SDI scores (r = -0.28, -0.27), but

not with the SLEDAI-2K scores. **[Conclusions]** HRQoL measured by the EQ-5D was reduced in Japanese patients with SLE and associated with disease damage, rather than disease activity.

W9-6

Development of a quality indicator set for systemic lupus erythematosus in Japan

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Conflict of interest: None

[Objects] The aim of this study was to develop a quality indicator (QI) set systematically for Japanese SLE patients that we can evaluate easily using electronic health data. [Methods] We used a validated process that combined available scientific evidence and expert consensus to develop a QI set for SLE. First, we performed a literature review to retrieve all clinical practice guidelines (CPGs) and QI development studies. Second, we extracted the candidate QI items that can be evaluated using electronic health data. Third, we used a modification of the RAND/UCLA Appropriateness Method. [Results] We found 3621 articles through the initial search. Finally, 34 literatures were identified. We selected the remaining 12 indicators as the final QI set through the RAND/UCLA Appropriateness Method. The areas covered included assessment of disease activity, treatment, and drug toxicity monitoring. All the indicators can be measured by using existing electronic health data alone, without medical record review, and all are process indicators. [Conclusion] We identified 12 QIs for assessment of SLE patients based on administrative data. This study may contribute to the spread of QIs in the area of rheumatology in Japan.

W10-1

The prognosis of 64 Lupus nephritis (LN) patients in Kurashiki Central Hospital (KCH)

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Conflict of interest: None

[Object] LN is a major organ involvement of systemic lupus erythematosus and it often associate with poor prognosis. We evaluated patients of LN in KCH. [Methods] We retrospectively investigated 64 biopsy proved LN patients in KCH from January, 2006 to October, 2017. We examined sex, onset age, and long-term prognosis. We also investigated pathological assessment of kidney biopsy (based on ISN/RPS classification), treatments, and complete or partial remission (CR/PR) rate of selected 39 LN patients with sufficient laboratory and clinical data. [Results] Five- and ten-year survival rate of 64 LN patients (onset age 34.0±17.9 year old, 57 females) were both 98.4%. We pathologically classified 0 patient into class I, 3 into class II, 8 into class III, 11 into class IV, 6 into class III/IV+V, and 11 into class V. The patients of class III or IV achieve CR earlier than those of class III/IV+V or V. Thirty percent of LN patients were administered pulses of intravenous methylprednisolone (IVMP), and had a tendency to respond well. Patients treated intensive immunosuppressive therapy (IVCY, multi-target therapy, and high dose MMF) achieve CR earlier. [Conclusions] Long-term prognosis of LN patients were good. Early remission may inducted by adding IVMP and intensive immunosuppressive therapy.

W10-2

Improved outcome of lupus nephritis (LN): A single center retrospective cohort study

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Conflict of interest: Yes

[Object] To examine the outcome of LN in our facility. [Methods] Japanese patients (pts) who underwent first-time renal biopsy between 1976 and 2015 in our facility and were diagnosed with ISN/RPS Class III to V were analyzed. A primary endpoint was defined as doubling serum creatinine, end stage renal disease or death. Survival was calculated using Kaplan-Meier method. The proteinuric remission was defined as urine protein <0.5 g/gCr. [Results] 140 pts with median age of 34 years were included. Median observation period was 105 months. Class III (±V), 35 pts; IV (±V) 82 pts; pure V, 23 pts. The renal and life prognosis was significantly better after 2000 (89 pts) compared to before 2000 (51 pts, P=0.02). We further compared the outcome of 3 major initial treatments among pts with moderate to severe proteinuria (>2 g/gCr) at the renal biopsy: IVCY (8 pts), calcineurin inhibitors (18 pts) and multi-target therapy (MMF + tacrolimus, 17 pts), Proteinuric remission was achieved as follows: 12.5%, 50%, 76.5% at 6 months and 50%, 66.7%, 82.4% at 12 months, respectively. No pts with multi-target therapy reached primary endpoint, although there was no statistical significance for long-term prognosis among 3 treatments. [Conclusions] The prognosis of LN has been improved in recent years.

W10-3

Utility in combination of mycophenolate mofetil and taclolimus in treatment of lupus nephritis

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Conflict of interest: None

[Object] To assess the utility and safety profile of mycophenolate mofetil (MMF) and tacrolimus (Tac) combination therapy in lupus nephritis. [Methods] We retrospectively studied the patients with lupus nephritis who were administered MMF (n=29) with or without Tac, and assessed the utility and safety profile at 6 months after MMF initiation. Definition of responder was as follows: >50% decrease of proteinuria within 25% change of baseline serum creatinine level. [Results] Disease duration was longer and the proportion of recurrence case was higher in non-responder group. In addition, initiation dose of prednisolone (PSL) and the MMF dose at 3 months were significantly lower in non-responder group. Although the baseline SLEDAI was significantly higher in combi-

nation therapy (MMF + Tac) group, urine protein level decreased more rapidly in this group. Serious infection occurred in higher proportion in combination therapy group. [Conclusions] Factors associated to renal damage, including longer disease duration and recurrence of lupus nephritis, and factors associated to treatment intensity, such as PSL and MMF dose, influenced the efficacy. Although the combination therapy (MMF + Tac) showed rapid response, it seemed to be necessary to consider about incidence of serious infection.

W10-4

Long-term efficacy and safety of tacrolimus in patients with lupus nephritis

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Conflict of interest: None

[Objectives] The aim of this study was to reveal the long-term efficacy and safety of tacrolimus (TAC) in patients with lupus nephritis (LN). [Methods] The subjects of this study were 78 LN patients who received TAC from January 2007 to December 2015. We examined continuation rates, adverse effects, and the changes of eGFR, proteinuria, serum C3, serum anti-dsDNA levels and corticosteroid doses. [Results] Sixty-one patients had active LN and 57 did serological activity. The continuation rate at 1, 3, 5 and 10 years was 81.5, 74.2, 68.8 and 53.8%, respectively. Discontinuation for adverse events occurred in 12.8% of the patients. The serological markers remarkably improved and corticosteroid doses were reduced during the observation period. [Conclusion] TAC is a safe and effective drug for the long-term treatment of LN.

W10-5

Identification of Effective Predictors of Intravenous Cyclophosphamide and Mycophenolate Mofetil in the Selection of Induction Therapy for Lupus Nephritis

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Conflict of interest: None

[Object] This study aims to identify response predictors of IVCY and MMF, which are the primary induction therapies for LN. **[Methods]** We examined 29 patients with LN who received induction therapy (IVCY, 16; MMF, 13) from 1994 to 2015. Their baseline characteristics and the ratio of CR at week 24 were analyzed. **[Results]** At the baseline, the IVCY group demonstrated a longer time since the diagnosis of SLE and frequent flares than the MMF group; however, the differences observed were not statistically significant. Moreover, there was no difference in age, sex, complement levels, anti-dsDNA antibody titers, anti-Sm/RNP antibody positivity rates, proteinuria, and abnormality in urine sediment between both groups. Regarding patients with CR at 24 weeks, the univariate analysis revealed that in addition to a longer time since the diagnosis of SLE and frequent flares, the anti-RNP antibody positivity rate was higher (OR 8.15; $P = 0.07$) in the IVCY group than the MMF group. Furthermore, a significant difference was observed in the positivity rate of anti-RNP antibody (OR 6.09; $P = 0.03$) in the multivariate analysis. **[Conclusions]** Although IVCY and MMF are equivalent treatment options for LN, this study suggests that IVCY might be more effective for patients with the anti-RNP antibody.

W10-6

Adjunct treatment in patients with lupus nephritis

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Conflict of interest: None

[Object] To examine the impact of adjunct treatment on lupus nephritis (LN) [Methods] The study involved 32 consecutive patients diagnosed with active LN and treated with multitarget therapy. The following parameters were assessed at discharge and months 6 and 12: body weight, body mass index (BMI), daily salt intake level, blood pressure, HbA1c level, LDL-cholesterol level (LDL-C), and smoking status. The following outcome variables were assessed: urinary protein level, complete remission (CR), SLEDAI remission, and urine sediments. [Results] Each parameter such as body weight (51.5 kg, 53.7 kg, 54.0 kg), BMI (20.3, 21.2, 21.3), HbA1c (6.0%, 6.0%, 5.8%), LDL- C (135 mg / dL, 112 mg / dL, 103 mg / dL) remained favorable at discharge and months 6 and 12, respectively. Daily salt intake level at month 6 was associated with improvement of proteinuria at months 6 and 12. Blood pressure level at month 12 was associated with CR and SLEDAI remission at month 12. Patients who underwent dietary counselling guided with regular 24-hour urine collection showed higher remission rates, defined as the absence of active urine sediments. [Conclusions] Our results suggest that adjunct treatment may contribute to the improvement of long-term outcome in patients with LN.

W11-1

Treatment and clinical course of elderly onset rheumatoid arthritis

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Conflict of interest: None

[Object] To investigate the clinical course of patients with elderly onset rheumatoid arthritis (RA) at our hospital. [Methods] We compared the characteristics, treatment and response of 55 patients whose onset of RA was over 80 years old (elderly onset group: EO) with 119 patients at 40-59 years old (non-elderly onset group: NE) retrospectively. [Results] The mean DAS28-ESR (DAS) and HAQ at the diagnosis of EO were significantly higher than NE (4.91 vs 4.41, 1.2 vs 0.5). For the first treatment, in EO, 87.3% were treated by csDMARD, and none by MTX. The rate of PSL use was significantly higher than NE (56.4% vs 30.3%). Three months later, DAS and HAQ in PSL user significantly decreased more than those in non-PSL users (ΔDAS 2.55 vs 0.83, ΔHAQ 0.9 vs 0.3). One year later, the rate of MTX user in EO was significantly lower than those in NE (9.1% vs 78.1%), whereas the rate of bDMARDs was not different between two groups (11.4% vs 14.0%). HAQ in EO was significantly higher than that in NE, whereas DAS was similar in both groups. The infected patients were more in EO than in NE (5 vs 2patients). [Conclusion] For the patients with elderly onset RA, it is important to make a treatment strategy aiming at early functional recovery while avoiding the risk of infection and other complications.

W11-2

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

[Object] Of the treatment of rheumatoid arthritis (RA), biologic agent therapies are chosen, if disease activity remains moderate or high despite

csDMARDs therapy. We investigated the tendency to choose biologic agent 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 75 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 between TNF inhibiters and ABT. [Results] From 2005 to 2010, etarnercept (ETN) was used the most. After the advent of ABT, ABT was used the most. Drug continuation rates increased. In 2011-2014, concomitant MTX rate of TNFi (73.3) was higher than that of ABT (33.3). 2 years drug continuation rates due to adverse events; TNFi was 88.6%, and ABT 96.4%. [Conclusions] Increasing of drug continuation rates seemed for accumulation of experience.

W11-3

Efficacy and safety of biologics in the management of elderly onset RA patients

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Conflict of interest: None

[Object] Purpose of this study is to reveal efficacy and safety of biologics (BIO) in elderly onset RA (EORA) patients. [Methods] We retrospectively investigated medical records of 92 EORA patients, who had visited our hospital from April to August in 2017, and had been treated with biologics. [Results] Mean observation period was 66 months. Mean age was 68.5 years, female 58, RF-positive 71%, and anti-CCP antibody-positive 67% (antibody titer over 100 U/mL approximately 60%) at diagnosis. At the baseline, average DAS28-ESRCRP was 5.82, and HAQ-DI 1.50. Thirty patients was started to treat with BIO monotherapy, 14 received BIO by switching from csDMARDs, and 48 had BIO with csDMARDs. The number of patients who received each BIO were as follows: 9 IFX, 20 ETN, 10 ADA, 7 CZP, 12 GLM, 16 TCZ, and 18 ABT. The continuation rate of the first BIO was 35.9%. Reasons of BIO-cessation were remission in 20, adverse events in 19, insufficient response in 18 and patients hope in 2. Among 19 adverse events, 7 were infections, 5 were injection-site reaction, and 3 had malignancies. [Conclusions] Most EORA patients (approximately 60%) had high disease activity with high titer of anti-CCP. Although infection rate was high, 22 % of cases could stop BIO because of remission. BIO may be useful in EORA.

W11-4

The clinical investigations of elderly-onset rheumatoid arthritis (EORA) patients

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Conflict of interest: None

[Object] Our purpose is to clarify the therapeutic effect and safety of bDMARDs against EORA. [Methods] From 2008 to October 2017, the patients who newly onset RA and who had been treated for 3 years or more, were extracted from our patient database, and EORA cases were identified. The outcomes up to the third year after the beginning of treatment were retrospectively analyzed. Cases of developing severe complications of grade 2 or higher after the treatment, and a case of discontinuation of treatment related adverse events were taken as dropout examples. Comparison of treatment efficacy was performed with non-EORA and non-bDMARDs EORA group. [Results] There were 2,700 applicable cases in the observation period, and 1,420 cases were treated with more than 3 years. 64% of cases treated with immunosuppressive drugs in this period, 32% of cases receiving bDMARDs, 39% and 11.7% of EORA (176 cases). In EORA, the use frequency of golimumab was high in bDMARDs, and there was no significant difference in complications. However, as the age rises, the frequency of outpatient depression decreases, so statistical analysis was difficult at age over 80 years. [Conclusions] The bDMARDs treatment for EORA has been shown to be safe to administer until 80 years of age.

W11-5

Single center cohort study for better management of elderly onset RA

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Conflict of interest: None

[Object] Purpose of this study is to reveal clinical problems of elderly onset RA (EORA) patients for better management. [Methods] We retrospectively investigated medical records of EORA patients, who had visited our hospital from April to August in 2017. [Results] Mean observation period was 56 months. Median age was 68 years old, female 129, RF-positive 65.6%, anti-CCP antibody-positive 67.4% (antibody titer over 100 U/mL approximately 30%), and average CRP 3.2 mg/dL at the point of diagnosis. Respiratory complications were seen in 50 cases, including 28 interstitial lung disease, 9 COPD, and 4 non-tuberculous mycobacteriosis, 7 tuberculosis and 5 bronchiectasis. Other Complications were diabetes 18%, hypertension 40%, and hyperlipidemia 24%. Cerebrovascular and cardiovascular events had occurred in 10.4%, history of malignancy was seen in 14 and newly developed malignancy was seen in 15 cases. Corticosteroids were prescribed in 31%, csDMARDs 86%, and bDMARDs 43%. Infectious adverse event were occurred in 35 patients (16.5%). [Conclusions] RF/anti-CCP antibody positive rate was higher than previous reports. It is necessary to adjust anti-rheumatic therapy for poor prognostic cases, but the frequency of infection and malignancy was high in EORA patients.

W11-6

Elderly rheumatoid arthritis patients without ACPA positivity may have higher incidence rate of severe adverse events during abatacept treatment

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Conflict of interest: Yes

[Object] Abatacept has been considered to be relatively safe in rheumatoid arthritis patients, and it is often used in the elderly patients. However, we sometimes see patients with severe adverse event (AE) during abatacept treatment. We studied the predictive factors for discontinuation of abatacept due to AEs in elderly patients. [Methods] Participants were consecutive 195 RA patients older than 65 years treated with abatacept in the TBC Registry system. Multivariate Cox regression analysis was used to find predictive factors for, and Kaplan-Meier analysis was used to calculate cumulative incidence rate of discontinuation due to AEs. [Results] Mean age was 74.2, disease duration was 12.9 years, and DAS28-CRP score was 4.40. 84.6% of patients was anti-CCP antibody positive. Cumulative incidence of discontinuation due to AEs was 10% in 3 years. Cox regression analysis revealed that the anti-CCP antibody negative was an independent predictor for discontinuation due to AEs (HR: 14.0, p=0.001). Anti-CCP antibody negative group had higher discontinuation rate due to AEs compared to the positive group (44.0 vs 5.8%, p=0.036). [Conclusion] Elderly patients who are negative for anti-CCP antibody seemed to have high incidence rate of severe adverse events when treated with abatacept.

W12-1

The Difference in the Clinical Characteristics between Cytomegalovirus Disease and Asymptomatic Cytomegalovirus Reactivation in Rheumatic Diseases

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Conflict of interest: None

[Object] Cytomegalovirus (CMV) infection is one of the most common opportunistic infections in rheumatic diseases. The CMV antigenemia test becomes positive (CMV reactivation) regardless of the symptoms. The aim of this study was to determine the difference in the clinical characteristics between patients with symptomatic and asymptomatic reactivation in rheumatic diseases. [Methods] We retrospectively examined patients with CMV infection at our department, from 2008 to 2016. Patients positive for CMV reactivation were divided into two groups based on the symptoms they experienced, namely, CMV disease (with any symptoms) and asymptomatic CMV reactivation (without symptoms). The CMV antigenemia assay was used to assess the difference in the clinical characteristics between the two groups. [Results] In the multivariate analysis, the odds ratios are 8.82 (95% confidence interval (CI) 1.64-47.30, P value=0.01), 0.81 (95% CI 0.69-0.95, P value<0.01), and 1.26 (95% CI 1.05-1.50, P value=0.01) for oral candidiasis, serum albumin and CMV antigenemia count, respectively. [Conclusions] Patients with CMV reactivation who presented with hypoalbuminemia, oral candidiasis, and high CMV antigenemia count during the first positive diagnosis are highly at risk for CMV disease in rheumatic diseases.

W12-2

Clinical characteristics of cytomegalovirus reactivation in patients with rheumatic disease

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Conflict of interest: None

[Object] This study investigated risk factors for the reactivation of cytomegalovirus (CMV) infection among patients with rheumatic disease. [Methods] Between March 2012 and April 2016, 264 patients with CMV reactivation were enrolled in this study and divided into two groups: Group 1 patients had been initially treated for rheumatic diseases and group 2 patients for disease relapse. CMV reactivation in these two groups was analyzed. [Results] The mean patient age was 59.3 ± 18.4 years and 179 (67%) were female. Compared to patients without CMV reactivation, those with CMV reactivation were older (p=0.04) and had been treated with high-dose prednisolone (PSL) (p<0.01) or pulse methylprednisolone (p<0.01). In a multivariate analysis, CMV reactivation was associated with age (p<0.01) and the maximum PSL dose (p<0.01). Both the maximum PSL dose (p=0.02) and the platelet count (p<0.01) were significantly lower in patients treated for relapse than in those who had initially been treated. [Conclusions] Patient age and the maximum PSL dose may be risk factors for CMV reactivation. Among the patients treated for disease relapse, a low platelet count may be indicative of CMV reactivation.

W12-3

The risk factor of cytomegalovirus infection in rheumatic disease patients treated with moderate to high dose prednisolone

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Conflict of interest: None

[Object] To investigate risk factors of cytomegalovirus (CMV) infection in rheumatic disease (RD) patients treated with moderate to high dose prednisolone (PSL 0.5mg/kg/day). [Methods] Two hundred fifty-one patients who have treated with moderate to high dose PSL between January 2012 to October 2016 were enrolled. The clinical and laboratory data associated with onset of CMV infection within one year were analyzed. [Results] The underlying diseases were angiitis (n=65), SLE (n=63), PM/DM (n=41) and RA (n=27). Eighty-six patients were treated with pulsed methyl-PSL, 155 patients with immunosuppressive drugs. CMV antigenemia test was examined for 759 cases, 48 patients were diagnosed with CMV infection. The median interval to onset was 35.5 days. By ROC analysis, a level of $5/10^4$ WBCs was determined to be the optimal threshold value (sensitivity 87.2%, specificity 92.9%). Concomitant comorbidity of diabetes mellitus (odds raio 3.25) and low levels of serum albumin before the administration of PSL (odds raio 3.25) were identified as significant risk factors for CMV infection. [Conclusions] CMV antigenemia screening test may be important for RD patients treated with moderate to high dose PSL, especially in cases with concomitate diabetes mellitus and hypoalbuminemia at the treatment.

W12-4

Risk factors for cytomegalovirus (CMV) reactivation in patients with connective-tissue disease (CTD); single-center prospective cohort study

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Conflict of interest: None

[Object] To identify risk factors relevant with CMV reactivation in patients with CTD prospectively. [Methods] Consecutive CTD cases who started immunosuppressive therapy from February until October 2017 were enrolled. Serum CMV-IgG was screened before the induction therapy, and CMV pp65 antigen was subsequently monitored weekly. Risk factors for CMV reactivation were statistically analyzed. [Results] 45 cases were enrolled. Mean age was 60.2 y/o, and female was 31.1%. The underlying diseases were AAV 13, PM/DM 9, SLE 7, GCA 6, and others 11. The initial dose of PSL was 49.9 mg/day, and mPSL pulse was conducted in 9 (20.0%). Concomitant immunosuppressive therapies were IVCY 18, CNI 7, MMF 5, HCQ 3, TCZ 1, ABT 1, and RTX 1. No CMV reactivation occurred in 6 CMV-IgG negative cases. Among 39 CMV-IgG positive cases, CMV reactivated in 11 cases (28.8%), and CMV infection occurred in 1 cases (hematopoietic injury). CTD recurrence (p=0.022), mPSL pulse therapy (p=0.012), IVCY (p=0.001), and low lymphocyte count 1 week after treatment initiation (p<0.001) were significantly related with CMV reactivation. [Conclusions] While no CMV reactivation occurred in CMV-IgG negative cases, treatment regimen and low lymphocyte count were associated with CMV reactivation in CMV-IgG positive CTD cases.

W12-5

A Study of cytomegalovirus (CMV) reactivation following immunosuppression treatment for rheumatic diseases, comparison between non-serial and recurrent reactivation

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Conflict of interest: None

[Object] CMV reactivation following immunosuppression often becomes the problem. In some cases CMV disappears by antiviral treatment immediately but in other cases are recurrent. We retrospectively examined the differences between non-serial and recurrent reactivation. [Methods] We examined 30 cases that underwent antiviral treatment from 2016 to 2017. We diagnosed as the reactivation using CMV antigenemia (C7HRP) method. [Results] Non-serial group were 17, recurrent group were 13 patients. The maximum amount of glucocorticoids was average of 45 and 37 mg/day, the glucocorticoid pulse therapy was administered in 7 and 3 and the immunosuppressant was used simultaneously in 11 and 5 cases. Initial CMV+ cell count (/5 WBC) was 5.9 in non-serial, 3.5 in

recurrent group. A period to reactivation is for 44, 37 days, WBC counts/lymphocyte at the reactivation were 7850/1759/μl, 7907/859/μl, antiviral treatment were administered 18 and 13 days respectively. There were no significant differences between two groups. The median days until recurrence were 34 days. The lymphocyte count at the recurrense was significantly lower than that of non-serial groups (median 670 vs 1736) (P=0.003). [Conclusions] Prolonged low lyphocyte level was the risk of the recurrent reactivation.

W12-6

A study on 8 cases with EB virus positive treated with biologics

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Conflict of interest: None

Object Since Epstein-Barr virus (EBV) is related to lymphoproliferative disorder with the immunosuppressive therapy including methotrexate. Yet, recently it was reported that abatacept and tocilizumab would not increase the amount of EBV. Thus, the objective of this study was to examine the cases with EBV-Positive rheumatic disease patients treated with biologics in our department. *Methods* We observed 8 cases with EBV-DNA positive in the peripheral blood who were treated with etanercept (2), tocilizumab (1), or abatacept (5) from 2013 to 2016. EBV-DNA was measured by a real-time PCR method. *Results* Biologics were initiated in 5 out of 8 cases after the confirmation of its negative conversion, but in the remaining 3 biologics were initiated in spite of presence of EBV-DNA. Of the 5 cases, 1 case with tocilizumab developed EBV-associated lymphoma and tocilizumab was stopped. Three out of the 5 cases received biologics after more than 6 months-sustained negative results and maintained EBV-DNA negative. Of 3 cases with positive, 1 case with the highest amount of the virus DNA before the treatment initiation showed elevated DNA and biologics was discontinued. *Conclusions* Unlike the previous report, we presented that biologics may increase EBV load in patients with rheumatic disease.

W13-1

Otolaryngologic evakuation and prognosis of dysphagia in inflammatory myositis patients with positive anti-TIF1-gamma-antibody

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Conflict of interest: None

[Object] Inflammatory myositis with positive anti-TIF1-gamma antibody (ab) often complicates refractory dysphagia. The detail of otolaryngologic evaluation has not known. [Methods] This is a retrospective single center study. We included inflammatory myositis patients with dysphagia and those who had comprehensive nasopharyngolaryngoscopic evaluation by otolaryngologists between 1/2015 and 7/2017. [Results] Ten patients, age of 64.3 (12.0) were found; 3 of anti-TIF1-gamma, one each of anti-ARS, anti-MDA5, Anti-Mi2, and anti-RNP. Six patients complicated with advanced cancer (Stage 3/4); 3 of esophagus, one each of stomach, breast, and 2 ovary. All patients have abnormal otolaryngologic examination and eight patients required nutritional support therapy. All 3 TIF1-gamma-positive patients persisted to have severe dysphagia at 8 weeks, whereas 4 of 6 TIF1-gamma-negative patients improved dysphagia. [Conclusions] This case series with nasopharyngolaryngoscopic evaluation confirmed severe refractory dysphagia in inflammatory myositis patients with positive anti-TIF1-gamma antibody.

W13-2

In-vitro study of cytotoxic T lymphocyte-mediated muscle injury in polymyositis

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Conflict of interest: None

Objectives: Cytotoxic T lymphocytes (CTLs) play assumingly a crucial role in myoinjury of polymyositis (PM). Although the presence of CTLs in non-necrotic myofibers is hallmark histopathology of PM, the pathological significance of the CTLs is unclear. In addition, detailed mechanisms of the myoinjury by CTLs are poorly understood. The aims of this study are to clarify the pathological significance of CTLs in the myofibers and the mechanisms of cell death of myoblasts and myotubes. Methods: C2C12 cells were transfected with genes encoding MHC class I ($H2K^b$) and OVA peptide to generate myoblasts ($H2K^bOVA$-myoblasts) and were differentiated to myotubes ($H2K^bOVA$-myotubes). These cells were co-cultured with OT-I CTLs. Results: Analysis with time-lapse confocal microscopy revealed that OT-I CTLs invaded into $H2K^bOVA$-myotubes. The myotubes invaded by CTLs died earlier than uninvaded ones. OT-I CTLs lacking perforin1 or granzyme B did not show cytotoxicity against myoblasts but against myotubes. The mechanism of CTL-induced cell death was apoptosis in myoblasts and non-apoptosis in myotubes. Conclusions: Our *in vitro* model revealed that CTLs invade into myotubes and contribute to myoinjury. The patterns of CTL-induced cell death were different between myoblasts and myotubes.

W13-3

Pulmonary Cytokine production in Interstitial lung disease associated with myositis; ARS vs anti-MDA5 ab

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Conflict of interest: None

[Object] Interstitial lung disease (ILD) is a critical complication that determine prognosis. ILD is frequently developed in patients with ARS and a-MDA5 Ab. The clinical features are different between two types of ILD. To determine whether pulmonary cytokine production is different between 2 types, we performed analysis of cytokines in broncho-alveolar fluid (BALF). [Methods] Cytokine, ferritin, albumin levels in BALF from 10 ARS patients withILD and 6 a-MDA5 Ab+ patients were measured using multiplex cytokine array and ELISA. Cytokine and ferritin levels were adjusted albumin concentration. [Results] BALF IL-5, IL-6, IFN and IP-10 was elevated in patients with a-MDA5 Ab compared to ARS ones ($p<0.05$). IL-a, MCP-1 and ferritin levels had tendency to be higher in a-MDA5 Ab + patients than ARS ($P<0.1$). In this study, no difference was found in serum ferritin levels between two groups. [Conclusions] In the lung of a-MDA5 Ab patients, activation of type 1 IFN system and macrophage are found, which might contribute to the development of resistance to immunosuppressive therapy.

W13-4

Association between serum High-mobility Group Box 1 (HMGB1) and Polymyositis/Dermatomyositis

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Conflict of interest: None

[**Object**] Macrophage activation is likely involved in the pathomechanisms of polymyositis (PM)/dermatomyositis (DM). High-mobility group box 1 (HMGB1) is released from macrophages and acts as a inflammatory mediator. We aimed to study the association between serum HMGB1 and PM/DM. [**Methods**] We retrospectively measured serum HMGB1 levels in patients with PM/classic DM/clinically amyopathic DM (CADM) and healthy controls (HCs) using ELISA kits and compared them (n = 29, 11, 6, and 29, respectively). We also analyzed their association with clinical information. [**Results**] Mean serum HMGB1 levels in patients with PM/classic DM/CADM were significantly higher

than those in HCs (13.6 and 5.5 ng/mL, respectively; $p<0.001$). Mean serum HMGB1 levels in patients with PM and classic DM were significantly higher than those in patients with CADM (12.9, 19.3, and 6.6 ng/mL, respectively; $p<0.05$ in both comparisons). Mean serum HMGB1 levels in patients with anti-ARS antibodies were significantly higher than those in patients with anti-MDA5 antibodies and others (17.8, 8.8, and 7.3 ng/mL, respectively; $p<0.05$ in both comparisons). Serum HMGB1 levels decreased in 8 weeks post treatment (mean levels, from 14.2 to 6.2 ng/mL, $p<0.05$). [**Conclusions**] Association between serum HMGB1 and PM/DM was suggested.

W13-5

The clinical features and type 1 IFN signatures in dermatomyositis patients with anti MDA5 antibody

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Conflict of interest: Yes

[Object] We investigated the clinical features and type 1 IFN signatures of MDA5 antibody positive dermatomyositis (MDA5-DM) patients. [Methods] Thirty-eight patients with active inflammatory myositis were included into this study. All serum samples were obtained at the time of diagnosis. We divided these patients into three groups, anti-MDA5 Ab positive group (MDA5 group), anti-ARS Ab positive group (ARS group) and double negative group (DN group). Double positive patients were grouped into MDA5 group. [Results] MDA5 group had 15 patients (11 CADM and 4 DM), ARS group had 10 patients (3 DM, 2 CADM, 4 PM, 1 ILD only), and DN group had 13 patients (5 DM, 1 CADM and 7 PM). 12, 9 and 2 of them had ILD respectively. MDA5 group had significantly higher serum type 1 IFN activities ($p<0.0001$), and had lower WBC ($p<0.001$) and complement C3 ($p<0.05$) than other groups. 9 of MDA5 group, 1 of ARS group, and 1 of DN group were treated with the triple combination therapy. 5, 1 and 1 of them respectively deceased during the 3.2±3.7 years follow-ups. [Conclusions] MDA5-DM showed the different clinical phenotypes from those of other groups, and showed the different serum profiles in type 1 IFN signature and complement. These factors may associate with the etiology of MDA5-DM.

W13-6

IFN gamma induces PD-L1 expression in lymph nodes and muscles in a mouse model of polymyositis

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Conflict of interest: None

[Object] Peripheral Th1 cells, which produce IFNγ, are decreased in active polymyositis and dermatomyosits patients. IFNγ-/- mice (GKO) developed severer C protein-induced myositis (CIM), which is a mouse model of polymyositis, than wild type mice (WT). IFNγ induces the programmed death 1 ligand 1 (PD-L1) expression on tumor cells and inhibits the local immune reaction. Compared to WT, GKO exhibit enhanced antigen-specific cytotoxicity of CD8+ T cells as well as PD-L1-/- mice. Assuming that IFNγ induces the PD-L1 expression on muscles and immune cells, and plays a protective role in human and mouse myositis, we aimed to clarify the effect of IFNγ on the PD-L1 expression in CIM. [Methods] CIM was induced in GKO and WT. The PD-L1 expression on mononuclear cells from the spleen, lymph nodes (LNs), and muscles was quantitatively assessed with flow cytometry. Its localization in the muscle tissues was assessed with immunohistochemistry staining. [Results] The level of PD-L1 expression on macrophages, dendritic cells, and T and B cells from LNs and muscles was lower in GKO than in WT. PD-L1 was expressed on mononuclear cells and endomysium at the inflammation sites of the muscle tissues from WT, but not from GKO. [Conclusions] IFNγ induces the PD-L1 expression in LNs and muscles in CIM.

W14-1

The importance of ultrasound survey of the elbows of the patients with rheumatoid arthritis ~the survey of KURAMA cohort~

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Conflict of interest: None

[Object] Evaluation of elbows in patients with rheumatoid arthritis (RA) tended to be underestimated and there were few studies about survey of elbows with ultrasound (US) in RA patients. In this study, we aimed to evaluate the association between US scores of elbows and functional score in RA patients. [Methods] We recruited 95 RA patients in remission from KURAMA cohort and performed US survey of elbows. We evaluated their elbow function by questionnaire, and then analyzed the correlation between US score of elbows and functional scores. [Results] Among 95 RA patients, 4 patients (4.2%) had synovitis in elbows by physical examination, but 40 patients (42.1%) had synovitis with US survey. There were weak positive correlations between US score of elbows and HAQ ($p=0.04$) and PREE (Patient-rated Elbow Evaluation) score ($p=0.04$). In particular, there was a positive correlation between US scores of elbows and PREE-F ($p=0.02$), which is a score of daily activity of elbows. [Conclusions] We found synovitis of elbows in nearly half of RA patients in remission. There were positive correlations between US scores of elbows and HAQ or PREE. If there is a synovitis with US in RA patients in remission, treatment enhancement may lead to improvement of their ADL.

W14-2

Association between joint regions with ultrasound-determined synovitis and systemic inflammatory markers

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Conflict of interest: None

Objective We analyzed the association between joint regions with ultrasound-determined synovitis and systemic inflammatory markers. **Methods** We enrolled 152 patients with untreated arthritis and performed musculoskeletal ultrasound on 40 joints and determined a semiquantitative grade for power Doppler (PD) signals. We analyzed the associations between PD scores in 8 joint regions and CRP/MMP-3 levels using multiple linear regression models with forced entry method. **Results** Mean age was 55 years and 112 patients were female. Median CRP and MMP-3 were 0.36 and 65.7. Median total PD score was 2. Standard regression coefficients for 8 joint regions were -0.009 for MCPs, 0.05 for PIPs, 0.372 for wrists, 0.183 for elbows, 0.628 for shoulders, 0.377 for knees, 0.261 for ankles, and -0.0131 for MTPs in a regression model to explain CRP using PD scores as dependent variables. Standard regression coefficients for the same joint regions were -5.134, -4.449, 24.061, 27.839, 22.508, 64.108, 36.501, and 2.539 to explain MMP-3. **Conclusion** Systemic inflammatory markers such as CRP and MMP-3 do not accurately reflect the inflammation in small joints. Conversely, it is necessary to weight the large joints for the global ultrasound synovitis score to represent the severity of systemic inflammation.

W14-3

The comparison of the ultrasonographic findings between intravenous administration and subcutaneous injection of Tocilizumab

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Conflict of interest: Yes

[Object] There are two administration routes for tocilizumab (TCZ), intravenous administration (IV) or subcutaneous injection (SC), in patients with rheumatoid arthritis (RA). We compared ultrasonographic synovial findings between two administration routes for TCZ. [Methods] Total 76 patients who treated TCZ, 27 patients in IV group and 49 patients in SC group, were included in this cross-sectional study. Ultrasonographic examination was performed in MCP, PIP, wrist and MTP joints and finger flexor tendon and wrist extensor tendon. The gray scale (GS) and power Doppler (PD) findings were assessed by the semi-quantitative method (0-3). GS score and PD score (both 0-156 points) were defined as the sum total of each score. [Results] Clinically, DAS 28-ESR improved from 5.3 at baseline to 2.4 at ultrasonographic examination in IV group, and it improved from 5.2 to 2.8 in SC group. US findings were not significantly differenced in both groups, GS score: 11.7 vs 10.9, PD score: 5.3 vs 5.7, max PD grade: 1.3 vs 1.4 in IV and SC respectively. [Conclusions] Ultrasonographic findings between IV and SC of TCZ were not significantly differenced. Both administration routes of TCZ are effective for the treatment in patients with RA.

W14-4

Prospective Study of Bio-Free Remission Maintenance Using Ultrasonography in Rheumatoid Arthritis Patients: 52-Week Result

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Conflict of interest: None

[Object] After obtaining low disease activity (LDA) by administration of adalimumab (ADA) and MTX, we investigated the usefulness of joint ultrasonography (US) in RA patients who discontinued ADA in a multicenter prospective study. [Methods] Thirty one patients in sustained LDA for 6 months with ADA and MTX were enrolled. According to the patient's request, patients were divided into ADA discontinuation group (19 cases) and continuation group (12 cases), and in the discontinuation group, comparison was made between the relapse group and the non-relapse group. US examined at 38 joints including toes. Modified Total Sharp Score (mTSS) was evaluated. Correlation between various clinical indicators or integral value of US score and ΔmTSS was examined. [Results] DAS28-ESR at the baseline was not significantly different between the relapse group and the non-relapse group. Although US total score was increasing in the relapse group, it was not significant. mTSS progression was found in 2 cases, and a signal on the US was observed at the joints where bone erosion advanced. However, the integral value of US score was not correlated to ΔmTSS. [Conclusions] US provided limited value as a tool to predict both clinical relapse and radiographical progression in RA patients who discontinued ADA.

W14-5

Analysis of patients who discontinued Biologics in imaging remission (echo remission) ~ Is it possible to stop Biologics if echo remission? ~

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Conflict of interest: None

[Object] We analyzed the prognosis when stopping the biologics in imaging remission. [Methods] In 969 cases of biologics administration, 50 cases were able to analyze joint echo before and after discontinuation, among which 21 cases were with echo remission. Definition of echo remission was set to power doppler grade 0 in all 22 joints of fingers and wrist joints. [Results] Patient background was 16 women out of 21 patients. Age 52.5 years, observation period after discontinuation was 12 months. 16 out of 21 patients (76%) maintained echogenic remission after discontinuation of biologics, and 5 cases relapsed. There was no significant difference in various factors in comparison between groups. In remission maintenance group, DMARDs (MTX 12, SASP 1) were used in 13 cases, and MTX was used in 4 cases in relapse group. [Conclusions] When stopping the biologics in echo remission, it was possible to maintain echo remission after discontinuation with high probability. When achieving echo remission, it is reasonable to consider the choice to consider discontinuing biologics. The reason why there was no significant difference compared with the relapse group was considered to be due to the small number of cases in the relapsed group. It seems that accumulation of future cases is necessary.

W14-6

Automated classification of rheumatoid arthritis on ultrasonography using deep learning

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Conflict of interest: None

[Object] In this work, we developed a deep learning convolutional neural network algorithm for classification of ultrasound images on rheumatoid arthritis patients. To obtain a large amount of teacher images from few cases, teacher images were created using moving images. Our aim is to confirm the validity of these teacher images. [Methods] Ultrasound images were acquired from the wrist and finger joint of rheumatoid arthritis patients. Five hundred ultrasound images in 72 patients were used as conventional group. Five hundred ultrasound images in 5 patients were used as movie based group, and two thousand ultrasound images were used as long movie group. Labeling of normal blood vessel, synovial blood vessel (grade 1,2,3) was done manually. We constructed deep neural network using Convolutional Neural Network (CNN) in matlab (Mathworks, MA, USA) programming environment. We investigated the correct answer rate of these groups. [Results] The correct answer rate of conventional group, movie based group and long movie based group were 68±14%, 62±17% and 69±16%. An error rate of grade1, grade2 and grade3 were 23±18%, 32±19% and 45±17%. [Conclusions] Performance of deep learning is improved by using movie image even in few cases.

W15-1

The diagnostic performance of temporal artery biopsy (TAB) in Japanese patients with giant cell arteritis

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Conflict of interest: None

[Object] To investigate sensitivity and specificity of TAB for the diagnosis of giant cell arteritis (GCA) in Japanese patients. [Methods] To calculate sensitivity and specificity of TAB for the diagnosis of GCA, we performed a retrospective chart review with all the patients visiting our hospital during April 2009 and August 2017, who subsequently underwent TAB. We also confirmed the final diagnosis for the cases without GCA. [Results] TAB was performed in 24 cases (13 with GCA, 11 without GCA). The sensitivity of TAB for the diagnosis of GCA was 11 of 13 (85%). All the TAB specimens with positive results showed granulomatous arteritis with giant cells. One of the two false-negative cases was subsequently diagnosed with GCA from the TAB of other side, and another did not have any cranial symptoms but met the ACR criteria. None of the 11 cases without GCA showed vascular inflammation. The final diagnosis for them was as follows; fever of unknown etiology (3); polymyalgia rheumatica (2); and polyarteritis nodose, suspected histiocytosis X, lymphoma, nonarteritic ischemic optic neuropathy and unknown diagnosis (1 each). [Conclusions] The sensitivity and specificity of TAB was 85%, and 100%, similarly to those in western countries. The TAB is useful for the diagnosis of GCA in Japan.

W15-2

Clinical Features of Giant Cell Arteritis with or without Cranial Manifestations

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Conflict of interest: None

[Object] To compare the clinical characteristics and prognosis of giant cell arteritis (GCA) with cranial manifestations and those without. [Methods] We examined 25 GCA patients diagnosed in our hospital between April 2005 and September 2017 (mean age was 73.4±8.7 years and 19 were female) to identify clinical features and prognostic differences between patients with cranial manifestations and those without. [Results] 10 (40%) had intracranial manifestations (I-GCA group) and 15 (60%) had isolated extracranial manifestations (E-GCA group). Age at disease onset was older in I-GCA group (median 80 vs 69 years, p=0.03) and longer diagnostic delays were seen in E-GCA group (1.3 vs 4.0 months). I-GCA group had more temporal artery (80 vs 0 %, p<0.01) and vertebral artery (89 vs 20 %, p<0.01) involvement while E-GCA group had more aortic arch (33 vs 93 %, p<0.01) and descending aorta (44 vs 93 %, p=0.03) involvement. Initial steroid dose was higher in I-GCA group (median PSL 30 vs 20 mg, p<0.01). The relapse rate was 73/1000 patient-year in I-GCA group and 80/1000 patient-year in E-GCA group. There was no difference in the number of vascular events between two groups. [Conclusions] Our data suggests that GCA with cranial manifestations shows different clinical features from that without.

W15-3

Follow up study of color duplex ultrasonography in temporal arteries of 20 patients with giant cell arteritis

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Conflict of interest: None

[Objectives] It is reported that color doppler ultrasonography (CDU) of temporal arteries is useful as an examination of giant cell arteritis (GCA). We analyzed CDU and clinical features of patients with GCA retrospectively. [Methods] Analyze the CDU and clinical features of 20 patients with GCA hospitalized in our hospital from 2004 to July in 2017. [Results] Average age was 75.0 years old ±10.1. Male/female were 7/13. Time after starting treatment was 1579 days ± 1024. Nineteen patients met ACR classification criteria (1990) and one was diagnosed by temporal artery biopsy. Ultrasonographers and trained rheumatologists evaluated the CDU. Vessel wall thickness was measured in the thickest portion of parietal or frontal ramus of temporal arteries, where biopsy was often performed. Sixteen patients (80%) showed halo signs before treatment. They totally disappeared in six patients within six weeks, in 13 within five years. Average of vessel wall thickness significantly decreased from 0.65 mm to 0.32 mm after induction of remission (p=0.0001). Halo signs relapsed in one patient out of three on clinical relapse. The vessel wall thickness didn't increase in those who kept remission. [Conclusions] It was indicated that CDU is useful for evaluation of treatment effect and relapse of GCA.

W15-4

Diagnosis and treatment of giant cell arteritis and Takayasu arteritis (26 cases in single -center)

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Conflict of interest: None

[Object] We examine diagnosis and treatment for patients with giant cell arteritis (GCA) and Takayasu arteritis (TA). [Methods] We examined retrospectively about the dose of steroid, examination at the time of diagnosis, use of immunosuppressant and biological drugs in our patients with GCA (G) and TA (T). [Results] (G) were 13 members (1 male, 12 female), (T) were 13 (3 male, 10 female). The mean age was 76 ± 3.9years and 40 ± 20years, the mean initial dose of prednisolone (PSL) was 0.8 ± 0.2 mg / kg / day versus 0.8 ± 0.2, but no difference was observed. The maintenance dose was 5.4 ± 1.7 mg / day vs 13.5 ± 13.74. Patinets treated with PSL only were 8vs2, with PSL and immunosuppressant were 4vs2, and with Tocilizumab were 1vs2. 11 patients (G) were underwent temporal arterial echo, and all were positive. Temporal artery biopsy was performed in all cases and positive in all. In (T), carotid echo was performed in 12 patients, 11 were positive, CT was performed and positive in al cases. PET-CT was performed in 8, and 4 were positive. There were no deaths and blindness cases in (G), and 9 cases were relatively remission. 3 people died in (T), and 8 were relatively remission. [Conclusions] The prognosis was better in (G), and the maintenance dose of prednisolone was smaller.

W15-5

Complication and comorbidity of large vessel vasculitis

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Conflict of interest: None

[Object] Large vessel vasculitis (LVV) is the arteritis in aorta and its major branches, and classified into Takayasu arteritis (TAK) and giant cell arteritis (GCA). The aim of this study is to analyze complications and comorbidities of LVV. [Methods] 141 patients with LVV (GCA:11 cases) in our institution during 2008-2017 were enrolled to this study. The prevalence and clinical courses of complications and comorbidities were evaluated. [Results] Surgeries were undertaken in 38 patients (Aortic valve replacement, 13; aortic root substitution, 8; other valve replacement, 4; coronary artery graft, 4; percutaneous transluminal angioplasty of renal artery, 4). Although more than half of the former two surgeries were performed at the time of diagnosis, 13 cases were operated after more than 10 years. Comorbidities included ulcerative colitis (9 cases), sternoclavicular joint arthritis (3), osteomyelitis (2), uveitis (2), and amyloidosis (1). Most of these comorbidities preceded LVV for about a few years. [Conclusions] More than one-fourth of LVV patients were undergone surgery, indicating the needs for early detection and sufficient treatments. LVV shares some comorbidities with spondyloarthropathy, sug-

gesting similar pathomechanisms among these diseases.

W15-6

Identification of Risk Factors for Recurrence in Polymyalgia Rheumatica

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Conflict of interest: None

[Object] To identify risk factors for reccurence in patients with polymyalgia Rheumatica (PMR). [Methods] Cox proportional hazards regression analysis was performed 76 patients with PMR who had been treated by2015 EULAR/ACR recommendations between January2015 and October 2017 in our center. [Results] On univariate analysis, 6 variables were identified as significant risk factors affecting PMR recurrence: elevated ESR (P=0.0453), high CRP (P=0.03), high γ-GT (P=0.0059), increased platelets (P=0.0138), high IgA (P=0.048), arthralgia/myalgia limited to shoulders and hips (P=0.0109), and the maximum dose of prednisolone used (P=0.0059). These 7 variables were introduced into the multivariate analysis, and the following 2 variables were retained as independent significant risk factors: the maximum dose of prednisolone (P<0.01) and limitation of arthralgia/myalgia to shoulders and hips (P<0.05). [Conclusions] These results indicate that the initial dose of prednisolone and the absence of peripheral joint pains may be associated with the recurrence in PMR patients.

W16-1

Clinical characteristics of ANCA-associated vasculitis in children

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Conflict of interest: None

Background There are many unknown points in childhood onset ANCA-associated vasculitis. **Objective** To clarify the clinical features of ANCA-associated vasculitis in children. **Methods** The patients with ANCA-associated vasculitis were included, who came to our hospital from April 2006 to Oct 2017. Symptoms and laboratory findings at the onset of these patients were examined. **Results** In total,7 children (1 boy and 6 girls) were enrolled. The number of patients with granulomatosis with polyangiitis (GPA) and microscopic polyangiitis was 2 and 5, respectively. The age of disease at onset was 12.0 (7.5-13.5) years. The periods until diagnosis was 11.0 (3.5-15.5) months. The most common initial symptoms were school urinalysis in three cases. Next, fever, fatigue, and edema of the lower extremity as were seen in 2 patients respectively. The organ lesion was kidney in five patients. Four patients had lung lesions concomitantly. Five patients had crescentic glomerulonephritis in their kidney biopsy. In fluorescent staining, lesions of pauci-immune type were recognized in all six patients. Two patients had end-stage renal failure, but there were no deaths. **Conclusion** Pediatric patients with ANCA-associated vasculitis never had a good prognosis including cases discovered by school urinalysis at initial stage.

W16-2

Consideration of rituximab administered to ANCA-associated vasculitis in our hospital

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Conflict of interest: None

[Object] ANCA-associated vasculitis (AAV) is a disease that complicates various organ lesions and follows a fatal course. AAV patients have been treated with corticosteroids and cyclophosphamide (CY) as remission induction therapy. Recently, rituximab (RTX) has attracted attention as one of treatment options. However, there are some discussion about selection criteria of RTX, maintenance therapy and adverse events. We examined AAV patients treated with RTX at our facility. [Methods] We enrolled 8 patients using RTX for patients with AAV under treatment at our hospital and compared their patient profiles. [Results] The mean age was 70.75 years old (2 men and 6 females, MPA 5 cases and GPA 3 cases). As an organ lesion, there were 2 cases of only kidney lesion, 2 cases of only lung lesion, 4 cases with multiple lesion, and the mean BVAS was 11.75. There were 5 cases of initial remission induction, 3 cases of re-induction of remission, and 2 cases of re-induction were combined with immunosuppressant including oral CY. As reasons for selection of RTX, 2 cases due to cytopenia. [Conclusions] We suggested RTX therapy for AAV as reinduction therapy for refractory cases and as an initial remission induction considering complications.

W16-3

Over a year or more after rituximab treatment for patients with refractory or relapsed ANCA-related vasculitis

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Conflict of interest: None

[Purpose] We retrospectively analyzed 15 cases which more than 1 year passed since introduction of rituximab (RTX) therapy for refractory or relapsed ANCA-related vasculitis (AAV). [Patients] Patients were 27-81 years old, two men and thirteen women. Diagnosis was 10 cases of Granulomatosis with Polyangitis (GPA), 3 cases of Microscopic Polyangitis (MPA), 2 cases of Eosinophilic Granulomatosis with Polyangitis (EGPA). Maintenance therapy after RTX administration, a patient was received PSL alone, other were received immunosuppressant (4 cases of cyclosporin, 5 cases of tacrolimus, 6 cases of azathioprine, 1 case of methotrexate). [Result] They received treatment with RTX (375mg/m2/week two or four times), and the lesion of AAV was improved. All patients were successfully reduced PSL. Although some complications [brain abscess (n=1), Pneumocystis jiroveci pneumonia (n=3), herpes zoster (n=2)] were occurred after the initiation of RTX. [Conclusions] After remission induction therapy with RTX for refractory or recurrent ANCA-related vasculitis, there was few cases with relapsed vasculitis. All cases were able to reliably reduce PSL in maintaining remission at low dose.

W16-4

Clinical investigation of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) in our department-Third report

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Conflict of interest: None

Objective: We investigated the relationship between clinical features and treatment responses and outcomes in AAV, especially microscopic polyangiitis (MPA). Subjects and Methods: This was a retrospective study of 75 AAV patients, who were hospitalized in our department over the past 7 years. Results: The 5-year survival rate with MPA is 79%. In three of our patients with MPA, intravenous cyclophosphamide (IVCY) was given for alveolar hemorrhage, but there were no cases in which it was done to target interstitial pneumonia (IP). Eight of 9 MPA patients who died had pulmonary lesions, and the cause of death in 7 was pulmonary infection. There were 36 patients with MPA for which remission induction therapy was used for the first time. Remission induction was unsuccessful in 2 of 4 patients in the initial therapy. These 2 patients had

motor nerve lesions of long duration and residual foot drop. The 2 patients in whom remission induction was successful despite motor nerve impairments had nerve lesions of short duration, and their motor nerve impairments improved. Discussion: In MPA, it is thought that IP may affect vital prognosis because of lung infection. Nerve damage in MPA suggests that early treatment may be involved in remission induction and improvement of nerve damage.

W16-5

Long-term renal outcome in pulmonary-limited microscopic polyangiitis

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Conflict of interest: None

[Object] To investigate long-term renal outcome of pulmonary-limited microscopic polyangiitis (MPA). [Methods] We retrospectively examined the patients who met the MPA diagnostic criteria and received induction therapy. We divided them into 3 groups, pulmonary renal, renal-limited and pulmonary-limited MPA and evaluated estimated glomerular filtration rate (eGFR) for 5 years. [Results] Twenty-five patients with pulmonary renal, 28 with renal-limited, and 19 with pulmonary-limited type were enrolled. At baseline, significantly higher eGFR, lower incidence of active sediment, lower BVAS, and lower titer of MPO-ANCA were observed in pulmonary-limited type comparing with other types ($p<0.01$, $p<0.01$, $p<0.01$, $p=0.02$). The eGFR of patients with pulmonary renal and renal-limited types was significantly improved ($p=0.01$, $p=0.03$) whereas that of pulmonary-limited was deteriorated ($p=0.05$), resulting no difference of eGFR at year 5 in all types comparison. By multivariate analysis, eGFR at baseline was independently associated with the deterioration of renal function (OR4.4, 95%CI 2.70-6.65, $p=0.01$). [Conclusions] Renal outcome of pulmonary limited MPA was not significantly different from that of pulmonary renal and renal-limited MPA for 5 years observation.

W16-6

Clinical characteristics of antineutrophil cytoplasmic antibody-associated vasculitis complicated with pneumomediastinum

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Conflict of interest: None

Background: Vasculitis is thought to be one of the causes of pneumomediastinum, however, few cases of antineutrophil cytoplasmic antibody-associated vasculitis (AAV) with pneumomediastinum have been reported. Object: This study aimed to characterize AAV complicated with pneumomediastinum. Methods: We retrospectively collected hospitalized cases in our department from April 2016 to September 2017. We analyzed medical records and collected microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA) based on diagnostic criteria of Ministry of Health, Labor and Welfare. Results: Thirty AAV (24 MPA, 6 GPA) cases were analyzed. Fourteen cases were admitted by new-onset and recurrence. These cases needed initiation or increase of glucocorticoid (GC). Other 15 cases were hospitalized for treating complications. The other case was hospitalized for evaluation of MPA. Three patients developed pneumomediastinum during their hospitalization. All of them were MPA with interstitial pneumonia (IP). Two of them were new-onset, the other was recurrent, treated with remission induction therapy. Pneumomediastinum was complicated within one month from initiation or increase of GC. Conclusion: Treatment and activity of AAV with IP may be associated with development of pneumomediastinum.

W17-1

Diagnostic rate of autoinflammatory diseases evaluated by fever pattern in cases over 16 years of onset age

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Conflict of interest: None

[Object] To investigate diagnostic rate of autoinflammatory diseases (AID) by fever pattern. [Methods] Final diagnosis of the patients over 16 years of onset age with polymorphisms of AID responsible genes analyzed from 2005 to 2016 in our institute was evaluated by fever pattern with information of clinical manifestations and course. [Results] All 87 individuals (onset:16~64 (median 30.5) years of age, Male: Female=27:60) were classified into following four groups: 1. Periodic fever (n=27, 31%), 2. Recurrent fever lacking of regular period (n=41, 47%), 3. Persistent fever of unknown origin (n=11, 13%), 4. No fever, but with probable manifestations of AID (n=8, 9%). Diagnostic rate of AID in Groups 1 and 2 was 10/27 (37%) including FMF (n=9) and PFAPA (n=1), 7/41 (17%) including FMF (n=5), CAPS (n=1), and TRAPS (n=1), respectively. No one was diagnosed as AID in Group 3 and 4. However, 4 cases in Group 4 had AID associated arthropathy. [Conclusions] Diagnostic rate of AID was low overall, but mostly identified in patients with periodic fever. Some clinically probable AID cases lacking responsible gene polymorphisms were identified. Prudent clinical differential diagnosis as well as genetic test is important.

W17-2

Diagnostic rate of autoinflammatory diseases evaluated by fever pattern in cases under 16 years of onset age

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Conflict of interest: None

[Object] To investigate diagnostic rate of autoinflammatory diseases (AID) by fever pattern. [Methods] Final diagnosis of the patients under 16 years of onset age with polymorphisms of AID responsible genes analyzed from 2005 to 2016 in our institute was evaluated by fever pattern with information of clinical manifestations and course. [Results] All 140 individuals (onset: 0.3~15 (median 5.0) years of age, Boys: Girls=79:61) were classified into following four groups: 1. Periodic fever (n=72, 51%), 2. Recurrent fever lacking of regular period (n=47, 34%), 3. Persistent fever of unknown origin (n=12, 9%), 4. No fever, but with probable manifestations of AID (n=9, 6%). Diagnostic rate of AID in Groups 1 and 2 was 50/72 (69%) including PFAPA (n=33) and FMF (n=17), 14/47 (30%) including CAPS (n=6), FMF (n=3), TRAPS (n=3), PAPA (n=1), and PFAPA (n=1), respectively. No one was diagnosed as AID in Group 3 and 4. [Conclusions] Diagnostic rate of AID vary by fever pattern and mostly identified in patients with periodic fever. Evaluating effectiveness of colchicine, cimetidine and glucocorticoids during the attack was necessary in diagnosing atypical FMF and PFAPA in cases with polymorphism in non-exon 10 of *MEFV*.

W17-3

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 inflammation that occurs in the absence of pathogenic autoantibodies, autoreactive T lymphocytes or other infective causes. Autoinflammatory syndrome is known to be important for the differential diagnosis of unknown fever. Methods: We examined the responsible genes including *MEFV*, *TNFRS-*

F1A, *NLRP3*, *MVK*, *NOD2*, *IL1RN*, *NLRP12*, *PSTPIP1*, *PSMB8*, *NLRC4*, and *PLCG2* in the genomic DNA derived from 213 patients with unknown fever using the next-generation sequencer (MiSeq). Results: 1) We diagnosed as FMF (M694I) in 9 patients (4.2%) and detected another *MEFV* mutations, such as E84K, R202Q, E225K, R304R, R354Q, P369S, and R408Q in 55 patients (25.8%). 2) We identified *TNFRSF1A* mutations, such as T61I and V125M in 6 patients. 3) We identified the less than 1% of frequency of mutations derived from East Asia healthy individuals in 10, 5, 8, 5, 3, and 1 location of *NLRP3*, *NOD2*, *NLRP12*, *PSTPIP1*, *NLRC4*, and *PLCG2*, respectively, in the patients with unknown fever. Finally, we diagnosed as TRAPS and CAPS in 3 and 1 patients, respectively. Conclusions: These exhaustive analyses suggest that we could find the *MEFV* mutations from 11 responsible genes derived from autoinflammatory syndromes in 30.0% of the patients with unknown fever.

W17-4

Secondary failure to infliximab in ADA2 deficiency: a case report

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Conflict of interest: None

[Introduction] The deficiency of Adenosine deaminase 2 (ADA2) is an autoinflammatory disease caused by autosomal recessive mutation in the *CECR1* gene. The clinical features are fever, livedo reticularis, and early-onset lacuna infarction. Although there is no established treatment, anti-TNF-α therapy is considered to be effective. Here we describe an infant with ADA2 deficiency, who developed secondary failure to infliximab (IFX) by anti-drug antibodies. [Case] A 4-month-old girl was admitted because of fever, erythema, and elevated CRP levels. The patient was diagnosed with ADA2 deficiency because of mutations in the *CECR1* gene and decreased ADA2 activity. Disease was well controlled with IFX 5 mg/kg/8 weeks and PSL. At one year and six months, fever recurred accompanied by the low blood IFX level and the elevated anti-drug antibody titer. IFX was switched to adalimumab with methotrexate (MTX). The patient remained symptom-free for 2 months with adalimumab and PSL 0.05 mg/kg/day. [Discussion] To the best of knowledge, this is the first report of ADA2 deficiency with secondary IFX failure. In the treatment of ADA2 deficiency patient with IFX, addition of MTX might be considered for the prevention of anti-drug antibodies.

W17-5

Investigation of pathogenesis of Adult Onset Still's Disease by transcriptome analysis of each immune cell subset

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Conflict of interest: Yes

[Object] Adult onset Still's disease (AOSD) is a rare systemic inflammatory disease. Its pathogenesis is still unknown. We performed lymphocyte subset flowcytometry analysis and transcriptome analysis of AOSD patient's PBMC to explore the pathogenesis. [Methods] We recruited 17 AOSD patients (45.8±14.6 years old) from February 2002 to September 2017, who fully fulfilled the Yamaguchi's criteria. We sorted each lymphocyte subset of the patients or healthy controls (HC) (N=15, 55.6±15.3 years old) and performed RNA-seq analysis. [Results] Percentages of CD16 negative monocyte ($p < 0.001$), Tfh ($p < 0.005$), and CD8 positive T cell ($p < 0.05$) in the Pt's PBMC were significantly higher than in HC's. In the B cell subsets, Switched Memory B cell ($p < 0.01$), Plasmablast (PB) ($p < 0.005$) were also higher than in HC's. Only the percentage of Naïve B cell was lower than in HC's ($p < 0.005$). [Conclusions] Through our transcriptome analysis, not only innate immunity but also acquired immunity, especially B cells, suggested to be important for the pathogenesis of AOSD. Newly onset and the refractory cases tend to have more PB ratio. Any cytokine balance might affect AOSD's PB differentiation, or PB itself might be a key player as cytokine producer. It is required to accumulate newly onset cases in the future.

W17-6

Clinical research of Pustulosis Associated Osteoarthritis in our hospital

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Conflict of interest: None

[Object] Although pustulosis associated osteoarthritis (PAO) is a disease having osteoarthritic symptoms associated with palmoplantar pustulosis (PPP), its clinical findings are unclear. We examined the clinical findings of PAO outpatients in our hospital. [Methods] The subjects are 72 PPP patients with extra-articular symptoms who visited our department from 1978 to 2015 (24 males and 48 females). The average age at the initial examination was 52.9 years old, the mean onset age was 47.7 years old, and the average observation period was 30.3 months. We also examined the affected area of osteoarthritic lesions, onset of joint and skin eruption, hematologic findings, treatment contents and its effect. [Results] We observed 52 cases of precordial lesions (72%) as for the main joint symptoms. In terms of the onset of rash and osteoarthritis, rash preceded about 29 months on average. PSL and SASP tended to be used in combination with NSAIDs for cases with strong symptoms of joints or elevated inflammations. Only one case confirmed improvement of symptoms after tonsillectomy. [Conclusions] The precordial lesions were about 70% and the rash tended to precede the osteoarthritis. PSL and SASP tended to be used concomitantly for cases of strong symptoms or elevated inflammations.

W18-1

Clinical and radiographic features of respiratory symptoms associated with primary Sjogren's Syndrome in our hospital

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Conflict of interest: None

[Object] Primary Sjogren's syndrome (pSS) is often associated with various respiratory symptoms. The most typical manifestations are chronic interstitial lung disease and tracheobronchial disease. There are very little reports concerning about clinical and radiographic features of respiratory symptoms associated with pSS in Japan. We aimed to analyze clinical features and chest radiographic findings of respiratory symptoms associated with pSS using the database of our institution. [Methods] We retrospectively investigated pSS patients with respiratory symptoms registered in our database from Apr.1 in 2015 to Apr.1 in 2016. We surveyed clinical and radiographic features of pSS patients with respiratory symptoms. [Results] We confirmed 13 pSS patients with respiratory symptoms. Mean age was 69.2±6.5 years. As for radiographic findings, 7 cases were NSIP pattern and 2 cases were UIP pattern. Bronchiectasis were found in 7 cases, while 2 cases had multiple cystic lesions. 6 cases deteriorated radiographically and among them, both of 2 UIP pattern cases were included. [Conclusions] pSS is associated with various respiratory symptoms. Further investigations are required in which cases therapeutic interventions are necessary.

W18-2

Examination of the change of the salivation ability in ten years of Sjogren's syndrome

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Conflict of interest: None

Objectives: We evaluated a change of the saliva quantity in the SS patient who was able to do 10-year long-term observation in a gum examination. Methods: We examined 24 patients with SS that enforced minor salivary gland biopsy from 2005 through 2009 in our course, and all patients met Japanese or ACR/ EULAR criteria. and was able to chase as of July, 2017. It enforced a gum examination in the case mentioned above and measured a change of the quantity of saliva in ten years from a diagnosis. In addition, we examined clinical data. Result: As for the quantity of mean saliva at the time of the diagnosis, 6.56 ± 6.00ml/10min, ten years later were 7.91 ± 6.10ml/10min. Anti-SSB antibody-positive percentage was higher (18.75% VS 62.5%, $p<0.05$), and anti-centromere antibody (ACA)-positive rate was higher (18.75% VS 62.5%, $p<0.05$), and a serum IgG normalcy was higher (22% VS 75%, $p<0.05$) in the saliva decrease group than saliva increase group. On the other hand, the decrease in quantity of saliva did not relate to ESSDAI at the time of the diagnosis. Conclusion: We suggest that quantity of saliva of SS patients with anti-SSB antibody positive, ACA positive and normal IgG decrease.

W18-3

Clinicopathological characteristics of primary Sjögren's syndrome in the presence or absence of germinal-center like structures

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Conflict of interest: None

[Objectives] Few studies have clarified the clinical differences due to the presence of germinal-center like structures (GC) in patients with Sjögren's syndrome (SS). We compared the clinicopathological characteristics of patients with GC in our SS cohort. [Methods] We studied 25 patients with GC (GC+SS) and 78 patients without GC (GC-SS) who had undergone labial salivary gland biopsy. All SS patients met the Japanese and/or American College of Rheumatology criteria. We analyzed clinicopathological data of SS at diagnosis. [Results] No significant differences were seen in age, sex, laboratory data, EULAR Sjögren's Syndrome Disease Activity Index score, and treatment. The focus score [A1] was 4.43±3.70 in the GC+SS group and 2.27±1.75 in the GC-SS group ($p<0.001$). The incidence of malignant lymphoma in the GC+SS group was higher than that in the GC-SS group (12.0% vs 1.3%). [Conclusions] GC was found to be related to the incidence of malignant lymphoma in a Japanese SS cohort and should be evaluated routinely during clinical practice when treating patients with SS.

W18-4

Clinical features and prognosis of 56 patients with child-onset Sjogren syndrome in our hospital

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Conflict of interest: None

[Objective] To compare the clinical feature of child-onset Sjogren syndrome (SS) children with that of the adult-onset SS using the new guidance of juvenile SS diagnosis (juvenile criteria). [Methods] We retrospectively examined the diagnosis and the clinical features of child-onset SS patients less than 16 years old at the time of the first visit to our hospital from 1980 to 2017 based on medical records. We analyzed the validity of the juvenile criteria compared with the criteria of Ministry of Health and Welfare of Japan (adult criteria). [Results] Fifty-six patients were enrolled. Fifty-three cases met both criteria, 2 cases met adult criteria and "probable" in juvenile criteria, and one case diagnosed in juvenile criteria only. Twenty-six cases of secondary SS included SLE (69%), MCTD (15%) and RA/JIA (8%). Anti SS-A antibody was positive for 91% of patients. 61% of patients completed transition to internal medicine. Four patients experienced the pregnancy. A patient had a miscarriage, two patients had premature babies. No neonatal lupus was born. [Conclusions] Juvenile criteria enables the child who does not meet other criteria to be follow up. Pediatric rheumatologists need to inform the risk of neonatal lupus erythematosus to patients because of high positive SS-A antibody.

W18-5

Japanese Cardiac Neonatal Lupus Prevention Project: from a nationwide survey of cardiac neonatal lupus to an investigator-initiated clinical trial of hydroxychloroquine using telemedicine

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Conflict of interest: None

[Object] The recurrence rate of cardiac neonatal lupus (cardiac NL) in anti-SS-A antibody-positive mothers increases to 15-18%. HCQ was shown to be effective to prevent the recurrence of cardiac NL and a clinical trial is ongoing in the U.S. [Methods] First, we conducted a nationwide survey of cases of congenital complete heart block (CCHB) developed between 1/2006 and 12/2016 for 184 institutions. Second, we started a single-arm interventional study (J-PATCH) from 9/2017. Briefly, anti-SSA positive mothers with <=10 weeks pregnancy and a previous child with cardiac NL will receive 400mg/d of HCQ throughout pregnancy. Primary endpoint is advanced heart block (II or III). PI will exam patients and prescribe HCQ in cooperation with local experts. Participants can choose office visit or doctor's visit for the initial visit. Telemedicine will be used thereafter. [Results] There were 112 anti-SSA CCHB cases; 100 cases of survival, 8 cases of death after birth and 4 cases of in utero death, 78.5% case requiring pacemaker, 4 cases with previous child with cNL. We will report an update of J-PATCH in the meeting. [Conclusions] Conducting a clinical trial in pregnant women with rare diseases is extremely difficult but utilization of telemedicine may allow nationwide recruitment of patients.

W18-6

Examination of anti-aquaporin 4 antibody positive rate and anti-AQP4 antibody positive optic neuropathy complication rate in Sjogren's syndrome patients

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Conflict of interest: None

[Object] Anti-aquaporin (AQP) 4 antibody positive optic neuritis is refractory and recurrent optic neuritis, and its visual prognosis is poor. In recent years, studies on the relevance between anti-AQP4 antibody and Sjogren's syndrome (SjS) have been reported, but there are few reports and there are still many unknown points such as the frequency of complication. The aim of this study was to investigate the positive rate of anti-AQP4 antibody and the complication rate of optic neuritis in SjS patients. [Methods] The study involved 71 patients obtained consent for anti-AQP4 antibody measurement with SjS consisting of 7 male and 64 females patients with a mean age of 61.9±22.0 years. 44 patients had primary SjS and 27 patients had secondary SjS. [Results] The positive rate of anti-AQP4 antibody was 7.0% (5/71), and the complication rate of optic neuritis was 2.8% (2/71) in SjS patients. All cases with complicated optic neuritis had anti-AQP4 antibody. Furthermore, in the case of optic neuritic complications, the anti-AQP4 antibody titer was significantly

higher than the non-complication cases. [Conclusions] In SjS patients, there are a number of cases with anti-AQP4 antibodies. In the positive case of anti-AQP4 antibody, we should pay attention to the complication of optic neuritis.

W19-1

Mid-term clinical outcome of total hip arthroplasty for rheumatoid arthritis

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Conflict of interest: None

[Object] In recent years, total hip arthroplasty (THA) for rheumatoid arthritis (RA) has been decreasing. It is important to clarify the difference in clinical outcome of each model or fixed method in follow-up of RA patients after THA. [Methods] 59 patients of RA (86 hips) performed THA from March 1985 to October 2015. 41 patients were observable for more than 5 years. The average postoperative follow-up period was 8 years and 6 months. JOA score was used as clinical evaluation. The bone reaction of each fixed method was evaluated radiographically. [Results] The JOA score had improved from the preoperative average of 39.5 points to the average of 78.3 at the final follow-up period. Revision surgery due to aseptic loosening was performed on 4 hips in cemented THA and 2 hips in hybrid. In the cemented stem, the clear zone was confirmed on the proximal of the stem in 16 hips. In the cemenless stem, spot welds were observed on the proximal of the stem in 8 hips and rigid fixation was achieved. 3 hips recognized grade 3 stress shielding in the classification of Engh. [Conclusions] In the RA patients with good bone quality, it was considered that selection of proximal fit type cementless stem was effective. On the other hand, cemented stem was required careful observation.

W19-2

Long-term outcome of treatment with cementless total hip arthroplasty in patients with rheumatoid arthritis; Minimum 9-year results

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Conflict of interest: None

[Object] The aim of this study was to clarify the long-term clinical and radiographic results of cementless total hip arthroplasty (THA) for patients with rheumatoid arthritis (RA). [Methods] Forty-two total hip arthroplasties in 29 patients with a diagnosis of RA were performed from 2001 to 2008. Eight patients (fifteen hips) were lost to follow-up, leaving 27 joints of 21 patients for review at a mean 10-year follow-up after surgery. There were 3 men and 18 women with an average age of 58.8 years. The average follow-up period was 10.8 years. We evaluated the Japanese Orthopaedic Association (JOA) hip scores, radiographic changes and survivor rates of components. [Results] Two patients (3 hips) was infected from 3-year to 7-year after primary arthroplasty. The infected THA was performed one stage revision THA. An additional 1 patient (1 hip with MOM THA) was performed revision THA due to adverse reactions to metal debris. Except 4 revision hips, the mean preoperative JOA hip score of 41.0 improved significantly to 83.0 postoperatively at final follow-up. No femoral and acetabular components showed radiographic loosening, but one femoral and two acetabular components showed radiolucent line. [Conclusions] Cementless THA in patients with RA appears to be a promising treatment.

W19-3

The Fitting of the tapered wedge stem to the femoral canal in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] The purpose of this study was to evaluate the fitting of the tapered wedge stem to the femoral canal in patients with rheumatoid arthritis (RA). [Methods] Twenty RA patients underwent THA with the tapered wedge stem were included in this study (4 males, 16 females, average age 69.4 y.o). THA was performed for the destruction of hip joint in 12 patients and for femoral neck fracture in 8 patients. We used Taperloc in 8 patients and Microplasty in 12 patients. The JOA score for clinical evaluation, canal flare index (CFI), stem alignment and the type of stem fixation described by Nakata for radiographic evaluation, and intraoperative fracture and early subsidence of the tapered wedge stem as a complication were investigated. [Results] Mean JOA score elevated from 52.7 to 85.4 at the final follow-up (mean 28.9 months). Mean CFI was 3.63, stem was inserted 0.6°valgus in coronal plane and 5°flexion in sagittal plane. Stem fixation was achieved by ML-Fit in 12 cases, FLR-Fit in 3 cases, DIA-Fit in 2 cases, and MP-Fit in 3 cases. Femoral fracture during stem insertion was observed in one case as an intraoperative complication. [Conclusions] This study revealed that ideal fixation in accordance with the stem concept and good clinical results were obtained in many cases in RA patients.

W19-4

Change of Lumbar and Femoral Bone Mineral Density after THA in Rheumatic Arthritis Patients

Hyonmin Choe[1], Yutaka Inaba[1], Ken Kumagai[1], Shintaro Watanabe[1], Shunsuke Yamada[1], Michiaki Suzuki[1], Chika Ohsako[1], Naomi Kobayashi[1], Akiko Nagaoka[1], Yuichi Mochida[2], Kengo Harigane[2], Kagayaki Sahara[2], Tomoyuki Saito[1]
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Conflict of interest: None

[Object] We evaluated the change of lumbar and femoral bone mineral density (BMD) after Total hip arthroplasty (THA) in rheumatoid arthritis (RA) patients. [Methods] 23 RA patients (28 hips) who underwent THA and assessed BMD before and 1 year after THA were enrolled in this study. Medication for osteoporosis at the time of surgery and 1year after THA were noted. Change of lumbar and femoral BMD after THA were compared among RA patients with no medication, bisphosphonate, parathyroid hormone (PTH), vitamin D. [Results] Lumbar and femoral BMD were significantly decreased after THA, overall. Patients with no medication has significant reduction of BMD, whereas patients with bisphosphonate has significantly higher lumbar BMD and patients with PTH has significantly higher femoral BMD compared with patients with no medication. There was no difference between patients with no medication and vitamin D in change of BMD after THA. [Conclusions] BMD in RA patients were significantly decreased after THA. Medication for osteoporosis is necessary in RA patients after THA so that they can prevent the bone fragility fractures that may severely disable daily activity of patients.

W19-5

Which factor is related to nonunion after tibiotalocalcaneal arthrodesis for rheumatoid arthritis?

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Conflict of interest: None

[Object] This study was aimed to identify the risk factors for nonunion after tibiotalocalcaneal (TTC) arthrodesis with an intramedullary nail for rheumatoid arthritis (RA). [Methods] This study included 22 patients who underwent unilateral TTC arthrodesis with an intramedullary nail for RA. Three were male and 19 were female with an average age at surgery and follow-up periods of 63.1 years old (range, 44-79) and 53.0 months (range, 12-141), respectively. [Results] The tibiotalar nonunion rate was 0%, while the subtalar nonunion rate was 22.7% (five joints). Subtalar

curettage and longer timing of full weight bearing (FWB) after surgery significantly reduced nonunion in multivariate analysis ($P = 0.0352$ and $P = 0.0024$, respectively). The cut-off value for the timing of FWB for joint union was 35 days after surgery. [Conclusions] Nonunion rate in the subtalar joint after TTC arthrodesis was still high. Subtalar curettage and FWB at least 35 days after surgery are recommended for achieving joint union.

W19-6

Outcomes and tasks of total ankle arthroplasty for RA cases

Makoto Hirao[1], Kosuke Ebina[1], Yuki Etani[1], Akira Miyama[1], Atsushi Goshima[1], Hideki Tsuboi[2], Shigeyoshi Tsuji[3], Jun Hashimoto[3], Hideki Yoshikawa[1]
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Conflict of interest: None

[Object] Outcomes after total ankle arthroplasty (TAA) for rheumatoid arthritis (RA) cases were evaluated. The influences of biologic treatment on the outcomes after TAA were also evaluated. [Methods] TAA combined with additive techniques (augmentation of bone strength, control of soft tissue balance, adjustment of the loading axis) for rheumatoid arthritis (RA) cases were evaluated after mean follow-up period: 7.1 years. JSSF foot ankle, SAFE-Q scale was evaluated. Radiographic findings were also evaluated. [Results] This procedure significantly improved the clinical scores of the JSSF RA foot and ankle scales. Of 50 ankles, 48 had no revision TAA surgery. Prostheses sinking at the talus side was seen in 8 ankles; 2 required revision TAA. The social functioning score of the SAFE-Q scale at final follow-up was significantly higher in the biologic treatment group. The biologic treatment group showed a significantly lower dosage/usage of prednisolone, and disease activity at final follow-up. [Conclusions] TAA is recommended for the treatment of rheumatoid arthritis. The prevention of talar component subsidence remains a challenge in patients with the combination of subtalar fusion, rheumatoid arthritis, and higher social activity levels.

W20-1

The long-term outcome with more than 20 years of shortening oblique osteotomy at the metatarsal neck for the rheumatoid forefoot and the postoperative mid-hindfoot deformity

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Conflict of interest: None

[Object] Patients with rheumatoid arthritis sometimes require surgical reconstruction of MTP joint. Our center has performed shortening oblique osteotomy (SOO) at the metatarsal neck since 1985. We investigated patient satisfaction with SOO and the relevant factors among patients who could be followed up for more than 20 years. [Methods] The study population included 36 feet. The average age at the time of the operation was 45years and the average follow-up period was 25years. We checked the radiographic images of 14 feet for which preoperative and postoperative X-rays were available, as well as the clinical evaluations, and satisfaction questionnaire results related to 26 feet. [Results] Values of the HVA; 18°, the M1M2 angle; 3.5°, and the M1M5 angle; 4.3° were statistically significant improvement. The average overall satisfaction with the operation (assessed by a VAS [worst, 0 mm; best, 100 mm]) was 62. The item, which correlated to the satisfaction of SOO was condition of the foot at walking and the mid-hindfoot deformity score in the JSSF. The ratio of severe flat foot and loss of ankle motion were higher in the low-satisfaction group. [Conclusions] The state of the mid-hindfoot affects the results after SOO, and management of the whole foot is important.

W20-2

Short-term results of forefoot surgery in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To compare with joint-preserved and joint-resected arthroplasty for rheumatoid arthritis (RA) forefoot, and to evaluate underachievement factors. [Methods] We investigated some background factors, X-rays indexes, clinical scores and complications for 44 toes of 35 cases following up more than one year after the initial operation. 13 toes of ten cases were resected, and 31 toes of 25 cases were preserved. [Results] Preserved group showed better results in X-rays indexes and clinical scores. 4 cases of correction loss and 3 cases of callus recurrence were observed. Each item in SAFE-Q scores were better after a year in both groups. [Discussion] We experienced many cases in a short term. There is no report that examined toe-length difference between the next one. In the complication group, the shortening quantities of the 1 toe line and the 5 line were significantly less, and toe-length difference between 1 and 2 toe, and that between 4 and 5 toes were less too. [Conclusions] Preservated group was advantageous, and it is indicated that quantities of osteotomy and the toe-length difference between the adjacent toes are associated with postoperative results. Enough resection quantities in each toe are important for getting good result for the forefoot surgery in RA.

W20-3

Changes in radiological findings and plantar pressure following forefoot reconstructive surgery for patients with rheumatoid arthritis

Hyunho Lee[1,2], Hajime Ishikawa[1], Asami Abe[1], Yumi Nomura[1], Eriko Hasegawa[1], Chinatsu Takai[1], Daisuke Kobayashi[1], Hiroshi Otani[1], Satoshi Ito[1], Yasuaki Tokuhashi[2], Kiyoshi Nakazono[1], Akira Murasawa[1]
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Conflict of interest: None

[Object] To evaluate changes in radiological findings and plantar pressure after rheumatoid forefoot surgery with the patient's background. [Methods] Eighty-four feet in 60 patients with the age of 61.5 YO and the disease duration of 19.3 yrs. were evaluated. Peak pressure for plantar pressure, background characteristics for pain/general health -VAS, DAS28-ESR (DAS28), SDAI, JSSF scale, HAQ-DI, HVA, M1/2, M1/5, talocalcaneal angle, medial longitudinal arch, calcaneal pitch angle and lateral talo-first metatarsal angle were measured just before surgery and at one year after surgery. Distribution of peak pressure was measured in 9 sections. Maximum and minimum peak pressures and Δ pressure were also measured. [Results] There was no change in VAS, DAS28 or HAQ-DI. However, significant improvement was noted in SDAI and magnitude of pain, deformity and walking ability according to the JSSF scale. Significant reduction was also noted in HVA, M1/2 and M1/5. No change was found in radiograph data at either midfoot or hindfoot. Peak pressure at the 1st IP, 2nd-4th MTP, maximum peak pressure and Δ pressure decreased and minimum peak pressure increased significantly. [Conclusion] By the forefoot surgery for patients with RA, the transverse arch of the foot was restored and Δ pressure decreased.

W20-4

Comparison of plantar pressure before and after surgery of forefoot joint-preserving arthroplasty in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] The purpose of this study is to compare plantar pressure before and after surgery of forefoot joint-preserving arthroplasty in patients with RA. [Methods] The subject was 17 feet of 16 RA patients performed forefoot joint-preserving arthroplasty in our hospital from 2014 to 2016. Mean of the patients age was 62 years old, mean body weight was 48.1kg, mean disease duration was 19.1 years, and mean pre-operative DAS28 was 3.2. Walking plantar pressure was investigated by used F-scan DL. According to the ratio of the length from heel to toes, the whole of foot was divided into hindfoot (30%), midfoot (20%), forefoot (30%), and hallux (20%). The period of foot contact was divided into loading response phase, mid stance phase, terminal stance phase, and pre-swing phase. We investigated peak pressure and mean pressure in each phase before and 1 year after surgery. [Results] The peak pressure and mean pressure at hallux in pre-swing phase 1 year after surgery were significantly increased (P=0.005 and P=0.012, respectively). There were no significant differences in other walking phases in hallux. [Conclusions] After forefoot joint-preserving arthroplasty, the plantar pressure at hallux in pre-swing phase was significantly increased.

W20-5

A new radiographic grading system for the severity of dorsal subdislocation/dislocation of metatarsophalangeal joints relevant to the clinical symptoms

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Conflict of interest: None

[Object] To establish a new radiographic grading system to assess the severity of dorsal subdislocation/dislocation of lesser metatarsophalangeal (MTP) joints, and to examine the usefulness of this system. [Methods] We examined the radiographs of 172 toes of 36 patients with RA who underwent the joint-sparing surgery at the lesser MTP joints. MTP overlap distance (MOD) was determined as the distance between the end of metatarsal head and the base of proximal phalanx on the axis of metatarsal bone. ROC analysis was performed on MOD and callosities, and a grading system was created according to the degree of MOD. Subsequently, we evaluated 112 toes of 16 RA outpatients who do not require foot surgery, and examined the correlation with MOD grade and callosities and plantar pain, and examined inter-observer agreement. [Results] According to ROC analysis, MOD <0 mm was determined as grade 0, 0 ≦ MOD <5 mm as grade 1, 5 ≦ MOD <10 mm as grade 2 and MOD ≧ 10 mm as grade 3. In patients who did not require surgery, grade 3 was significantly accompanied by callosities or pain. The value of inter-observer agreement was 0.88, and Cohen's kappa coefficient was 0.74. [Conclusions] MOD was measured easily and MOD grade was able to evaluate each toe and reflected clinical findings.

W20-6

The examination of the cases that enforced re-operations after the forefoot operation in RA patients

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Conflict of interest: None

[Object] Our concept for correction of a forefoot deformity is to preserve the function of the metatarsophalangeal joint. We have performed the correction for hallus valgus with Swanson implant and a shotening oblique osteotomy of the metatarsal neck for forefoot deformity of the lateral toes. We were examined the cases that enfored some kind of re-operations after surgery. [Methods] 495 patients with RA were operated on from 1981 to 2016. The average age at operation was 60.2 year old (43 men, 452 women). The X rays evaluated the HV angle, M1-M5 angle and etc. [Results] The re-operation was performed to 76 patients. There were removal of Swanson implant (7cases). [Conclusions] It was thought that foot care was important including the infection prevention after the operation.

W21-1

Prognosis and causes of deaths of SLE patients of our institute during past 25 years

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Conflict of interest: Yes

[Object] We aim to know the prognosis and causes of deaths of our SLE patints during past 25 years. [Methods] We reviewed clinical data concerning prognosis of our patients from 1992 to July 2017. [Results] Total patients are 510 (61 males, average age 48.1). 5 year survival rate and 10 yeare survival rate at 1992 are 93.3% and 89.2%. 5 year survival rate and 10 yeare survival rate at 2006 are 95.6% and 92.7%. Total died patient are 54. The 1st cause of death is active SLE, 19 cases (35%). The 2nd and 3rd cause of death are active SLE with infection and malignant neoplasm, each 9 cases (17%). The 4th cause of death are infection, 6 cases (11%). There are 23 deaths until 2005 with 9 cases with active SLE. There are 31 deaths since 2006 with 10 cases with active SLE. [Conclusions] In our institute, prognosis of SLE patients since 2006 improved comparing with that until 2005. Most prominet causes of deaths are active SLE itself. Since 2006, death rate due to active SLE slightly decreased.

W21-2

The clinical feature of late-onset systemic lupus erythematosus

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Conflict of interest: None

[Object] Late-onset systemic lupus erythematosus (SLE) tend to present with atypical manifestations. In this study, we assessed the characteristic features of late-onset SLE in our hospital. [Methods] We collected the demographic, clinical and laboratory data at onset from SLE patients who visit our department from Apr. 2016 to Sep. 2017. We compared the data from late-onset SLE (≧50 years old at onset) with those from early-onset SLE (<50 years old at onset). [Results] A total of 223 SLE patients (30 late- and 193 early-onset SLE) were enrolled. Skin rash (30.0% vs 62.2%, p = 0.001) and anti-DNA seropositivity (67.9% vs 90.6%, p = 0.003) were less common in late-onset SLE while vasculitis occurred more frequently (10.0% vs 1.1%, p = 0.02) as compared to early-onset SLE. There were no significant difference in the female to male ratio (3.29 vs 5.03, p = 0.44), disease activity (SLEDAI; 13.8±11.5 vs 12.0±7.4, p = 0.41), pleuritis (20.0% vs 15.8%, p = 0.60), pericarditis (16.7% vs 7.03%, p = 0.15), arthritis (36.7% vs 49.7%, p = 0.24), and secondary Sjögren syndrome (13.3% vs 18.8%, p = 0.61) between them. [Conclusions] The results suggest that the pathological mechanism of late-onset SLE can differ from that of early-onset SLE.

W21-3

The change of immunosuppressive therapy for 194 cases of systemic lupus erythematosus from 2012 to 2017: Could the approval of hydroxychloroquine and mycophenolate mofetil have reduced the glucocorticoid dose?

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Haruka Takahashi[1,3], Yusuke Nakamichi[1], Shuhei Sano[1], Tatsuo Mori[1], Nanase Honda[1,2], Michiru Kina[1], Eisuke Takamasu[1], Kae Onishi[1], Takayasu Kise[1], Satoshi Watanuki[1,4], Yuji Miyoshi[1], Yoshiki Nagai[1,3], Shoji Sugii[1]
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Conflict of interest: None

[Objective] We reported the status of the immunosuppressive therapy for all systemic lupus erythematosus (SLE) cases in our department in the 57th meeting. Thereafter hydroxychloroquine (HCQ) and mycophenolate mofetil (MMF) have been approved in clinical practice of SLE in Japan. This study is performed to examine the change of the immunosuppressive therapy for SLE in the 5 years. [Methods] Clinical data in 2012 and 2017 were collected retrospectively from the medical records of 244 cases of SLE who were under management in our department on 1 Apr 2012. [Results] Of the 244 cases, 194 cases were still under management in our department. As for the 194 cases, female was 91%, age in 2012 was 48.0 ± 15.3 years old, disease duration in 2012 was 12.8 ± 10.4 years, SLEDAI score was 2.80 ± 2.64. Although the ratio of the cases on glucocorticoid was the same (86.1%), its dose was decreased (6.54 ± 6.91→5.35 ± 7.61 mgPSL/day). As for the ratio of the patients under other drugs, HCQ (3.1%→34.0%) and MMF (0.0%→4.6%) were significantly increased and tacrolimus was tended to be increased (12.4%→17.5%), mizoribine had a tendency of decreasing (10.3%→7.2%). [Conclusions] Clinical application of HCQ and MMF might reduce the dose of glucocorticoid in patients with SLE in Japan.

W21-4

The effectiveness of multitarget therapy for renal and non-renal manifestations of systemic lupus erythematosus

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Conflict of interest: None

[Object] To examine the impact of multitarget therapy on various manifestations of systemic lupus erythematosus (SLE). [Methods] Between 2009 and 2015, a total of 32 consecutive patients underwent kidney biopsy and were diagnosed with active lupus nephritis (LN). They were all given multitarget therapy and analyzed retrospectively. Relevant parameters including SLEDAI-2k criteria were assessed at baseline and months 6 and 12. [Results] At baseline and months 6 and 12, patients had the following manifestations: arthritis (53%, 0%, 3%), myositis (6%, 0%, 0%), active urine sediments (81%, 22%, 19%), proteinuria (97%, 25%, 6%), rash (31%, 6%, 9%), pleurisy/pericarditis (28%, 0%, 0%), low complement (75%, 25%, 19%), increased DNA binding (88%, 16%, 13%), fever (34%, 0%, 0%), thrombocytopenia (16%, 3%, 0%), and leukocytopenia (28%, 0%, 3%). Patients with NPSLE were excluded from the study because they were treated with another regimen using intravenous cyclophosphamide. [Conclusions] Our results suggest that multitarget treatment is highly effective in most patients with inflammatory or hematological manifestations. Some cases with discoid lupus erythematosus, active urine sediments, or serological activity remain unresolved, however, and additional strategies for these patients are required.

W21-5

Concentrations of mycophenolic acid in systemic rheumatic disease

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Conflict of interest: None

[Object] We analyzed concentrations of mycophenolic acid (MPA) in Japanese patients with systemic rheumatic diseases and investigated safety and correlation with efficacy or adverse events. [Methods] MPA concentrations of 16 patients (SLE 13, SSc 2, AAV 1) were analyzed retrospectively. [Results] Mycophenolic mofetil (MMF) doses were decided by each doctor according to the patients' conditions, ranged 500 to 3000mg. Median duration of treatment was 170 days, and median trough concentration was 1.95μg/ml (ranged 0.5 to 12.5μg). Some patients had high trough concentrations at early phase of treatment. Prednisolone was administered 29.3mg on average before the treatment. The dose was significantly reduced, and the diseases were also improved after the treatment. MMF was discontinued in only one patient because of a hematologic adverse event and renal impairment (eGFR 11ml/min, daily dose of 500mg, and trough concentrations ranged 1.1to 4.2μg/ml). Some other patients had loose stool. [Conclusions] MPA concentrations in Japanese patients showed similar level to past foreign reports, and MMF was used safely for a long time. Adverse events may have little correlation with trough concentrations, and we have to consider patients' conditions when deciding MMF dose.

W21-6

Remission and flare in patients with systemic lupus erythematosus (SLE)

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Conflict of interest: None

Aim: To clarify remission and flare in SLE patients. **Methods:** Patients were classified according to the DORIS definition, which consists of clinical or complete remission without prednisolone (ClinR or ComR), clinical or complete remission on treatment with 5 mg/day or less prednisolone (ClinROT or ComROT), and non-remission (NonR). **Results:** Cumulative total of 111 ClinROT, 35 ComROT, 65 NonR and 2 ClinR were observed in 83 patients during the observation of 24.7±8.6 years. Kaplan-meier cumulative remission rate at 2, 4, 6, 8, and 10 years were 86.4, 70.6, 53.8, 35.0, and 18.9%, respectively. At the final visit, 19 (23%) ClinROT and 21 (25%) ComROT were observed, that lasted 10.9±8.7 and 6.1±6.4 years, respectively. Although remission without prednisolone did not exist at the last visit, around half of ClinROT and ComROT had been taking 2.5 mg/day of prednisolone. NonR with 13.1±9.2 years of unremitted duration were 43 patients (52%) and 14 of them had never achieved remission. Unremitted duration was significantly longer than remitted one. SLEDAI, frequency of renal involvement, and SLICC/ACR damage index were significantly higher in 43 NonR than 40 remitted patients. **Conclusion:** Relapsing-remitting nature of SLE was clarified and steroid-free remission was hard to achieve.

W22-1

Evaluation of prediction factors for complete remission and life prognosis in lupus nephritis

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Conflict of interest: None

[Object] To evaluate the prediction factors for complete remission and life prognosis in lupus nephritis. [Methods]: Two hundred and one cases who underwent renal biopsy at our hospital and community hospitals from 1993 to 2016 were enrolled in this study. We retrospectively analyzed the complete remission rate at 12 months after therapy induction and evaluated the predictive factors for complete response and life prognosis. [Results]: In 181 cases, we were able to examine the therapeutic response and life prognosis at 12 months after therapy was introduced. Multivariate analysis showed that female gender, lower index of activity as assessed by the NIH histological scoring system, and the absence of podocyte foot process effacement as assessed by electron microscope were predictive factors for achieving complete remission at 12 months. Kaplan-Meier analysis showed that achieving a complete response at 12 months was correlated with better life prognosis. [Conclusions]: Our results suggested that the predictive factors for complete remission at 12 months after therapy induction were female gender, lower histological activity, and the absence of foot process effacement. Also, we found that complete remission at 12 months after the induction of therapy was related to life prognosis.

W22-2

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

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Conflict of interest: None

[Object] Our goal is to assess the correlation between renal pathology and clinical course of LN. [Methods] 60 patients with LN proven by renal biopsy from 2001 to 2017 were enrolled. We assess the correlation among clinical characteristics, laboratory data, and pathohistological findings. [Results] Female were 49. Mean age was 44.3±2.2 years old. According to ISN/RPS classification, I, II, III, IV, III/IV+V, and V were 3, 3, 13, 11, 26 and 4 cases, respectively. Intensive therapies included mPSL pulse therapy (50%), IVCY (20%) and oral immunosuppressants (48.3%). In all cases, oral PSL was administrated and the average of initial PSL dosage was 31.2±2.1 mg daily. After 1 year, 54 patients had remission, but 6 had poor prognosis. In LN III/IV+V and LN V, proteinuria levels were higher and ds DNA antibodies levels were lower than those in LN III/IV only. In LN III/IV+V, renal dysfunction tend to be severe and resistant to treatment. [Conclusions] In LN exhibiting LN V, severe proteinuria was observed. In LN III/IV+V, renal function and prognosis tended to be poor.

W22-3

The relevance of anti-ribosomal P / anti-dsDNA antibodies and the histological findings and remission rate of lupus nephritis

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Conflict of interest: None

Objectives: Anti-ribosomal P antibody (Anti-P) is frequently detected in patients with SLE. We investigated the relevance of anti-P/anti-dsDNA antibodies (anti-dsDNA) and the histological findings and remission rate of lupus nephritis (LN). **Methods:** Twenty-nine patients who were histologically diagnosed with LN in our hospital from 2005 to 2017 were evaluated. Anti-P was analyzed by an immunoblot assay using total ribosomal proteins of brine shrimp. Laboratory and histological findings and therapeutic response at 6 months were compared. **Results:** Six patients (20.7%) had anti-P, twenty (69.0%) had anti-dsDNA, five (17.2%) had both antibodies and eight (27.6%) had neither. Five patients having both antibodies were ISN/RPS Class III/IV±V, and one having anti-P only was Class V. The number of positive antibodies (0,1,2) were correlated with the extent of endocapillary proliferative glomerular lesions and the frequency of Class III/IV. Patients with both antibodies were associated with low complement at 6 months after the initiation of the treatment. **Conclusion:** Patients with anti-P and anti-dsDNA were associated with Class III/IV, endocapillary proliferative glomerular lesions, and low complement levels at 6 months after the initiation of the treatment.

W22-4

Clinical features and outcomes of podocyte injury in patients with lupus nephritis

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Conflict of interest: None

[Object] To clarify the occurrence of podocyte injury and its association with therapeutic response in patients with lupus nephritis (LN). [Methods] Consecutive patients with LN with available electronic microscopic findings in our institute were included. Patient characteristics and laboratory data and pathological classification were retrospectively collected and compared. [Results] 27 patients (22 female, mean age 43.7 years) were enrolled. The ISN/RPS classification of lupus nephritis were two (unclassified), one (class II), there (III), three (IV), nine (V), six (III+V), and three cases (IV+V). Two cases identified as lupus podocytopathy showed FSGS pattern. Foot process effacement (FGE) was observed in 18 cases (67%). During the mean observation period of 50.1 months, 19 patients (70%) achieved complete response (CR, urinary protein/urine creatinine ratio<0.5 mg/gCr or proteinuria by dipstick test <±). The rate of CR was significantly higher in the FGE positive group (83%) than in the FGE negative group (44%, p=0.04). The duration to CR achievement was also significantly shorter in the FGE positive group (median eight months vs two months, p=0.05). Two cases with lupus podocytopathy did not achieve CR. [Conclusions] The pathological type and FGE may be associated with renal prognosis in LN.

W22-5

The histological findings and renal prognosis in lupus nephritis: A cross-sectional analysis of the Yokohama City University Registry

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Conflict of interest: Yes

The histological findings and renal prognosis in lupus nephritis: A cross-sectional analysis of the Yokohama City University Registry. [Object] In lupus nephritis (LN), Class III and IV based on the ISN/RPS 2003 Classification have been shown to have poor renal prognosis. Here we investigated the association between pathological findings which are not assessed in the classification and renal prognosis. [Methods] LN patients who visited our department from April 2016 to September 2017 were enrolled in this cross-sectional study. We analyzed the associations between serum creatinine (Cre) level and histological findings of renal biopsy specimens, including tubulointerstitial involvement (TII) and thrombi. [Results] The biopsy specimens were classified into Class I/II/III/IV/V (6/10/44/62/7). TII and thrombi were found in 59.5% and 13.0%, respectively. In sera, lupus anticoagulant, anti-caldiolipin, anti-β2GPI and anti-SS-A antibodies were positive in 37.6%, 28.6%, 21.3% and 58.2%, respectively. Serum Cre levels in patients who had TII or thrombi were significantly higher than those in patients who did not (0.93 vs 0.69 mg/dL, $p < 0.01$, and 1.02 vs 0.79 mg/dL, $p < 0.05$). Serum Cre level was not related to the classification and anti-β2GPI and anti-SS-A seropositivity.

W22-6

Inflammatory cells in urine reflects renal pathological injuries in lupus nephritis

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Conflict of interest: None

[Objectives] To investigate whether urinary inflammatory cell analysis is useful to access renal pathological injury in lupus nephritis (LN). [Methods] 26 patients who had been diagnosed as LN and referred to Niigata University Medical and Dental Hospital between 2003 and 2017, were participated in this study. $CD3^+$ and $CD14^+$ cells were measured by urinary inflammatory cell analysis, and transcutaneous kidney biopsy was simultaneously performed. The number of $CD3^+$ and $CD14^+$ cells was compared with renal pathological findings, which were classified into ISN / RPS classification. The severity of these was scored from 0 to 4, and it was compared with the group where the total number of $CD3^+$ and $CD14^+$ cells was significantly increased (group positive, n = 12) and not (group negative, n = 14). [Results] The group positive contained 2 cases of type III and 10 cases of type IV, whereas the negative contained 6 cases of type III, 4 cases of type IV, and 4 cases of type V. The severity score of adhesion, endocapillary hypercellularity, cellular and fibrous crescent formation, duplication, and interstitial cell infiltration were significantly higher in the group positive than in the negative. [Conclusion] Urinary inflammatory cell analysis reflects actual renal pathological findings of LN.

W23-1

Expression of SLAMF6 and its functional significance in podocytes of lupus nephritis

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Conflict of interest: None

[Object] Lupus nephritis is one of the most serious manifestations of systemic lupus erythematosus (SLE). The alteration of the structural protein in podocytes is known as a mechanism of proteinuria in LN. It has been shown that the expression of signaling lymphocyte activation molecule family 6 (SLAMF6) is enhanced in CD4+T cells of SLE patients. We sought to examine the functional role of SLAMF6 in lupus podocytes. [Methods] We evaluated the co-expression of nephrin, a podocyte marker, and SLAMF6 in kidney of normal controls and LN patients, also in B6 and MRL/*lpr* mice. We analyzed the expression of SLAMF6 in podocytes and CD4+T cells of kidney and spleen in B6 and MRL/*lpr* mice by flowcytometry. We treated human podocytes with IgG from healthy individuals and LN patients, and analyzed the expression of SLAMF6 by real-time PCR. [Results] The expression of SLAMF6 was increased in nephrin positive cells from LN patients and MRL/*lpr* mice compared to control. Also, the SLAMF6 expression in CD4+ T cells increased in MRL/*lpr* mice compared to control. The level of SLAMF6 mRNA elevated in podocytes exposed to LN-derived IgG. [Conclusion] The expression of SLAMF6 is enhanced in LN podocytes, suggesting that the possibility of cooperating with CD4+T cells contributing to its dysfunction.

W23-2

Increased interferon-alpha production by myeloid cells upon activation of STING pathway in systemic lupus erythematous

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Conflict of interest: None

[Object] Type I interferon (IFN) contributes to the pathogenesis of systemic lupus erythematosus (SLE). Stimulator of interferon genes (STING) is a cytosolic DNA sensor located in the endoplasmic recticulum and mediates the production of type I interferon (IFN). We investigated STING pathway in myeloid cells from SLE patients. [Methods] Blood samples were obtained from healthy controls (HCs) and SLE patients. Peripheral blood mononuclear cells (PBMCs) were stimulated with a STING ligand, 2'3'-cGAMP. The expression of STING and the proportion of IFN-α-producing cells was investigated by intracellular staining and flow cytometory. [Results] The proportion of IFN-α producing cells was increased among monocytes, conventional dendritic cells (cDCs), and plasmacytoid dendritic cells (pDCs) from patients with SLE. The frequency of IFN-α producing cells were markedly increased in these myeloid cells from SLE patients with active disease. The expression of STING was sifnificantly increased in these cells in SLE patients compared with those in HCs. [Conclusions] These results suggests that the increased STING expression in myeloid cells is associated with their enhanced IFN-α production in SLE.

W23-3

Analysis of CD26-negative T cell subsets in the pathophysiology of steroid-resistant systemic lupus erythematosus

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Conflict of interest: None

[Object] CD26 is a T cell costimulatory molecule, 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 exhibited $CD28^{nega}CD57^+Perforin^{hi}Granzyme\ B^{hi}$ cytotoxic potential. SLE patients with a large number of these subsets 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. [Conclusions] Our data strongly suggest that $CD26^{nega}$ cytotoxic T cells are involved in the pathophysiology of steroid-resistant SLE. We are currently investigating whether these subsets are affected during active and subsequent inactive stages of SLE.

W23-4

Membrane vesicles in SLE sera induce type-I IFN via STING pathway

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Conflict of interest: None

[Object] 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 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. Thus we studied the role of STING in the production of IFN-I and IFN-I inducing factors in SLE sera. [Methods] We evaluated both the IFN-I bioactivity and the type-I IFN-inducing activity (IFN-I-IA) in SLE sera by using several different reporter cell lines. In order to study the involvement of STING, we established the STING-deficient reporter cell lines (STING-KO) using the CRISPR/Cas9 system. [Results] Serum-induced IFN-I-IA was higher in SLE than those in other autoimmune diseases or healthy controls. And the enhanced IFN-I-IA in SLE was reduced in STING-KO. Membrane vesicles from SLE sera also showed higher IFN-I-IA than healthy controls. [Conclusions] Our findings suggest that SLE sera have a potential to induce IFN-I production through STING and membrane vesicles seem to possess IFN-I-inducing activity.

W23-5

Hydroxychloroquine affects S100 proteins in systemic lupus erythematosus

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Conflict of interest: None

[Object] To reveal effects on S100A8 and S100A9 by HCQ and association with disease activity in SLE. [Methods] Serum levels of S100A8 and S100A9 were measured by ELISA in samples of SLE patients with HCQ treatment at time points of screening, 3 months and 6 months. Disease activity was scored according to SLENA-SLEDAI and CLASI. Immunologic activity was defined by the levels of C3, C4, CH50, anti-dsDNA body, white blood cells, lymphocytes and platelets. We demonstrated the effect on DAMPs and activation of THP-1 cell line by HCQ. [Results] We enrolled 64 patients. In 50 cases HCQ dose was based on ideal weight and in 14 cases by small dose. Improvement of immunologic activity related with HCQ dose. Regardless of HCQ dose, HCQ significantly lowered levels of S100A8 and S100A9. Elevated levels of S100A8 and S100A9 were seen in patients with photosensitivity and lupus nephritis (LN) and significantly lowered in LN patients. Levels of S100A8 and S100A9 associated with CLASI score. HCQ suppressed the activation of monocytes stimulated by LPS and levels of S100A8 and S100A9 in supernantants lowered. [Conclusions] HCQ lowered levels of S100A8 and S100A9 and might suppress disease activity. We suggested that HCQ may affect TLR 4 and suppress the activation of monocytes and expressions of DAMPs.

W23-6

Evaluation of trans-eQTL effects via alternative splicing of autoimmune disease susceptibility genes in human immune cells

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Conflict of interest: None

[Object] Although genome-wide association studies (GWAS) have identified many susceptibility loci for autoimmune diseases, the mechanisms of disease are yet unknown. Here, we evaluated biological significances of splicing QTL (sQTL) effects caused by disease susceptibility variants by integrating sQTL analysis, trans-eQTL analysis and existing GWAS results. [Methods] We collected peripheral blood from 105 healthy volunteers. RNA-seq data were obtained from FACS isolated 5 immune cell populations (B cells, $CD4^+$ T cells, $CD8^+$ T cells, Monocytes, NK cells). We quantified expression level using HISAT2 and Cufflinks. We conducted sQTL analysis by Matrix eQTL and trans-eQTL analysis by Sparse decomposition of arrays. Then, we integrated these results with GWAS catalog. [Results] Of 11,491 genes examined, 1,841 genes were identified as sQTL (FDR < 0.05). Among them, 67 sQTLs had GWAS SNPs in strong linkage disequilibrium ($r2 > 0.8$). It was revealed that SLE GWAS variant rs2764208 has an sQTL effect on SNRPC gene and enhances interferon related pathway as trans-eQTL effects. [Conclusions] GWAS variants having sQTL effects may be involved in disease by changing gene functions qualitatively, and their biological impact on the cells can be evaluated by their trans-eQTL effects on other genes.

W24-1

The role of lymph nodes in the induction of autoantibodies in lupus model mice

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Conflict of interest: None

[Object] To investigate the involvement of the lymph nodes (LNs) in autoantibody production, which is a crucial step in the development of autoimmune diseases by using model mouse of SLE. [Methods] Female New Zealand Black and white (NZBW) mice were used in this study. They are model mouse spontaneously developing lupus like nephritis with the appearance of anti-DNA antibody. Follicular helper T cell (TFH), plasma cell, germinal center (GC) of the LNs were evaluated by immunohistochemistry and flow cytometry. A comparison was made between young NZBW and NZBW which developed nephritis and became positive for urine protein. In order to exclude the involvement of the spleen, the same evaluation was carried out for NZBW who underwent splenectomy before onset. [Results] In the LNs, TFH, GC B cells and plasma cells increased. When lymphocytes in the LNs were cultured, it was shown that anti-DNA antibody was detected in the culture supernatant. In female splenectomized NZBW developed nephritis similarly to NZBW without splenectomy. [Conclusions] Although LNs have hardly been studied as organs to produce autoantibodies, the present study shows that autoantibodies are produced in the LNs, suggesting examination of the LNs is also necessary for understanding the mechanisms of autoimmune diseases.

W24-2

Synergistic enhancement of IL-6 production of human peripheral blood monocytes by anti-Sm and anti-RNP antibodies

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Conflict of interest: None

[Object] Anti-Sm antibodies have been found to be associated with neuropsychiatric manifestation in SLE (NPSLE). We examined the effects of anti-Sm on the expression of IL-6 in human monocytes to elucidate the roles of anti-Sm in NPSLE. [Methods] Highly purified peripheral blood monocytes obtained from healthy donors were cultured with monoclonal anti-Sm antibody (anti-Sm mAb), monoclonal anti-U1 RNP antibody (anti-RNP mAb) or control murine IgG1 or IgG3. After the various periods of incubation, IL-6 levels in the culture supernatants were measured by ELISA, and the expression of IL-6 mRNA was determined using RT-PCR. [Results] Both anti-Sm mAb and anti-RNP mAb significantly increased the IL-6 production of monocytes in a dose-dependent manner, although the latter was more potent than the former. Of note, anti-Sm mAb synergistically enhanced the production of IL-6 of human monocytes in the presence of anti-RNP mAb. Anti-Sm mAb significantly enhanced the expression of IL-6 mRNA in human monocytes in the pres-

ence of anti-RNP mAb (p=0.0212). [Conclusions] These results demonstrate that anti-Sm mAb and anti-RNP mAb synergistically upregulate the expression of IL-6 in human monocytes. The data suggest that anti-Sm might play an important role in BBB damages in NPSLE.

W24-3

Role of serum autoantibodies in blood brain barrier damages in neuropsychiatric systemic lupus erythematosus

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Conflict of interest: None

[Object] To elucidate the roles of serum autoantibodies in the development of blood-brain barrier (BBB) damages in neuropsychiatric systemic lupus erythematosus (NPSLE). [Methods] Paired serum and CSF samples were obtained from 101 NPSLE patients (69 patients with diffuse psychiatric/neuropsychological syndromes [diffuse NPSLE] and 32 patients with neurologic syndromes [focal NPSLE]). Serum anti-NR2 subunit of NMDA receptor (anti-NR2), anti-Sm, and anti-ribosomal P were measured by ELISA. Blood-brain barrier (BBB) function was evaluated by Q albumin (CSF/serum albumin quotient x 1,000). [Results] Q albumin was significantly higher in acute confusional state (ACS) than in non-ACS diffuse NPSLE or in focal NPSLE. Anti-Sm, but not anti-NR2 or anti-P, was significantly elevated in ACS compared with the other 2 groups of NPSLE. Multiple regression analysis confirmed the significant contribution of anti-Sm (p=0.0030), but not anti-NR2 (p=0.4687) or anti-P (p=0.2662), in the elevation of Q albumin. [Conclusions] These results confirm that the damages of BBB play a crucial role in the development of diffuse NPSLE, especially ACS. More importantly, the data demonstrate that serum anti-Sm might play a most important role in the disruption of BBB in NPSLE.

W24-4

The Influence of Various Autoantibodies for the Mortality of Long-term Prognosis in Patients with Diffuse Psychiatric/Neuropsychological Syndromes in Systemic Lupus Erythematous

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Conflict of interest: None

[Object] Neuropsychiatric manifestations in SLE (NPSLE) still remain one of the difficult complications and one of the factors that influence the long-term mortality in patients with NPSLE, especially diffuse psychiatric/neuropsychological syndromes (diffuse NPSLE), have not been fully elucidated. The aim of this study is to clarify the effects of various autoantibodies on the overall mortality in patients with diffuse NPSLE. [Methods] Forty-eight patients with diffuse NPSLE who had been admitted from 1992 to 2012 were exhaustively collected for the study. The medical charts were reviewed for various clinical parameters. The relationship of various serum autoantibodies with overall mortality was analyzed. [Results] Of 48 patients, 12 patients [25.0%] died during the observation periods (3280 ± 2243 days [mean ± SD]). The 5-year, 10-year, 15-year and 20-year mortality rates were 82.9%, 79.7%, 64.4% and 53.7%, respectively. Among various autoantibodies in the sera, the presence of anti-P at the onset of diffuse NPSLE, significantly decreased survival duration even on the multivariate analysis (RR 2.56, 95% CI 1.293-5.949, p=0.0006). [Conclusion] These results indicate that the presence of anti-P in the sera is a significant risk factor for the poor prognosis of diffuse NPSLE.

W24-5

Results of Safety and Efficacy of Belimumab 200mg SC in the Japanese SLE patients: Results of the Japanese population from the BEL112341 Pivotal Phase III, Randomized, Placebo-controlled Study of Belimumab in Patients with Systemic Lupus Erythematosus

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Conflict of interest: Yes

[Object] BEL112341 (NCT01484496) assessed the efficacy and safety of belimumab (BEL) compared to placebo (PBO), both added to standard of care therapy over 52 wks in SLE patients. [Methods] 839 SLE subjects were randomized to BEL (559) and PBO (280), whose age ≧18 yrs with a SELENA SLEDAI (SS) score of ≧8, were to be dosed weekly through W51, with a final evaluation at W52. The primary endpoint was the SLE responder index response rate at W52. [Results] The response rate was significantly higher for BEL [340/554 (61.4%)] compared with PBO [135/279 (48.4%)] [OR: 1.68 (95%CI: 1.25-2.25), p=0.0006]. The results in the Japanese (JP) was higher for PBO [12/16 (75.0%)] compared with BEL [7/13 (53.8%)]. But the OR with model adjustment to stratification factors including SS at baseline was 1.02. The safety profile in BEL was generally favorable and similar to that of PBO in the Overall and JP. [Conclusions] The efficacy and safety results in BEL112341 were similar to that in BEL IV studies; no new safety issues are identified. The response rate in JP may have been contributed by the small sample size, enrollment not to be stratified by country and imbalance in disease activity including SS between BEL and PBO. The safety profile was similar between the JP and Overall. GSK funded this study.

W24-6

Effects of Belimumab on Disease Activity Across Multiple Organ Domains in North East Asian Patients with SLE: Phase III trial (BEL113750)

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Conflict of interest: Yes

[Object] Organ manifestation domain score improvement was assessed with Intravenous (IV) belimumab (BEL) plus standard SLE care (SoC) in active, autoantibody-positive SLE. [Methods] BEL113750 (NCT01345253) was 52-week trial of BEL 10mg/kg or placebo (PBO), plus SoC, in patients with SLE with SELENA SLEDAI (SS) ≧8. The primary-endpoint was the SLE Responder Index at W52. The improvement was defined as a reduction in SS domain score or BILAG improvement by at least 1 category on domain score from BL to W52. Worsening was also assessed for all domains. [Results] MITT population comprised 677 patients. SS organ system involvement at BL were similar for both treatment groups, with immunologic, mucocutaneous, musculoskeletal and renal domains most prominent. Statistically significant improvements were observed at W52 in treatment differences vs PBO for the SS immunologic (14.93%), musculoskeletal (19.43%), and renal (20.74%) domains. Improvement in favour of BEL were observed on general, mucocutaneous, musculoskeletal and hematology domains of BILAG. No statistically significant differences in worsening for any domains. [Conclusions] BEL improved disease activity in multiple organ domains such as immunologic, musculoskeletal, mucocutaneous and renal domains. GSK funded this study.

W25-1

Quantitative and functional changes of CCR6+ type3 innate lymphoid cells in murine collagen-induced arthritis

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Conflict of interest: None

[Object] Innate lymphoid cells (ILCs) are a group of lymphocytes that lack antigen-specific receptors. ILCs are classified into three subsets, based on their patterns of cytokine production. ILC3s produce Th17 cytokines, which play critical roles in inflammatory arthritis. In this study, we tried to evaluate the ILCs in collagen induced arthritis (CIA) model mice, in order to clarify the role of ILC3s in the development of rheumatoid arthritis (RA). [Methods] We isolated ILCs from peripheral blood, local lymph nodes and joints in normal and CIA model mice by flow cytometry. We compared the absolute cell number, the polarization and gene expressions levels of the cytokines of each ILC subsets in normal and CIA mice. In addition, we measured the relationships between the frequency of ILC subsets in synovial fluid (SF) and clinical parameters of 23 RA patients. [Results] The gene expression levels of Th17 cytokines in CCR6+ILCs were elevated after the induction of arthritis, in addition to the skew toward CCR6+ILC3s in joints. The proportion of CCR6+ILC3s in SF had increased in some RA patients and had the positive correlation with swollen joint count and tender joint count. [Conclusions] CCR6+ILC3 may play some roles in pathogenesis of RA through its production of cytokines.

W25-2

Role of Sphingosine-1-phosphate receptor 3 (S1P3) signaling in collagen-induced arthritis (CIA)

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Conflict of interest: None

[Object] This study aimed to evaluate the role of S1P/$S1P_3$ signaling in murine CIA. [Methods] $S1P_3$ knock-out (KO) DBA/1J mice with CIA were studied in comparison with wild-type (WT) mice. Arthritis severity were evaluated by visual scoring and histological analysis. Murine primary fibroblast like synoviocytes (FLS) were obtained from CIA mice. We examined $S1P_3$ expression after TNFα treatment and cytokine production after S1P treatment in FLS. [Results] $S1P_3$ deficiency resulted in modest symptoms of arthritis and a significant reduction in synovial inflammation and bone erosions in histological analysis. TNFα treatment upregulated $S1P_3$ expression and S1P treatment enhanced IL-6 production in WT-FLS significantly. TNFα-priming enhanced S1P-induced IL-6 production, which is significantly higher in WT-FLS than in KO-FLS. This effect was not observed in MCP-1 production of WT-FLS. [Conclusions] S1P induces IL-6 production via $S1P_3$ upregulation by TNFα in CIA-FLS. $S1P_3$ inhibition is a good target of the therapy for arthritis.

W25-3

Fractalkine promotes differentiation into osteoclasts from human peripheral blood monocyte

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Conflict of interest: None

[Object] Fractalkine (FKN) is involved in the pathogenesis of rheumatoid arthritis (RA), and clinical trial of anti-FKN mAb for RA is currently conducted. In this study, we aimed to clarify the effect of FKN on differentiation into osteoclasts (OC) from human peripheral blood monocytes (MC). [Methods] $CD16^+$ and $CD16^-$ peripheral blood MC were purified from healthy donors. The MC were incubated with M-CSF + RANKL with or without FKN. The cells were stained for TRAP. TRAP-positive multinucleated (three or more nuclei) cells were counted as OC. The cells were seeded onto plates coated with calcium phosphate thin films, and the resorption lacunae were examined. The experimental protocol was approved by the Ethics Committees, Toho University (27060). [Results] Differentiation of $CD16^-$ MC into OC was induced by stimulation with M-CSF + RANKL. Co-culture with FKN dose-dependently upregulated the differentiation into OC. Calcium resorption was also enhanced by addition of FKN. On the other hand, $CD16^+$ MC treated with M-CSF + RANKL did not differentiate into OC with or without FKN. [Conclusions] FKN promotes OC differentiation from $CD16^-$ peripheral blood MC.

W25-4

Overexpression of RasGRP2 Involves Adhesion and Migration of Fibroblast-like Synoviocytes in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Object] Rheumatoid arthritis (RA) is an autoimmune polyarthritis characterized by tumor-like proliferation of fibroblast-like synoviocytes (FLS). We analyzed the expression and function of Ras guanine nucleotide-releasing proteins (RasGRPs) in FLS. [Methods] Synovial tissue samples were obtained from patients with RA or osteoarthritis (OA) who underwent knee joint replacement surgery. Synovial tissue samples were evaluated immunohistochemically for the presence of RasGRPs. FLS were isolated from patients' synovial tissue samples with type I collagenase and were cultured. [Results] RasGRP2 (also called CalDAG-GEFI) were overexpressed in FLS from some of our RA patients compared with those from OA patients. RasGRP2 protein was abundant in FLS and endothelium from RA synovial tissues, whereas scarcely found in OA synovial tissues. The expression levels of RasGRP2 mRNA was lower in FLS from RA patients treated with biologics than those from untreated RA patients. The stimulation of VEGF and TGF-β increased the expression of RasGRP2 in FLS. Overexpression of RasGRP2 promoted adhesion and migration of FLS through Rap-1 activation. [Conclusions] RasGRP2 was overexpressed in FLS from RA patients, and involved adhesion and migration of FLS, proposed as a potential therapeutic target for RA.

W25-5

The expression of cadherin 2 is induced by decoy receptor 3 in rheumatoid synovial fibroblasts

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Conflict of interest: None

[Object] Decoy receptor 3 (DcR3) is a secreted decoy TNF receptor and competitively binds and inhibits the TNF family including Fas-ligand, LIGHT, and TL1A. We newly revealed by microarray assay that DcR3 regulates gene expression in rheumatoid synovial fibroblasts (RA-FLS). The profiles indicated that cadherin 2/type 1/N-cadherin (CDH2) was upregulated by DcR3. CDH2 has been reported to be associated with cell

attachment and migration osteoblast differentiation. In this study, we studied CDH2 as one of the key molecules in DcR3 signalling in RA-FLS. [Methods] After RA-FLS were stimulated with DcR3, CDH2 mRNA was quantified by real-time PCR. The expression of CDH2 protein in RA and OA synovium were evaluated with immunohistochemistry. [Results] Real-time PCR revealed CDH2 mRNA in RA-FLS was induced by DcR3 in a dose-dependent manner. Immunohistochemistry revealed that CDH2 protein was expressed predominantly in sub-lining layer of RA synovium. [Conclusions] CDH2 suppresses the proliferation of RA-FLS through increasing the $p27^{Kip1}$ that inhibit cell-cycle progression. The present study demonstrated that the expression of CDH2 is induced by DcR3 in RA-FLS. DcR3 signalling may control the hyperplasia of RA synovium through CDH2 and $p27^{Kip1}$.

W25-6

Fucosylated cytokines are expressed on rheumatoid arthritis synovial tissues

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Conflict of interest: None

[Object] We previously reported that glycan in rheumatoid arthritis (RA) serum was higher than that in normal subjects serum. In this study, we examined fucosylated tumor necrosis factor (TNF)-α was expressed on RA synovial tissues. [Methods] To determine that the expression of fucosylated TNF-α was expressed on RA and osteoarthritis (OA) synovial tissues, we performed immunofluorescence. We determined the percentage of α (1,2)-fucosylated TNF-α in RA and OA synovial tissues by counting the total number of yellow cells, and divided this value by the total number of green cells in each tissue section. Each section was evaluated by an observer blinded to the experimental conditions. In order to indicate that the expression of fucosylated TNF-α was in RA synovial fluids, immunoprecipitation was performed. [Results] We found fucosylated TNF-α was expressed on RA synovial tissues. Fucosylated TNF-α on RA synovial tissues was significantly highly expressed compared with that on OA synovial tissues. In addition, fucosylated TNF-α in RA synovial fluids was significantly higher compared with in OA synovial fluids. [Conclusions] Fucosylated TNF-α was expressed in RA synovial tissues and synovial fluids. These data show that fucosylation was involved in RA.

W26-1

Production of Ro52/TRIM21 autoantibodies that react to PEP08 epitope in Ro52 clinically relate to the morbidity and severity of interstitial lung disease in connective tissue diseases

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Conflict of interest: None

[Object] Ro52 autoantibodies (Ro52-Abs) appear in sera of connective tissue diseases (CTD) patients with interstitial lung disease (ILD). It was reported that the generation of Ro52-Abs correlated to the morbidity of ILD, but its clinical significance is still controversial. In this study, we tried to determine epitopes of Ro52-Abs and examine the relationship between the generation of Ro52-Abs reactive to the determined epitope in Ro52 and the clinical morbidity and severity of ILD. [Methods] We selected 4 patients from ILD with high titer of Ro52-Abs in their sera and obtained monoclonal Ro52-Abs (moRo52-Abs) from the patients' PBMCs using a novel single B cell manipulating technology (ISAAC system). [Results] We obtained 12 moRo52-Abs. Western blotting analysis revealed that 11 of the 12 moRo52-Abs bound to coiled-coil (C-C) domain of Ro52. We then performed ELISA using the peptide library of the C-C domain of Ro52. Those 2 moRo52-Abs that were obtained from different patients bound with one peptide (PEP08). Finally, we assessed the relationship between PEP08-reactive moRo52-Abs with the clinical morbidity and severity of ILD. [Conclusions] Statistical analysis revealed that the production of PEP08-reactive Ro52-Abs correlated with the morbidity and severity of ILD in CTD.

W26-2

Association of GTF2I region polymorphism with systemic lupus erythematosus and systemic sclerosis in a Japanese population

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Conflict of interest: None

[Object] Genome wide association studies of SLE in Chinese and Korean populations recently demonstrated strong association with rs73366469, located upstream of *GTF2I* encoding a transcription factor. However, association with systemic sclerosis (SSc) has not been reported. In this study, we examined whether this SNP is associated with SLE also in the Japanese population, and whether the SNP is also associated with SSc. [Methods] Genotyping of rs73366469 was performed on 842 Japanese SLE patients, 446 SSc patients and 934 healthy controls using TaqMan SNP Genotyping Assay. Association study was performed by chi-square test. Correction for multiple testing was performed by calculation FDR q values using Benjamini-Hochberg method. [Results] Strong association of rs73366469 C was detected in SLE ($p=5.11\times10^{-16}$, $q=1.38\times10^{-14}$, OR=2.37), and also in SSc (p=0.0017, q=0.0051, OR=1.50). When the allele frequency was compared between patients with and without specific clinical symptoms or autoantibody profiles, significant difference was not observed. [Conclusions] Association between SLE and *GTF2I* rs73366469 was replicated in a Japanese population, and detected for the first time in SSc. This SNP appeared to be associated with occurrence of the diseases rather than their clinical phenotypes.

W26-3

Clinical significance of new citrullinated protein, inter-alpha-trypsin inhibitor heavy chain 4 (cit-ITIH4), in patients with RA

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Conflict of interest: None

[Object] To identify citrullinated protein (cit-ITIH4) in sera, and to evaluate the clinical significance in RA patients. [Methods] 1) Citrullinated protein expressions in sera were examined by Western blot in peptide GPI-induced arthritis (pGIA) and RA patients. 2) The detected proteins were identified by mass spectrometry. 3) In RA patients, the relationship between the expression of cit-ITIH4 and clinical features was analyzed, and cit-ITIH4 levels were compared before and after biological treatment. 4) The antibody response against cit-ITIH4 peptide was measured by ELISA. [Results] 1) The band of citrullinated protein at 120kD was specifically detected in pGIA and 82% of RA patients sera. 2) Cit-ITIH4 was identified, especially R438 site was commonly citlullinated in mice and humans. 3) Cit-ITIH4 levels were correlated with the levels of CRP, RF and DAS28-CRP, and were decreased after biological treatment in RA patients. 4) The antibody response against cit-ITIH4 peptide containing citrullinated R438 was significantly increased in RA patients. [Conclusions] These results suggested that serum cit-ITIH4 was specifically increased in RA patients, and could be a new serum marker of disease activity in RA patients.

W26-4

Ribavirin, an antiviral drug, down-regulates interferon signature in CD4 naive T cells from patients with SLE by increasing H3K9me2 levels

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Conflict of interest: None

[Objective] Recently, the association of IFN signature and epigenetic abnormalities is suggested. In this study, we analyzed H3K9me2, H3K9me3 and H3K27me3 levels, which are gene repressive histone lysine methylation, in CD4 naive T cells of SLE patients and examined the relationship with IFN signature. We also perform experiments using ribavirin as a candidate drug of improving IFN signature in SLE. [Methods] The expression of ISG of CD4 naive T cells obtained from SLE patients and healthy subjects was analyzed by qPCR. The levels of H3K9me2, H3K9me3, and H3K27me3 in the ISG region were analyzed by ChIP-qPCR. Furthermore, these cells were stimulated with type I IFN and CD3/CD28 beads and the expression of ISG under ribavirin treatment were analyzed by qPCR. In addition, H3K9me2, H3K9me3 and H3K27me3 levels were analyzed by ChIP-qPCR. [Results] In the CD4 naive T cells from SLE patients, high expression of ISG was observed as compared with healthy subjects, and H3K9me2 level was decreased in the MX1 region. Furthermore, an increase in the level of H3K9me2 in the ISG region was observed by ribavirin treatment. [Conclusion] Ribavirin is thought to be as a candidate drug for treatment of SLE by improving IFN signature through increasing H3K9me2 level in the ISG region.

W26-5

Immune cell subsets from PBMC in patients with MCTD

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Conflict of interest: Yes

[Object] Mixed connective tissue disease (MCTD) is a disease entity of unknown etiology characterized by overlapping clinical features of two or more connective tissue diseases and by elevated anti-U1RNP antibodies. In this study, we aimed to assess the immunophenotypic characterization of MCTD patients by flow cytometry (FCM). [Methods] Peripheral blood samples were obtained from 9 MCTD patients and 10 healthy controls (HC). Immunophenotypes were analyzed by FCM. Each one patient evolved to SLE and overlap syndrome was excluded. [Results] Among 26 immune cell subsets, the proportion of naïve B cells and monocytes, especially CD16-negative monocytes, was significantly higher in MCTD patients than in HC. Moreover, circulating plasma cells tend to increase in MCTD patients. [Conclusions] The increased CD40 expression on CD16-negative monocytes, and the increased number of plasma cells in the active stage of MCTD have been reported. Our results suggest that the increased number of CD16-negative monocytes, as well as plasma cells, is important for the pathogenesis of MCTD, indicating the peripheral blood compartment reflects the inflammatory milieu of the affected organs. We are currently investigating the molecular basis of these changes by using next generation sequencing techniques.

W26-6

The analysis of gene expression in monocytes from adult still's disease with DNA microarray

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Conflict of interest: None

[Object] Adult Still's disease (ASD) 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 ASD patients. [Methods] 1) Monocytes were isolated from healthy controls (HC), active-ASD and inactive-ASD. Differentially expressed genes (DEGs) were analyzed by DNA microarray and validated by quantitative PCR. 2) The correlation between validated DEGs and serum CRP, ferritin or plasma IL-1β, IL-6, IL-18, TNF-α in ASD was analyzed. 3) The production of IL-1β, IL-18 and the effect of autophagy were examined with DEGs overexpressing THP-1 cells. [Results] 1) In active-ASD, 67 genes expressed significantly higher than HC and inactive-ASD. After validation, PLAC8 was significantly higher in active-ASD. 2) In ASD, the expression of PLAC8 in monocytes had positive correlation with the value of serum CRP, ferritin and plasma IL-18. 3) In PLAC8-THP-1 cells, the production of IL-1β and IL-18 were decreased and autophagy was enhanced. The blockade of autophagy cancelled the inhibition of IL-1β and IL-18 production by PLAC8 overexpressing. [Conclusions] The overexpression of PLAC8 in monocytes might involve in the pathogenesis of ASD through the enhancement of autophagy.

W27-1

Two cases diagnosed with intravascular large B cell lymphoma in the department of Rheumatology

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Conflict of interest: None

Case 1: A 78-year-old woman was presented with fever, malaise, arthralgia and skin rush. Adult onset still's disease was suspected and admitted to our hospital. Laboratory findings showed elevated liver enzymes, LDH (938 IU/L) and sIL-2R (6,959 U/ml). Pathological examination of random skin biopsy specimen, but not of bone marrow, revealed that blood vessels of subcutaneous fat were infiltrated by CD20-positive large atypical lymphocytes. This finding resulted in the diagnosis with intravascular large B cell lymphoma (IVLBCL). Case 2: A 77-year-old woman was presented with Raynaud's phenomenon, bilateral legs

edema and bicytepenia (Hb 8.3g/dl, Plt 83,000/μl) with positive anti-centromere Ab. Connective tissue disease was suspected and admitted to our hospital. Physical examination revealed no skin change of sclerosis. Laboratory findings showed elevated LDH (573 IU/L) and sIL-2R (6,840 U/ml). Imaging study of ^{18F}FDG-PET indicated abnormal uptake in the retroperitoneum, stomach, spleen and bone marrow. Pathological examination of random skin biopsy specimen demonstrated the diagnosis with IVLBCL. [Clinical significance] In case with suspected to be connective tissue disease, we should consider IVLBCL as differential diagnosis. Random skin biopsy is useful method for the diagnosis.

W27-2

Diagnostic approach to fever of unknown origin in the field of autoimmune disorders

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Conflict of interest: None

Introduction: Fever of unknown origin (FUO) is caused by various disease and often makes a diagnosis difficult. The aim of this study is to determine the clinical features of patients with FUO in autoimmune disorders. Method: Medical records of 89 patients to meet the criteria of FUO by Petersdorf were reviewed between January 2013 and September 2017. Results: The causes of diseases were infections (n=8, 9.0%), non-infectious inflammatory diseases (n=53, 59.6%), malignant diseases (n=4, 6.5%), other diseases (n=13, 14.6%) and unknown (12.4%). 27 patients required hospitalization, the most frequent diseases were adult onset Still's disease (n=8), Behcet's disease (n=5), Systemic lupus erythymatosus (n=2) and drug fever (n=2). In the outpatient cases, they were polymyalgia rheumatica (n=8), Behcet's disease (n=6), familial Mediterranean fever (n=4) and microscopic polyangitis (n=4). These diseases had difficulty in diagnosis only by serological markers or imaging tests. In the most cases, the decision to clarify causes of FUO was based on the diagnostic criteria. Conclusion: Assessment of patients with FUO requires of knowledge of many diseases and diagnostic tools.

W27-3

Rat-bite fever caused by Streptobacillus notomytis, manifesting with septic arthritis, reactive arthritis, sepsis and purpura

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Conflict of interest: None

A 67-year old male presented with low grade fever, purpura in the extremities and peripheral arthritis affecting PIP, MCP and wrist on both hands and the left first MTP. Loxoprofen improved PIP, MCP arthritis and purpura, but a gram negative rod was isolated in an aerobic bottle after 138 hours of incubation. Meropenem was started, improving wrist arthritis. Sonography and CT scan revealed bone erosion in the MTP, leading to the diagnosis of septic arthritis. Arthrocentesis was not performed due to insufficient amount of synovial fluid. MTP arthritis improved after two weeks of meropenem administration. Genetic analysis revealed the gram negative rod was Streptobacillus notomytis. Further questioning revealed the patient may have had contacted with rats. [Conclusions] Streptobacillus notomytis was proposed to be a new species separated from Streptobacillus moniliformis, which causes rat-bite fever. There has been no report of human infection with Streptobacillus notomytis. Rat-bite fever causes reactive and septic arthritis and skin rash, all of which were found in our case. Streptobacillus is difficult to isolate; therefore there may be more cases than reported. Streptobacillus infection caused by contact with rodent should be included in the differential diagnosis of arthritis.

W27-4

A case of gonococcal arthritis in which joint echography played an important role in the diagnosis

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Conflict of interest: None

A 23-year-old woman visited an emergency hospital due to pain and swelling of multiple joints. She was transferred to our hospital for further examination. She had a fever, redness, swelling and tenderness of the left shoulder, right knee, left 4MP joints. There was leukocytosis and serum CRP were elevated, but autoantibodies detected were all negative. The joint echography showed synovial thickening with increased blood flow signal in the tendons, but not in the joint synovia. Arthritis induced by sexually transmitted infections was suspected because of multiple sexual contacts other than her partner and increased vaginal discharge. Neisseria gonorrhoeae was detected by PCR test and culture from the abscess of the Bartholin's gland. Then, diagnosis of gonococcal arthritis was made. After treatment with antibiotics, symptoms and joint echography findings improved remarkably. It was thought that taking precise medical history was important in patients with atypical symptoms or clinical course for RA. In addition, there have been few reports of gonococcal arthritis, and reports on the joint echography in this disease are rare. So, we present here a rare case of gonococcal arthritis along with previous literature.

W27-5

Case report of a patient with Sjogren's syndrome presenting with hyponatremia after intravenous cyclophosphamide (IVCY) therapy

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Conflict of interest: None

Cyclophosphamide (CPA) is reported to cause hyponatremia in patients with cancer under chemotherapy and in those with connective tissue diseases receiving oral CPA or IVCY treatment. We describe here a 53-year-old woman with anti-SS-A positive Sjogren syndrome who presented with hyponatremia as a side effect of IVCY. In addition to xerostomia, she had been complicated with extraglandular manifestations, including purpura and numbness in the lower extremities, and interstitial lung disease, which was resistant to daily oral prednisolone of 15 mg, although serum IgG levels decreased from 6,374 to 3,190 mg/dL. We therefore started IVCY (500mg/month). Nausea which was noticed during the 2nd and 3rd IVCY disappeared soon after IVCY. However, on the next day of 4th IVCY infusion, she developed nausea with confusion (JCS1-2), lassitude, and tachypnea. Lab data revealed hyponatremia (125 mEq/l) with relative elevation of serum ADH (3.1pg/mL). Serum and urine osmolarity concentrations were 271 and 324 mOsm/kg, respectively, and urine Na level was 66 mEq/L, suggesting the involvement of SIADH mechanism in our case. Drug-induced SIADH should be considered as a side effect of IVCY, especially in patients presenting with gastrointestinal symptoms as well as disturbance of consciousness.

W27-6

Two cases of drug-induced pleuritis caused by anti-tumor necrosis factor (TNF) agents likely via mechanisms other than drug-induced lupus (DIL)

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Conflict of interest: None

Drug-induced pleuritisding anti-TNF agents, especially due to DIL. We report two cases of DIP, both of whom developed pleural effusion (PF) after starting anti-TNF agents. PF resolved shortly after discontinuing the agents. Case 1: A 52-year-old woman (AS). She was receiving

MTX and PSL. Adalimumab (ADA) was added leading to remission of AS. She developed a right-sided PF with elevated CRP 3 months after starting ADA. The PF was exudative. Bacterial and mycobacterial culture were negative. Antinuclear (ANA) and anti-histone Ab (AHA) were negative. ADA was discontinued and the PF improved and disappeared completely 4 months later. Case 2: A 74-year-old woman (RA). Etanercept (ETN) for active RA was started leading to remission of RA. Two months later, she presented with bilateral PF and pericardial effusion. CRP was elevated. ANA was positive (1:40). AHA was negative. Thoracentesis was not performed. ETN was discontinued, and the PF had improved 1 month later and disappeared completely 2 months after discontinuing ETN. In both cases, AHA were negative and ANA was negative or positive at low titer, suggesting that PF in these two cases was due to mechanisms other than DIL. DIP, in addition to infection, should be considered as DDx of PF during treatment with anti-TNF agents.

W28-1

Factors associated with decreasing serum 25(OH)D levels and the appearance of vitamin D deficiencies among Japanese patients with rheumatoid arthritis: Results from the IORRA cohort study

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Conflict of interest: None

[Object] This study was aimed to investigate factors that predict vitamin D deficiencies among Japanese patients with rheumatoid arthritis (RA). [Methods] In 2011 and 2013, Serum 25(OH)D levels were evaluated in 2534 Japanese RA patients (2179 women and 355 men). A vitamin D deficiency was defined as serum 25(OH)D levels <20 ng/mL. The predictive factors of decreasing serum 25(OH)D levels and the appearance of vitamin D deficiencies over a 2-year period were evaluated using multivariate logistic regression. [Results] The prevalence of vitamin D deficiencies was 73.3% in 2011 and 68.2% in 2013. Serum 25(OH)D levels decreased >5 ng/mL from 2011 to 2013 in 224 (8.8%) patients. Among the 677 patients who did not have a vitamin D deficiency in 2011, 214 (31.6%) were diagnosed as deficient in vitamin D in 2013. Serum 25(OH)D levels that decreased >5 ng/mL were significantly associated with female gender, younger age, and bisphosphonate disuse. The appearance of vitamin D deficiencies was significantly correlated with younger age, increased tender joint counts, and weekly methotrexate (MTX) dosage. [Conclusions] Gender, age, tender joint counts, bisphosphonate use, and MTX dosage were associated with increasing vitamin D deficiencies among Japanese patients with RA.

W28-2

Short-term daily teriparatide in osteoporotic patients with rheumatoid arthritis

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Conflict of interest: None

[Object] The aim of this study was to compare the efficacy of 6-month teriparatide treatment followed by 6-month bisphosphonate therapy with 12-month bisphosphonate therapy in rheumatoid arthritis (RA) patients who had not been previously treated for osteoporosis. [Methods] A total of 34 RA patients with osteoporosis were enrolled. Thirteen patients received 6-month teriparatide prior to 6-month minodronate therapy (PTH group), and 21 patients received 12-month minodronate therapy (BP group). Bone mineral density (BMD), and bone turnover markers were measured prior to and 6 and 12 months after the initiation of treatment. [Results] BMD of the spine was significantly increased after 6 and 12 months of treatment in both groups. In the PTH group, the mean percent change of BMD of the spine was significantly higher at 12 months after the initiation of treatment, as compared to the BP group (PTH group: 9.9±1.5%, BP group: 5.5±0.7%). [Conclusions] Therapy involving 6-month teriparatide followed by 6-month minodronate therapy increased spine BMD to a greater degree than 12-month minodronate monotherapy. The strategy of short-term administration of teriparatide for RA patients with osteoporosis might be useful when additional bisphosphonate therapy is considered.

W28-3

Investigation of the relationship between sarcopenia and clinical efficacy of denosumab (DMAb) in rheumatoid arthritis (RA) and collagen disease patients

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Conflict of interest: Yes

(OBJECTIVE) We investigated the relationship between sarcopenia and clinical effects of denosumab in RA and collagen disease patients. (METHODS). We analyzed 79 subjects (F:M 68/11, 54.1±13.4 y. o., BMI 21.3±2.9, RA 24, SLE 24, others 31, PSL4.5±3.3mg) from 142 patients treated with DMAb from July 2013. We measured muscle mass with In Body 770 and examined the relationship among SMI, ECW/TBW, phase angle, and changes of femur and L2-4 BMD 12 months after treatment of DMAb. (RESULTS) 32 patients showed the tendency of sarcopenia. Mean SMI was 5.92±0.8 kg/m^2. 15 patients did not show the increasing of femur BMD although L2-4 BMD increased. Compared the increased group and no increased group of femur BMD, ECW/TBW and phase angle of left lower limb showed the significant difference (0.393 ± 0.009 vs.0.401 ± 0.011 p = 0.0168, 4.59 ± 0.83 vs 3.92 ± 0.87, p = 0.0123 Wilcoxon signed ranked test). In multivariate analysis, Δ femur BMD was correlated with ECW/TBW and phase angle of the left lower limb (-0.4505, p <0.001, 0.4220, p = 0.0001, Spearman test). Even age, sex, BMI, and dosage of PSL were added in multiple regression analysis, these parameters showed the significant difference. (CONCLUSION) Sarcopenia might be correlated with the effect of DMAb on femur BMD increasing.

W28-4

Proximal tibia inclination do not affect the long-term patient-oriented results after High Tibial Osteotomy (HTO)

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Conflict of interest: None

[purpose] We assessed the relationship between lower limb alignment and bone morphology after High Tibial Osteotomy (HTO) and patient oriented long-term results. [methods] The subjects were treated by HTO more than 5 years ago and assessed with patient-oriented KSS (Knee Society Scoring System) (105 knees). We measured Femoral Tibia Angle (FTA), Medial Proximal Tibial Angle (MPTA), Joint Line Convergence Angle (JLCA) and assess the relationship with KSS score. We divided subjects at median value of each values and compare the scores. [results] MPTA did not correlate with any scores. On the other hand, FTA negatively correlated with total function. This means that the gain of valgus leads to the better outcome. JLCA negatively correlated with satisfaction and total function. This suggests that the decreased medial joint space leads to the poor outcome. Two group comparison suggests that larger JLCA group showed significant lower score. No significance was detect-

ed at other alignment. [conclusion] We confirmed that insufficient correction leads to the poor functional long-term outcome. In the larger JLCA subjects, satisfaction and functional long-term outcome significantly decreased. However, proximal tibia inclination did not affect the patient-oriented long-term result.

W28-5

A single intra-articular injection of fluvastatin-PLGA microspheres reduces cartilage degradation in rabbits with experimental osteoarthritis

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Conflict of interest: None

[Object] Statins are cholesterol-lowering drugs and various profitable effects were reported recently. This study investigated therapeutic effects of local administration of statin in experimental osteoarthritis (OA) model. [Methods] We assessed the effect of fluvastatin (FLU) which showed most potent chondroprotective effects among clinically used statins to OA chondrocyte. Gene expression and MMP-13 secretion to culture medium were assessed. Next, we made FLU-PLGA (poly lactic-co-glycolic acid) microspheres and release profile was assessed. Finally, effects of FLU-loaded PLGA microspheres (FLU-PLGA) were tested in rabbit OA model. Rabbits were divided into four groups; group 1-A: PLGA-treated group, group 1-B: PLGA contralateral control group, group 2-A: FLU-PLGA-treated group and group 2-B: FLU-PLGA contralateral control group. [Results] Expression of COL2A1 and ACAN were promoted and MMP-13 were inhibited by FLU. The secretion of MMP-13 was also inhibited. The release kinetics showed that the FLU was gradually released. Histological analysis revealed that OARSI scores were significantly lower in group 3. [Conclusions] This study indicates that a single intra-articular injection of FLU-loaded PLGA microspheres could be a novel therapeutic approach for treating patients with OA.

W28-6

Low 25 Hydroxy vitamin D [25(OH)D] plasma levels in patients with connective tissue disease (CTD) treated with high-dose glucocorticoid (GC) therapy is a risk factor for avascular necrosis of the femoral head (ANF)

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Conflict of interest: None

[Object] The onset of ANF is a severe problem in patients with CTD treated with GC therapy. Vitamin D deficiency has been reported in association with metabolic diseases, cardiovascular and immune function. It is known that vitamin D deficiency is common in CTD patients. In this study, we examined the relationship with the prevalence of ANF and vitamin D deficiency in patients treated with high-dose GC therapy. [Methods] Baseline characteristics, serum 25(OH)D and the onset of ANF were evaluated in patients underwent primary prevention of osteoporosis with active vitamin D3, bisphosphonate preparation after starting high-dose GC therapy in our department between 2008 and 2013. ANF was diagnosed with MRI image. [Results] There were 72 of female patients with CTD, age 56.6 years old, 36% after menopause, BMI 20.8, 25(OH)D 13.9 ng/ml. ANF occurred in 5 cases (SLE 2, AAV 2, DM/PM 1), age 57.0 years old, 60% after menopause, BMI 19.7, 25(OH)D 7.4 ng/ml. In all onset group, 25(OH)D was less than 10 ng/ml and was severely deficient in 25(OH)D, which was significantly lower than that in non-onset group (7.4 vs 14.4 ng/ml, $p < 0.001$). [Conclusions] It was suggested that severe 25(OH)D deficiency prior to high-dose GC therapy might be a risk of developing ANF in patients with CTDs.

W29-1

Ultrasound (MSKUS) findings of feeding vessels (FV) and bone surface irregularity (BSI) in wrist joints (WJ) of healthy volunteers (HV) ~second report~comparative review between young (YA) and elderly adults (EA)

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Conflict of interest: None

[Object] To elucidate the differences of distribution (DIS) of FV and BSI in WJ both YA and EA of HV. [Methods] The dorsal side of WJ was scanned with 2D-probe in HV. The DIS of FV in the capsule and the extensor (E.) tendon sheath (TS), and the evaluation of BSI at lunate (Lu) were examined with comparative review. [Results] The DIS of FV in YA HV (n=30: mean age 32.2±8.0) vs EA HV (n=21: mean age 66.0±7.2) were above (ab)-Trapezoid (Rt100 vs 100%, Lt100 vs 100%: $p=1.0$), EDC TS (Rt86.7 vs 81.0%: $p=0.59$, Lt66.7 vs 76.2%: $p=0.47$), EDM TS (Rt30.0 vs 52.4%: $p=0.11$, Lt30.0 vs 66.7%: $p<0.01$), ab-Capitate (Rt23.3 vs 42.9%: $p=0.14$, Lt30.0 vs 47.6%: $p=0.21$), ab-TFCC (Rt16.7 vs 19.0%: $p=0.83$, Lt30.0 vs 38.1%: $p=0.56$), distal radial side of radiocarpal joint (Rt20.0 vs 42.9%: $p=0.08$, Lt23.3 vs 28.6%: $p=0.68$), distal end of Ulna (Rt10.0 vs 42.9%: $p<0.01$, Lt16.7 vs 28.6%: $p=0.31$). FV from vascular channels (vc) were depicted at Lu (Rt53.3 vs 52.4%: $p=0.95$, Lt46.7 vs 66.7%: $p=0.16$), Radius (Rt20.0 vs 33.3%: $p=0.29$, Lt16.7 vs 23.8%: $p=0.54$), Triquetrum (Tr) (Rt10.0 vs 42.9%: $p<0.01$, Lt16.7 vs 33.3%: $p=0.17$) and Capitate (Ca) (Rt6.7 vs 33.3%: $p=0.013$, Lt10 vs 33.3%: $p=0.04$). BSI (transverse diameter) at Lu in both groups were 1.26±0.33 vs 1.14±0.2mm: $p=0.21$. [Conclusions] The frequency of FV in EA were significantly higher at EDM TS, distal end of Ulna and Tr/Ca vc compared to those of YA.

W29-2

Differences in ultrasound-detected ECU pathologies between early RA, established RA and non-RA

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Conflict of interest: None

[Object] To determine the correlation between ultrasound-detected ECU pathologies and rheumatic diseases condition. [Methods] We reviewed the reports of MSUS done in our division since April 2015. Cases with stored images of ECU pathologies were selected. Presence or absence of pathologies (synovial hypertrophy, hyperemia, retinaculum thickening, tendinosis and tendon subluxation) was determined. [Results] 52 cases were analyzed. The purpose of the examination was initial diagnosis in 22 and follow-up in 30. Diseases/disorders were RA in 39 (14 early RA and 25 established RA at the time of the examination) and non-RA in 13. Frequencies of synovial hypertrophy, hyperemia, retinaculum thickening and tendinosis were 100%, 100%, 7% and 7%, respectively among early RA. Those of synovial hypertrophy, hyperemia, retinaculum thickening, tendinosis and tendon subluxation were 72%, 84%, 24%, 44% and 36%, respectively among established RA. Among the 22 patients examined for initial diagnosis, synovial hypertrophy was significantly associated with RA and retinaculum thickening was significantly associated with non-RA, while hyperemia was associated with neither. [Conclusions] Distinguishing synovial hypertrophy from retinaculum thickening of ECU can be useful for the early diagnosis of RA.

W29-3

Ultrasound analysis for enthesitis and synovitis of knee joint in peripheral spondyloarthritis patients

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Conflict of interest: None

[Object] We focus site and trend of enthesitis and synovitis of knee

joint in peripheral spondyloarthritis patients using ultrasound. [Methods] We analyzed synovitis and enthesitis of various site, such as tendon of quadriceps femoris (QFT), patella tendon (PT), insertion of medial collateral ligament (MCL), insertion of lateral collateral ligament (LCL) and tendon of popliteus muscle (PoT) of 20 knees in 11 peripheral spondyloarthritis patients. [Results] Average age is 57.4 ± 20.0 years and male to female ratio is 4:7. Diagnosis are 1 Ulcerative colitis, 1 reactive arthritis and 1 giant cell arthritis and 8 undifferentiated spondyloarthritis patients. Proportion of enthesitis are QFT 20% (4/20), PT 30% (6/20), MCL 45% (9/20), LCL 30% (6/20) and PoT 70% (14/20). This trend is remarkable in elder patients, especially more than 65 years. Only slight to mild joint fluid and periarticular vasculature are sometime detected, however proliferative synovitis isn't detected. [Conclusions] In peripheral spondyloarthritis patients, enthesitis of PoT is often detected than other site, including QFT and PT. This result suggests the importance of checking for various site, especially PoT.

W29-4

Ultrasonographic findings of the soft tissue swelling surrounding the nail in patients with psoriasis and psoriatic arthritis

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Conflict of interest: None

[Object] Although nail lesions in patients with psoriasis (PsO) are known as a risk factor for psoriatic arthritis (PsA), pathological feature and the relationship with inflammation of the soft tissue surrounding the nail is unknown. We assessed the ultrasonographic findings of soft tissue findings surrounding the nail in patients with PsO and PsA and compared with other diseases. [Methods] Twenty-five PsO · 35 PsA · 23 rheumatoid arthritis (RA) · 28 ulcerative colitis (UC) and 13 Crohn's disease (CD) patients were included in this analysis. The distance between the proximal nail fold on the dorsal side of the nail matrix and the nail bed on the volar side of the nail matrix was measured by ultrasonography. [Results] The distance between the proximal nail fold and the nail bed was 2.58 ± 0.56 mm in PsA and 2.55 ± 0.58 mm in PsO patients (p=0.603). Among the 60 patients who combined PsO and PsA patients, 41 patients with nail lesion and 19 patients without nail lesion was compared. The distance was 2.68±0.62mm in patients with nail lesion and 2.30±0.41mm in without nail lesion (p<0.001), which was also swelling compared with the RA, UC and CD group. [Conclusions] In patients with PsO and PsA with nail psoriasis, soft tissue surrounding nail was observed in ultrasonographic findings.

W29-5

Screening research of peripheral enthesitis by ultrasonography in patients with inflammatory bowel disease

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Conflict of interest: None

[Objective] Traditionally, tender and swollen joint counts were assessed by clinical assessment. To date, the modern imaging tool such as ultrasonography (US) can detect the joint and enthesial inflammation more sensitively than clinical assessment. The aim of this study was to research the utility of US screening for detection of peripheral enthesitis findings in patients with inflammatory bowel diseases (IBD) such as ulcerative colitis (UC) and Crohn's disease (CD). [Methods] Total 42 patients including 27 patients with UC and 15 patients with CD were underwent gray-scale (GS) and power Doppler (PD) US examination in lateral epicondyle, triceps enthesis, quadriceps enthesis, proximal and distal patella tendon enthesis, Achilles tendon and fascia plantaris tendon enthesis. [Results] In the clinical assessment, 9 patients with UC and 7 patients with CD had tenderness in any enthesis. Active enthesitis in US was found in 16 patients with UC and 8 patients with CD. The concordance rate between clinical findings and US findings was relatively high and subclinical enthesitis was also found in many patients. [Conclusion] The enthesial findings in patients with IBD was compared between clinical and US examination. US screening might useful in patients with IBD.

W29-6

Early detection of ankle joint synovitis in rats by ultrasonography using ultra high frequency probe with Superb Micro-vascular Imaging

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Conflict of interest: Yes

[Objectives] Early detection of synovitis is critical for arthritis clinic. Ultrasonography (US) is capable to detect early rheumatoid synovitis. Although small animals are needed for basic research, diagnosis of their synovitis has been done by pathology. Recently developed ultrahigh frequency probe with Superb Micro-vascular Imaging (SMI) is expected to detect neovascularization of synovitis. The aim of this study is to validate the ability of US for detection of early synovitis in rats. [Methods] Non-swollen 15 ankle joints of env-pX rats, which develop spontaneous synovitis, were used with 3 healthy control rats. Using TOSHIBA Aplio i800 with PLI-2004BX probe, power Doppler (PD) and SMI analyses were performed by pixel counting to quantify blood flow signals. Cut off value of total normal capillary vessel area in the joints was set from calculating mean value of normal rats in pathological specimens. Neovascularization was defined, when number of vessels was beyond 3 which vessel area was beyond the normal value. [Results] Positive SMI signal was associated with neovascularization, while this was not proven in power Doppler. [Conclusions] US is able to evaluate early synovitis of the rat ankle joints with SMI.

W30-1

Relationship between treatment response, periodontitis and atherosclerotic vasculitis in patients with rheumatoid arthritis using FDG-PET/CT

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Conflict of interest: None

[Object] The aim of this study was to evaluate the relationship between treatment response to rheumatoid arthritis (RA), periodontitis and atherosclerotic vasculitis 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), and carotid artery. We also evaluated DAS28-CRP and clinical parameters. Wilcoxon's test and Spearman's rank correlation test were applied to assess the correlation between the periodontal SUVmax, carotid artery target-to background ratio (TBR) and the clinical parameters. [Results] There was no significant change in periodontal SUVmax, carotid artery TBR before and after

treatment. But, there were significantly negative correlations between periodontal SUVmax at baseline and ΔDAS28-CRP (r=-0.369, p=0.004). [Conclusions] Periodontitis might decrease the response to the biological therapies in RA patients.

W30-2

Cutoff value of 18F-FDG Positron Emission Tomography (PET) to distinguish polymyalgia rheumatica (PMR) from rheumatoid arthritis (RA)

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Conflict of interest: None

[Object] To analyze cutoff value of 18F-FDG Positron Emission Tomography (PET) to distinguish polymyalgia rheumatica (PMR) from rheumatoid arthritis (RA). [Methods] We retrospectively studied 40 patients (seventeen PMR patients and twenty-three RA patients) who had PET/CT from Aug 2009 to Oct 2017 by using classification and regression tree (CART) analysis. [Results] Univariate CART analysis revealed increased uptake of 18F-FDG of ambilateral shoulder joints (61.1% vs. 9.1%; $p<0.01$), ambilateral hand joints (38.9% vs. 9.1%; $p=0.049$), spinous process of lumbar vertebra (72.2% vs. 0%; $p<0.01$), pubis (66.7 vs. 9.1%; $p<0.01$), sternoclavicular joint (55.6% vs. 9.1%; $p<0.01$) and ambilateral femoral joints (55.6 vs. 0%; $p<0.01$) in PMR patients compared with RA patients. In contrast, increased uptake of 18F-FDG of ambilateral knee joints were shown in RA patients compared with PMR patients. multivariate CART analysis revealed increased uptake of 18F-FDG of spinous process of lumbar vertebra had been significantly risk factor of PMR. [Conclusions] Increased uptake of 18F-FDG of spinous process of lumbar vertebra may be an important finding for to distinguish PMR from RA.

W30-3

Changes in Cartilage Matrix are Correlated with Changes in Bone Erosion Volume in Patients with Rheumatoid Arthritis: A Multi-Modality Imaging Study

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Conflict of interest: None

Objective: To investigate the changes of bone and cartilage damage in the patients with RA receiving MTX and anti TNFα therapy using three tesla MRI and high resolution peripheral computed tomography (HR-pQCT). **Methods:** Twenty RA patients with MTX treatment were recruited into either a low DAS group (n=9, DAS28<3.2) or a high DAS group (n=11, DAS28>3.2). The high DAS group received additional anti-TNFα treatment to MTX from baseline (BL). All patients underwent MRI wrist scans and HR-pQCT scans of the MCP and wrist at BL and at 3 month (3M). **Results:** Anti-TNFα therapy in the high-DAS group resulted in a significant decrease of DAS28 CRP score, which was accompanied by decrease in mean T1rho values and erosion volumes at all measurement sites. The low DAS group in contrast, displayed an increasing trend in T1rho values and erosion volumes despite low disease activity. Changes in T1rho values and bone erosion volume were significantly positively correlated, and both of them were significantly correlated with changes in DAS28 CRP score. **Conclusion:** Anti-TNFα therapy seems to simultaneously prevent bone and cartilage from further destruction and might even partially repair preexisting cartilage degeneration and bone erosions within first 3 months of therapy.

W30-4

Radiological Changes Measured By 3T MRI and HR-pQCT Correlated with Clinical and Functional Assessments in RA Patients

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Conflict of interest: None

Objective. To investigate the correlations between changes of radiological quantitative assessments with changes of clinical and functional assessments from baseline to 3 months (3M) in RA patients. **Methods.** Twenty-eight RA patients (MTX and anti-TNFα group with high disease activity, N=18 and MTX-only group with low disease activity, N=10 at the baseline) underwent clinical (DAS28), functional (HAQ and MHQ) and radiographic (MRI and high HR-pQCT) assessments at baseline and at 3M. MR images were evaluated RAMRIS and quantitatively for the volumes of synovitis (SYN) and bone marrow edema-like lesions (BMEL). Erosion volumes were quantified using HR-pQCT. **Results.** MRI showed statistically significant decreases in both SYN and BMEL volume for the anti-TNFα group, and an increase in SYN volume for the MTX only group. The MTX group showed an increase in HR-pQCT bone erosion volume. Changes in SYN, BMEL, and erosion volumes were significantly correlated with changes in DAS28, HAQ, and MHQ. **Conclusion.** Quantitative measures were more sensitive than semi-quantitative grading for evaluating structural and inflammatory changes with treatment. Multimodality imaging with 3T MRI and HR-pQCT may provide promising biomarkers that may aid determine disease progression and therapy response.

W30-5

Investigation of bone microstructure using High Resolution peripheral Quantitative CT (HR-pQCT) in arthritis

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Conflict of interest: None

[Object and Methods] HR-pQCT is a high resolution quantitative CT for voxel size 0.06 mm, quantitatively analyzing the bone microstructure. In this study, We examined HR-pQCT in the distal radius of 95 patients with arthritis. Bone microstructure of 52 patients (59 ± 2 years old) with anti-CCP antibody (ACPA) negative (N group) and 43 patients with ACPA positive (P group) (58 ± 1 year old). was examined. [Results] The cortical porosity was significantly stronger in the P group than the N group ($p<0.05$). When examining left and right differences, the differences in the number of trabecular were significantly larger ($p<0.05$) in P group than in N group in the non-differentiated arthritis patients (UA). P group was further divided into two groups of UA and rheumatoid arthritis patients (RA) and compared. In RA, the cortical bone porosity was significantly stronger ($p<0.01$) than UA, a tendency to decrease the trabecular bone area ($p = 0.07$), a significant decrease in trabecular bone density ($p<0.05$). [Conclusions] In the study, P group showed enhanced cortical bone porosity and decreased trabecular, especially RA of P group. On the other hand, in UA of P group, the difference in the number of trabecular bilateral was observed, suggesting the effect of ACPA on the trabecula.

W30-6

Bone microstructure analysis of metacarpal head of rheumatoid arthritis 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 is mainly used of osteoporosis, but in recent years it has been applied of rheumatoid arthritis (RA). The purpose of this study is to analyze bone microstructure of metacarpal

head of RA patients by HR-pQCT. [Methods] 18 patients with RA (69.2 ± 8.0 years old, 14 females, 4 males) 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. In a total of 36 regions, Tb.vBMD, BV/TV, Tb.Th, Tb.N, Tb.Sp, SMI, Conn.D, DA were analyzed. [Results] Tb.vBMD was 131.4 ± 50.1 mg/cm^3, BV/TV was 24.0 ± 8.0%, Tb.Th was 213.1 ± 31.4 μm, Tb. N was 0.95 ±0.19 1/mm, Tb.Sp was 469.9 ± 56.6 μm, SMI was 1.68 ± 0.52, Conn.D was 4.57 ± 1.03 1 /mm^3, DA was 1.23 ± 0.09. [Conclusions] The bone microstructure of the metacarpal head of RA patients was analyzed by HR-pQCT. Three-dimensional quantification such as thickness, number and connectivity became possible, and it would be useful to understand periarticular osteoporosis by RA. In future, it is expected to be applied to pathophysiological analysis and drug efficacy analysis.

W31-1

Pregnancy outcome of rheumatoid arthritis patients who had received etanercept during pregnancy

Mikako Goto[1,2], Ken Nakajima[1,3], Chinatsu Takai[2], Shuko Mishima[2], Kayoko Kaneko[2], Misato Kawakami[1], Omi Watanabe[1], Atsuko Murashima[1,2]

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Conflict of interest: None

[Object] Analyze the pregnancy outcome of rheumatoid arthritis (RA) patients who received etanercept during pregnancy. [Methods] Our analysis was consisted of two cohorts. One cohort was patients who had consulted to Japan Drug Information Institution of Pregnancy during the establishment of the institution (2005) to Oct 2017. Another cohort was registration data of pregnant patients with RA. since 2012. We evaluated the patients who used etanercept during the first trimester. [Results] The total number of patients was 136. Outcome of them were 111 live births, 1 stillbirth, 6 spontaneous abortion, 0 elective termination and 18 loss of follow up. Three fetus had congenital anomalies (2 ventricular septal defect and 1 subvalvular pulmonary stenosis). [Conclusions] Our analysis showed that use of etanercept in the first trimester, will not increase the abortion and congenital anomalies rate. Limitations are the relatively small number of patients analyzed and absence of control cohort who had RA but did not take etanercept.

W31-2

The biological drugs increase the pregnancy and delivery in japanese patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To know pregnancy and parturition in women who had rheumatoid arthritis (RA) in forty years old or younger, we report the survey about marriage, pregnancy and parturition in japanese patients with RA. [Methods] In Simosizu hospital, 197 japanese women with RA were researched about their marriage, pregnancy and parturition. [Results] 160 patients were married. 135 patients (84.4%) experienced a total of 274 pregnancies. Outcome of their pregnancies were 231 childbirths (195: before developing RA, 36: after having developed in RA), 40 miscarriages, ectopic pregnancy, 2 stillbirths. After their delivers, 33 patients became RA (32 childbirth, 1 miscarriage), 10 patients became aggravation of RA, 1 patient. Twelve of 36 childbirths (after having developed in RA) were in 8 patients treated with biological drugs. They occupied 33.3% of childbirth after developing RA and 80% of them after biological drugs became available to RA. [Conclusions] Patients with RA had few pregnancies and delivers. But, Biological drugs resolve this problem.

W31-3

Tacrolimus concentrations during pregnancy and lactation in the patients with systemic lupus erythematosus

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Conflict of interest: None

Objectives: The purpose of this study was to investigate whether tacrolimus (TAC) blood concentration changes during pregnancy and lactation in the patients with systemic lupus erythematosus (SLE). Methods: We retrospectively analyzed TAC concentrations in SLE patients with TAC during pregnancy. We monitored TAC trough levels and SLE disease activity before pregnancy. After pregnancy, we monitored TAC trough levels and SLE disease activity monthly. TAC concentrations were also analyzed maternal blood at delivery, umbilical cord blood. Breast milk of TAC concentration was assessed before, and after 3 and 12 hours TAC administration. We also determined whether TAC concentrations affect SLE disease activity during pregnancy. Results: Twenty-one patients with 25 pregnancies were included. The mean age was 32.5 years, 19 cases were treated with TAC before pregnancy. The mean TAC dose during pregnancy was 2.3 mg/day. We found that TAC concentration at second trimester was significantly lower than before pregnancy ($p<0.0001$). TAC concentration was not affected SLE disease activity during pregnancy. The mean cord blood/maternal blood concentration ratio was 0.715 (0.36-1.00). Relative infant dose was 0.013-0.071%. Conclusions: TAC concentration was decreased during pregnancy.

W31-4

Importance of Preconception Care (PCC) for pregnancy with Lupus Nephritis (LN): experience at a single center in Japan

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Conflict of interest: None

Pregnancy with LN is tend to perinatal complications such as HDP, preterm birth, FGR and PROM. These risks are increased if active nephritis or hypertension is present during pregnancy, so EULAR recommends PCC. The aim of this study to reveal pregnancy outcomes in LN with and without PCC. 27 women 32 cases got live birth; 19 women 21 cases were PCC group, and the others were non-PCC group. In the PCC, 5 of 6 women who required treatment for LN before pregnancy were permitted next pregnancy with immunosuppressants. Treatment at the conception was steroid 20 (PCC 11, non-PCC 10), steroid with immunosuppressants 11 (10, 1), none 1 (PCC). Although there was no difference between PCC and non-PCC in the amount of steroid, age, delivery weeks, and birth weight, all 3 cases who flared nephritis and required to treatment during pregnancy were in non-PCC. Preterm birth was 17, PCC 13 (<34 weeks 6: PROM 3, HDP+renal dysfunction 1, FGR+abruptio placentae 1, FGR assosiated with APS 1), non-PCC 4 (3: HDP 1, PROM+HDP 1, uterine rupture after caesarean section 1). We support for next pregnancy throughout evaluating and managing the disease activity, APS, renal function, hypertension, and so on. There was no exacerbation of LN during pregnancy in PCC group, so PCC is very important for LN patients.

W31-5

Creatinine/Cystatin C ratio; A new biomarker for evaluation of muscle mass and strength in patients with rheumatoid arthritis - A study based on KURAMA cohort -

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Conflict of interest: None

[Object] Rheumatoid arthritis (RA) patients are prone to lose muscle mass and muscle strength (MM/MS) due to chronic inflammation and physical disability. We aimed to identify a useful biomarker in daily practice to evaluate MM/MS, and further analyzed the influence of RA treatment on MM/MS. [Methods] MM/MS data of 331 RA patients were collected from KURAMA cohort 2014. The data was analyzed with several possible biomarker candidates. 3-year longitudinal MS data was available in 106 out of 331 patients. Rate of change of MS in 3 years was analyzed with the biomarker and RA treatments. [Results] Among the biomarker candidates, Creatinine/Cystatin C ratio (Cre/CysC) showed the highest correlation with MM/MS (MM:ρ=0.44, $p<0.001$, MS:ρ=0.47, $p<0.001$). Longitudinal analysis resulted in decrease of MS in 85±24% in treatment group with non-bDMARDs, while MS change was 112±41% with TNF inhibitor (TNF-i), 101±22% with IL-6 inhibitor and 92±46% with CTLA4-Ig. Multivariate analysis showed that MS change correlated with DAS28-ESR (p=0.008) and TNF-i treatment (p=0.005). Cre/CysC also showed similar tendency as MS change. [Conclusions] Cre/CysC is a useful biomarker to evaluate MM/MS in RA patients. Improving disease activity and treatment by TNF-i have potential in increasing MM/MS.

W31-6

The correlation between lower limb load bearing axis and foot deformity in rheumatoid arthritis

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Conflict of interest: None

[Object] RA patients have risk of lower limb joint deformity and it is important to understand the pathology of foot deformity in the whole lower limb alignment. Then we examined how the load axis in the proximal from hindfoot is related to foot deformity. [Methods] We examined the relationship between mechanical ankle joint axis point (MAJA) and the parameters in hind-, middle- and forefoot [TCA, pronated foot index (PI), HVA, M1M2A, M1M5A, M2M5A] in 66 limbs of RA who underwent X-rays including HC view. [Results] MAJA was correlated with TCA, HVA and PI (r=0.52, 0.25, -0.38). Then MAJA was positively correlated with M1M2A (r=0.38), while it was negatively correlated with M1M5A and M2M5A (r=-0.19, -0.61), and TCA was negatively correlated with M2M5A (r=-0.26) [Conclusions] Lateralization of MAJA was correlated with hindfoot valgus deformity and related to the navicular valgus deformity, increasing HVA and decreasing spread foot. It was unclear that MAJA depended on or led to hindfoot valgus deformity. Then, MAJA was related to mid- and forefoot deformity. It was thought that inversion gait due to the hindfoot deformity led to increasing loading to the hallux and HVA, and decreasing loading to lesser toe and M2M5A, or forefoot deformity led to hindfoot deformity.

W32-1

The usefulness of the database for ultrasonography in rheumatoid arthritis. (Follow-up report) Application to joints other than fingers and wrist joint

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Conflict of interest: None

[Object] We have reported the usefulness of Filemaker database (FMDB) for joint ultrasonography (JUS) in rheumatoid arthritis (RA). We developed JUS application linked with new ordering system (ODS) along with medical system update in our hospital. We report on the effects of application to JUS other than fingers/wrist joints. [Methods] Following the input interface of FMDB, we developed new application which added input items of elbow/shoulder/knee/foot/toe joints with ODS management company. [Results] We have about 2,000 fingers/wrist JUS examinations per year, and JUS examinations of other than fingers/wrist joints also increased year by year. In conjunction with the ODS reservation system, JUS examination appointment frame setting has been automated, making it unnecessary to create a new record which had been prepared in the past. By converting JUS other than fingers and wrist joints into DB, information on RA cases without findings in fingers/wrist joints was also unified. [Conclusions] By developing a new application in cooperation with ODS, we could construct JUS-DB that was easy to introduce even under the same medical system of other hospital. The meaningful introduction of JUS-DB including elbow/shoulder/knee/foot/toe joints simplified the statistical reuse.

W32-2

Reduced atherosclerosis in mice with conditional deletion of Spleen tyrosine kinase

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Conflict of interest: None

[Background] Atherosclerosis is mediated by chronic inflammatory processes along with altered lipid metabolism. Spleen tyrosine kinase (Syk) serves downstream signaling of various cell surface receptors. Previous reports showed that Syk inhibitor prevented atherosclerosis in mice. Because of possible off-target effects of the pharmacological intervention, we would like to address whether Syk plays role in atherosclerosis in mice by utilizing Syk deficient mice. [Methods] We generated $Syk^{flox/flox}Rosa26CreER^{(T2)+/+}LDLR^{-/-}$. The Syk was knocked out by the oral administration of tamoxifen. Syk^{del}/del $LDLR^{-/-}$ received high-fat diet for 16 weeks. Then, we measured the volume of atherosclerosis lesions of aortic sinus and the ratio of atherosclerosis lesions to the whole aortic area. [Results] The ratio of area of atherosclerosis in aorta was in $Syk^{del/del}LDLR^{-/-}$ (2.6±0.4 %) [n=11] was significantly lower than that in $SYK^{+/+}LDLR^{-/-}$ (7.5±1.1 %) [n=9] [$p<0.01$]. The volumes of atherosclerosis lesions in aortic sinus in $Syk^{del/del}LDLR^{-/-}$ (0.09±0.01 mm^3) [n=15] was significantly lower than that in $SYK^{+/+}LDLR^{-/-}$ (0.14±0.01 mm^3) [n=16] [p=0.046]. [Conclusion] The atherosclerosis of aorta and aortic sinus in Syk conditional deficient mice was significantly decreased.

W32-3

A retrospective study on Treatments for TAFRO syndrome

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Conflict of interest: None

TAFRO syndrome is a rare systemic inflammatory disorder characterized by thrombocytopenia, anasarca, fever, renal insufficiency, and organomegaly. A total 216 cases of TAFRO syndrome, multicentric Castleman disease, and similar conditions have been registered in the Multicenter Retrospective Study of TAFRO Syndrome (UMIN000011809) between October 2013 and October 2017. Among them, 80 cases were fulfilled the diagnostic criteria for TAFRO syndrome. In this study, we retrospectively analyzed the efficacies of various treatments performed for this syndrome. The median age at onset was 53, and 44 were male. All patients received corticosteroids, but only 20% responded to this monotherapy, and secondary treatments were performed in the majority of them. Of the other therapeutic agents used, tocilizumab was used in 33 cases and it was effective in 14 cases (42%), cyclosporine was used in 29 cases and it was effective in 20 cases (68%), and rituximab was used in 13 cases and it was effective in 8 cases (61%). Twenty cases (25%) have died after the failure of these treatments. Thus, tocilizumab, cyclosporine, and rituximab were identified as potentially effec-

tive agents for this syndrome. This study also revealed the high mortality rate of this disorder.

W32-4

Effectiveness of immunoadsorption therapy for HPV vaccine-related neuroimmune dysfunction syndrome (HANS)

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Conflict of interest: None

[Object] To examine whether immunoadsorbance plasmapheresis (IAPP) using Human TR-350 is effective against HANS [Methods] Five girls (average age 18 years old, average age from appearance of vaccination to symptom appearance on average 9.8), which were symptoms unstable due to medication immunotherapy and the social life was difficult and IAPP consent was obtained Monthly symptoms became stratified and daily life was difficult to 15 months), a total of 6 IAPPs were implemented with target of plasma treatment volume of about 1.0 L. [Results] Average plasma throughput was 0.9 L on average. Improvement was found in HANS's core symptoms such as pain, disapproval of stature, learning ability disorder, movement disorder of the hand, and loss of vision. Especially pain decreased in all cases and decreased from 10 to 2.6 on the face scale. However, in 2 cases, symptoms recurred after about 1 to 2 months and again required adsorption therapy. Two cases showed macroscopic hematuria and abdominal pain from hemolysis accompanying poor blood loss. [Conclusions] Functional recovery was seen by IAPP than removal of any antibody associated with HPV vaccine. However, there are cases where it recurs and it is necessary to consider maintenance therapy after IAPP.

W32-5

Immune checkpoint inhibitors induced arthritis as immune-related adverse events

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Conflict of interest: None

[Background] Immune checkpoint inhibitors dramatically changed treatment of advanced cancers. However, it sometimes induces various kinds of immune-related adverse events (irAEs). Here I report arthritis as irAEs [Case 1and 2] A 56 year-old man with rheumatoid arthritis (RA) and a 79 year-old woman with RA were treated with Nivolumab for lung cancer. Their arthritis flared up after administration of Nivolumab, however they could to continue Nivolumab with temporally use of low dose corticosteroids. [Case 3] A 69 year-old man developed palmar flexor tenosynovitis after administration of Nivolumab. 20mg of daily prednisolone improved his arthritis. [Case 4] A 67 year-old man developed large joint of arthritis after administration of Nivolumab. After discontinuation of Nivolumab arthritis gradually resolved. [Case 5] A 78 year-old man developed psoriasis like rash and shoulder arthritis after administration of Pembrolizumab. Low dose of corticosteroids provided sufficient relief of rash and arthritis. [Conclusion] Immune checkpoint inhibitors sometimes induce arthritis, but it could be well controlled with low dose corticosteroids.

W32-6

A case report of disseminated gonococcal infection with difficulty in distinguishing from rheumatoid arthritis (RA)

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Conflict of interest: None

A 20-year-old woman visited her previous doctor, who prescribed antibiotics, with pharyngalgia, fever, exanthema and arthralgia. She was referred to our hospital for further examination and treatment, as no improvement was observed with joint steroids injection and oral steroids. Albeit an addition of Sapazosulfapyridine, she required hospitalization with polyarthritis. Arthrocentesis revealed 27000 cells/mm^3 and haematoid cloudy joint fluid. Its Gram stain and culture were negative. Due to progression of her hip joint destruction in MRI as well as negative autoantibodies and infection tests, seronegative RA was considered, which resulted in Methotrexate use and consideration of biological preparation. However, as bacterial phagocytosis, neutrophils and Gram-negative diplococci were identified in the reconfirmed joint puncture smear and the Gram stained specimen, she was diagnosed with gonococcal arthritis. In addition to detection of Gonococci with culture and its DNA exams, distinguishing gonococcal arthritis from RA by imaging is difficult. As seen in this case, diagnosis could be more complicated with previous treatment. Therefore, besides appropriate history taking, aggressive specimen collection and therapeutic diagnosis by antibiotics are required in suspicious cases.

W33-1

The long-term outcome of interstitial lung disease with anti-MDA5-antibody

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Conflict of interest: None

[Background] Interstitial lung disease associated with anti-MDA5-antibody (MDA5-ILD) sometimes deteriorates acutely, so called "rapidly-progressive ILD (RP-ILD)". However, some cases exhibit chronic or recurrent clinical courses. [Methods] We collected the medical charts of MDA5-ILD patients preformed remission induction therapy in our hospital. [Results] Number of the MDA5-ILD patients were 23. Sixteen cases were performed "triple therapy" using glucocorticoid, calcineurin inhibitor and cyclophosphamide. Three cases died of RP-ILD within six months even with triple therapy. Their KL-6 and ferritin elevated remarkably, reflecting activity of RP-ILD. Four cases died of infection after six months from the start of triple therapy. The transitions in serum ILD markers of the 4 cases were not different from those of survivors. Seven cases were survived even without triple therapy. In survival cases, the durations required for serum ILD marker normalization were 25.1±21.7 weeks in KL-6 and 20.3±15.4 weeks in ferritin. In 4 cases of survivors without triple therapy, KL-6 rose up again despite of maintenance therapy, resulting in glucocorticoid dose up. [Conclusions] Triple therapy for MDA5-ILD may be necessary for not only rescuing RP-ILD but also preventing disease recurrence.

W33-2

The Risk Factors for Opportunistic Infection during Treatment for Polymyositis/dermatomyositis

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Conflict of interest: None

[Object] Although concomitant infection are the predominant causes of death in patients with polymyositis (PM)/dermatomyositis (DM), intensive immunosuppressive therapy are necessary forsevere cases. Here we investigated the predictive risk factors for opportunistic infection by assessing cytomegalovirus (CMV) antigen test as a barometer for immunocompromised status. [Methods] We retrospectively analyzed clinical data, treatment regimen, and clinical outcomes including CMV antigenemia in the patients with PM/DM who had received initial treatment at six hospitals affiliated to Yokohama City University from 2003 to 2016. [Results] One hundred eighty-eight patients (PM 50, DM 92, and clinically amyopathic DM (CADM) 46) were recruited. The mean age was 56 ± 16 years and 136 (72%) were female. Fortynine patients (30%) had CMV antigenemia within 6 months from initiation of treatment. A multivariate analyses revealed that low PaCO2 (OR 0.67, p = 0.041), old age (OR 1.09, p = 0.040) and treatment with calcineurin inhibitors (OR 7.30, p =0.006) were independent risk factors for CMV antigenemia. [Conclusions] Appropriate monitoring for opportunistic infection is important, especially in patients who have low PaCO2 level and receive treatment with a calcineurin inhibitor.

W33-3

Clinical significance of anti-ARS antibodies which are positive by ELISA but not by immunoprecipitation

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Conflict of interest: None

[Background] After the ELISA for anti-aminoacyl tRNA synthetase (ARS) have been utilized in daily practice, we sometimes encounter patients that are positive for anti-ARS by ELISA but not by RNA immunoprecipitation (RNA-IP). We analyzed these cases and validated anti-ARS-positivity in other methods. [Methods] We examined medical records of patients who visited to our department from 2014 to 2017. In 1628 samples, we found 134 samples (78 cases) to be positive for anti-ARS by ELISA (MESACUP™) which were subsequently analyzed by RNA-IP. Some of the samples which showed discrepant results (ELISA positive, RNA-IP negative) were further analyzed by individual antigen-specific ELISA and protein-IP. [Results] In 17 who showed discrepant results, 15 had interstitial lung disease (ILD), but only 6 had myositis. Within 7 who analyzed by specific ELISA, anti-Jo1, anti-EJ and anti-KS were detected in 4, 2 and 2, respectively. Protein-IP showed the same result with antigen-specific ELISA in 5, but no antigen was immnoprecipitated in 2 cases. [Conclusion] Some anti-ARSs may recognize denatured ARSs and seem to associate strongly with ILD rather than myositis. Further accumulation and follow-up of such patients are needed to conclude whether they show some part of anti-synthetase syndrome.

W33-4

Transcriptome analysis of immune cell subsets in PBMCs to elucidate the pathophysiology of idiopathic inflammatory myopathies

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Conflict of interest: Yes

Object: Although type 1 IFN signature is presumed to relate to idiopathic inflammatory myopathy (IIM), the etiology is still unknown. To elucidate IIM pathophysiology, we performed RNA-seq of 17 immune cell subsets in PBMCs from IIM patients. Methods: 22 IIM patients and 32 healthy controls were picked up. The details of 22 IIM cases were as follows: 6 polymyositis, 15 dermatomyositis and 1 necrotizing myopathy. With 11 anti-ARS antibody and 2 anti-MDA5 antibody, 15 cases had interstitial pneumonia (IP) and 15 cases were in remission. 17 immune cell subsets in PBMCs were sorted by flow cytometry. Results: In IIM, plasmablast (PB), Th17 and CD16-negative monocyte increased, and only in exacerbation phase unswitched memory B cell decreased. Although the number was relatively low, Th17, Th2, Tfh and CD16-positive monocyte had more DEGs than other subsets. Pathway analysis showed genes related to mitochondrial dysfunction and oxidative phosphorylation were upregulated in Th17, Th2 and Tfh. Conclusions: Type 1 IFN-regulated genes did not increase significantly in PBMCs, suggesting it works locally in muscle. A group of IIM with high subset ratio of PB appears to show characteristic DEGs. More cases recruitment is needed for the analysis of IIM subtypes like antibody and IP profile.

W33-5

Minimally invasive muscle biopsy for patients with polymyositis and dermatomyositis

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Conflict of interest: None

[Object] While muscle biopsy is crucial to diagnose polymyositis/dermatomyositis (PM/DM), it has not been frequently performed in Japan because of its invasiveness. Minimally invasive muscle biopsy with conchotome is widely used in Scandinavian countries. Tibialis anterior (TA) had been reported to be suitable for this technique with utility and safety. In this study, we introduced the technique in Japan and evaluated its efficacy. [Methods] Minimally invasive muscle biopsy was performed in 12 cases suspected PM/DM clinically. Four or 5 muscle specimens, which were 3 mm in diameter, were obtained from 1 cm incision of the skin and muscle fascia on TA. Presence of necrotic fibers with infiltrating cells were evaluated as biopsy positive. [Results] MMT on TA were over 9/10 in all participants. Median serum CK levels was 2,176 IU/L. In two patients who underwent lower leg MRI, no significant finding was observed. Ten biopsies including the two from MRI negative cases were evaluated as histologically positive. All participants were diagnosed as PM/DM. [Conclusions] Positive biopsy rate in our study was comparable to previous reports with this technique. Regardless of other clinical features at biopsy site and sample size, minimally invasive muscle biopsy should be useful for PM/DM.

W33-6

Prognostic factors and treatment for interstitial pneumonia associated with anti-MDA5-positive amyopathic dermatomyositis

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Conflict of interest: None

[Object] It is currently recognized that anti-MDA5-positive amyopathic dermatomyositis (ADM) has a high mortality rate. However, its associated prognostic factors and optimal treatment strategies remain to be determined. [Methods] Here we analyzed retrospectively the clinical features and survival of 18 consecutive patients with anti-MDA5-positive ADM. HRCT images were evaluated for consolidation, ground glass opacities, traction bronchiectasis, bronchovascular bundle thickening, honeycombing, pleural effusion and mediastinal emphysema. [Results] We found that in patients who died, CRP and LDH levels were elevated and Alb and PaO2 were decreased relative to those in patients who survived. HRCT demonstrated consolidation, pleural effusion and vertical

emphysema predominantly in the patients who died. CsA was used in 5 cases and Tac in 13. The mortality rate was 60% and 38.4% in patients who received CsA and Tac, respectively. Plasma exchange (PE) was performed in 5 patients, all of whom died. [Conclusions] These observations indicate that prognostic factors in patients with anti-MDA5-positive ADM are consolidation, pleural effusion and mediastinal emphysema demonstrated by HRCT, as well as PaO2, CRP, LDH and Alb. We were unable to demonstrate the effectiveness of PE in this study.

W34-1

Identification of novel autoantibody in the synovial fluid of knee joint from patients with rheumatoid arthritis

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Conflict of interest: Yes

[Background] Rheumatoid arthritis (RA) is a chromic, autoimmune and inflammatory joint disease with a poorly understood etiology. Despite widespread diagnostic use of anti-citrullinated protein antibodies and rheumatoid factor, there is strong demand for novel biomarkers to improve the diagnosis this disease. [Objectives] The purpose of present study is to investigate novel autoantibodies in the synovial fluid of RA patients. [Methods] By using SEREX (Serological identification of antigens by recombinant cDNA expression cloning), we identified ten and several antigens from sera of RA patients. Synovial fluid of the knees was obtained from 48 RA and 48 osteoarthritis (OA) patients. Furthermore, AlphaLISA (Amplified Luminescence Proximity Homogeneous Assay) was used to analyze the antibody levels in synovial fluid using synthetic polypeptides as antigens. [Results] Significantly higher proportion of antibodies against lamin A (LMNA, $p<0.0000001$) and cell growth-regulating nucleolar protein (CGRN, $p<0.0000001$) were found in synovial fluid of RA as compared with OA. [Conclusions] We identified two novel autoantibodies in the knee synovial fluid of RA patients. These antibodies would have the potential to become diagnostic biomarkers and may play a critical role of pathogenesis of RA.

W34-2

Smoking is only factor affecting the change of the titer of anti-CCP-antibody in patients with rheumatoid arthritis

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Conflict of interest: None

Purpose: Anti-cyclic citrullinated peptide antibodies (CCPab) are known as useful markers for the diagnosis of rheumatoid arthritis (RA), but there were few reports on longitudinal analysis of it. In this study we analyze the affecting factor of changes of the titer of CCPab and relationships with bone mineral density (BMD). **Methods:** We analyzed 7-years date from the TOMORROW study, which is a 10-years prospective cohort for age and sex matched RA (n=208) and volunteers (Vo) (n=213). The titer of CCPab was measured five times and BMD was three times. The evaluation factor was time, sex, smoking, presence of RA, the use of bDMARDs, Disease activity score 28-CRP (DAS28) and MMP-3. All analysis was used by the mixed model linear regression. **Results:** In the longitudinal analysis of CCPab, there were significant positive correlations in time, RA and smoking in analysis for all patients, no significant correlations for Vo, and significant correlations in time and smoking not in bDMARDs, MMP-3 or DAS28 for RA. For analysis of BMD, there were only significant correlations between CCPab and BMD of thoracic spine. **Conclusions:** Longitudinal analysis of 7-years date from the TOMORROW study shows the possibility the titer of CCPab was increased by smoking regardless of disease activity of RA.

W34-3

Autoantibodies against Amyloid b-40 peptide in ACPA negative rheumatoid arthritis patients are high

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Conflict of interest: None

[Object] It is well known that various autoantibodies exist at high concentrations in the blood of rheumatoid arthritis (RA) patients. We developed an ELISA method using Amyloid-β peptide (Aβ-40) as an antigen (J Neurol Neurosurg Psychiatry 2017) and clarified that Amyloid-β autoantibodies are high in RA patients. In this study, we examined the relationship with ACPA negative RA. [Methods] The subjects were 174 patients with joint pain, 106 patients (age 55.6 ± 14.9 years) diagnosed with RA and 68 cases of unknown arthritis (UA) (59.5 ± 13.4 years old). [Results] The concentration of anti-Aβ-40 antibody was 17.0 ± 2.3 u in RA group, 11.2 ± 0.95 u ($p<0.02$) in UA group, and 8.3 ± 0.87 u ($p<0.002$) in healthy subject group. The concentration was significantly higher in the RA group. There was no correlation between ACPA and anti-Aβ-40 antibody ($r = 0.028$). However, the concentrations of anti - Aβ-40 antibody were high in ACPA negative RA patients. [Conclusions] Although no clear correlation was found between the titer of ACPA and the anti-Aβ-40 antibody value, anti-Aβ-40 antibody tended to be higher with ACPA negative RA. It was suggested that anti-Aβ-40 antibody might be involved as a factor in the onset of RA.

W34-4

Relation of respiratory disorders to anti-CCP antibody (ACPA) in patients with rheumatoid arthritis (RA)

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Conflict of interest: None

[Object] ACPA becomes positive before the onset of RA, and has been suggested to relate to the development of RA. Mori et al. reported the precise analysis between pulmonary disorders (PD) and ACPA (ARD 2012). We here studied the relation from reverse direction. [Methods] Subjects were 448 patients with RA, with the mean age of 59 years (15 - 90). Inclusion requirements were chest CT to evaluate PD at the first visit and measurement of ant-CCP Ab (ACPA). Relations among many factors were analyzed. [Results] In 448 patients, the prevalence of ILD, bronchiectasis (BE), and bronchiolitis (BRN) were 27.7%, 26.8%, and 19.2%, respectively, and prevalence of any PD was 42.8%. Median value of ACPA titer was 60.2 U/ml (0.4 - 6823). When it was divided into 4 according to PD, the median values in ILD group, BE group, BRN group and no-PD group were 125.5U/ml, 189U/ml, 78U/ml, and 27U/ml, respectively. Significant differences were found between ILD and no-PD, and BE and no-PD. The degree of PD (ILD and BE/BRN) significantly correlated with ACPA titer. Logistic regression analysis revealed that significant risk factors related to high ACPA titer (more than 175) were presence of BE or BRN. [Conclusions] It was suggested that pre-existence of airway disorder induces high ACPA titer.

W34-5

Relation of respiratory disorders to RF in patients with rheumatoid arthritis (RA)

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Conflict of interest: None

[Object] RF becomes positive before the onset of RA, and has been suggested to relate to the development of RA. We here studied the relation of pulmonary diseases (PD) to RF in RA. [Methods] Subjects were 448 patients with RA, with the mean age of 59 years (15 - 90). Inclusion requirements were chest CT to evaluate PD at the first visit and measurement of RF. Relations among many factors were analyzed. [Results] In 448 patients, the prevalence of ILD, bronchiectasis (BE), and bronchiolitis (BRN) were 27.7%, 26.8%, and 19.2%, respectively, and prevalence of any PD was 42.8%. Median value of RF value was 50.4 U/ml (0 - 2102). When it was divided into 4 according to PD, the median values in ILD group, BE group, BRN group and no-PD group were 100U/ml, 80U/ml, 58U/ml, and 33U/ml, respectively. Significant differences were found between ILD and no-PD, and BE and no-PD. The degree of PD (ILD and BE/BRN) significantly correlated with RF value. Logistic regression analysis revealed that significant risk factors related to high RF values (more than 180) were presence of BE, BRN, high ILD grade, and DAS-28ESR. Significant correlation was found between values of RF and anti-CCP Ab. [Conclusions] It was suggested that pre-existence of PD induces high RF value.

W34-6

Implications of anti-aminoacyl-tRNA synthetase antibodies in Sjögren's syndrome-associated interstitial lung disease

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Conflict of interest: None

[Object] The clinical features of interstitial lung disease (ILD) in autoimmune diseases, such as scleroderma or myositis, are known to be related to their disease-specific autoantibodies. Whereas, Sjögren's syndrome (SS) often be concurrent with other autoimmune condition, so it is still difficult to capture the essence of the SS-associated ILD (SS-ILD). Indeed, anti-aminoacyl-tRNA synthetase (ARS) antibodies can coexist with anti-SS-A antibodies. The purpose of this study was to investigate the clinical implications of anti-ARS antibodies in ILD with primary SS (pSS). [Methods] We retrospectively studied the clinical characteristics and autoantibody profile in consecutive 304 cases with SS from September 2014 at 2 hospitals. [Results] Of the 304, 59 patients showed both positive for anti-SS-A antibodies and ILD. Among them, 52 patients (including 20 pSS) were tested for anti-ARS antibodies and 7 patients (including 5 pSS) were positive. In 5 of them, myositis symptoms were absent or delayed from the occurrence of SS and ILD, and anti-ARS antibodies were detected later. [Conclusions] Five of the 20 (25%) patients with pSS-associated ILD were positive for anti-ARS antibodies. It is suggested that anti-ARS antibodies may have been involved in some cases considered as SS-ILD.

W35-1

Effects of tocilizumab on large joint in patients with rheumatoid arthritis. -Two-year follow up-

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Conflict of interest: Yes

[Objective] The purpose of this study is to assess effects of tocilizumab (TCZ) on large joint in patients with rheumatoid arthritis (RA). [Patients and Methods] 230 large joints in 20 patients were evaluated at baseline and at 1 and 2 years of TCZ treatment. Increase in more than 1 point of ARASHI change score was considered as progression of joint damage. [Results] Five shoulder joints, 3 elbow joints, 1 hip joint, 4 knee joints and 3 ankle joints showed the progression of joint damage during 2 years of TCZ treatment. On the other hand, 3 shoulder joints showed radiographic repair. Patients with joint damage progression had higher disease activity after TCZ treatment in comparison with patients without progression of damage. [Conclusions] The use of TCZ inhibited progression of joint destruction in certain large joints. However, joints of patients with inadequate control might show radiographic deterioration.

W35-2

The prognostic factor to achieve long term structural remission with RA treated with Tocilizumab

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Conflict of interest: None

[Background] There is a scarcity of reports about Tocilizumab (TCZ) therapy in RA patients with prognostic factor of long term efficacy. We analyzed association with long term radiological progression and clinical efficacy with RA receiving TCZ. [Methods] 26 patients included in this study. Disease activity was assessed using Clinical Disease Activity Index (CDAI). Joint damage scores were assessed using the van der Hiejde modified total Sharp score (mTSS) at baseline and 104 weeks (structural remission:ΔmTSS$\leqq$0.5, radiologic progression:ΔmTSS>0.5). [Results] Mean disease duration was 7 years. Mean age was 60 years. 19 patients were naïve to biologics. Concomitant medications included MTX in 23 patients. Radiologic remission rate was 73 % at 104 weeks. ΔmTSS with the patients who achieved clinical remission until 24 weeks was significantly lower than ΔmTSS with the patients who didn't achieve clinical remission until 24 weeks ($P<0.01$). Structural remission rate at 104 weeks with low MMP-3 titer group (MMP-3<230 ng/mL) were higher compared with high MMP-3 titer group (MMP-3>230 ng/mL). [Conclusions] This study demonstrates good long term radiologic outcome of TCZ in RA patients with low MMP-3 titer at baseline and achieved clinical remission until 24 weeks.

W35-3

Factors related to achievement at remission / low disease activity at 6 months of golimumab 50mg every 4 weeks therapy for patients with rheumatoid arthritis using RA database of FIT-RA registry

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Conflict of interest: Yes

[Objective] To investigate the factors related to achievement at remission or low disease activity (LDA) at 6 months of golimumab (GLM) 50mg every 4 weeks therapy for patients with rheumatoid arthritis. [Materials and methods] Seventy two RA patients treated by GLM 50mg every 4 weeks were extracted from FIT (Fukui, Ishikawa, Toyama)-RA database of multi-center study group in Hokuriku area. Forty three patients achieved at remission or LDA at 6 months of GLM therapy (R/L group). On the other hand, 29 patients showed moderate or high disease activity (M/H group). We compared R/L group and M/H group, and performed multivariate analysis to detect factors related to achievement at remission or LDA at 6 months. [Results] Dose of corticosteroid and value of rheumatoid factor at baseline were significantly lower in R/L group compared with M/H group. Moreover, the value of DAS28-CRP at baseline and 3 months were significantly lower in R/L group compared with M/H group.

Multivariate analysis indicated DAS28-CRP at 3 months (Cut off point: 2.63) after initiation of GLM therapy as independent factor of achievement at remission or LDA at 6 months. [Conclusion] When the patients with inadequate response of GLM 50mg every 4 weeks therapy, it might be necessary to enhance the treatment for RA.

W35-4

Efficacy of adding iguratimod therapy in rheumatoid arthritis patients who had inadequate response to biologic DMARDs

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Conflict of interest: None

[Object] 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] Subjects were 90 patients adding IGU who had inadequate response to Bio from August 2012 to March 2017. Previous treatment Bio. was ADA. And baseline mean concomitant MTX was 12.5 mg/week). And baseline characteristics were Mean age 53 years, mean duration of illness 5.7 years, corticosteroid use 8.9% (mean 2.8mg/day). The course of DAS28, SDAI, CDAI and remission rates were analyzed. [Results] Mean DAS28-ESR, SDAI, CDAI were significantly decreased from the initiation of IGU treatment at 24 weeks (3.12→2.26, 7.41→2.63, 6.70→2.29). Remission rates of DAS28-ESR, SDAI, CDAI were 70%, 71.1%, 72.2% at 24 weeks. There were almost no side-effect after adding IGU. [Conclusions] IGU might be a new RA treatment option for aiming remission in patients who had inadequate response to Bio.

W35-5

Middle term efficacy of iguratimod in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To assess the middle-term outcome of IGU therapy in patients with RA [Methods] Sixty-nine RA patients (14 males and 55 females) were enrolled in this study. Patients were divided into 3 groups: IGU group, Methotrexate plus IGU group, and biologics (Bio) plus IGU group. The differences of clinical course during three groups and predictive factors associated with low disease activity (LDA) were analyzed statistically. [Results] The survival rate of IGU at three years was 40.6%. Eight patients discontinued the IGU therapy due to insufficient response, 13 patients due to adverse events, eight patients added-on other drugs such as tacrolimus or Bio. Disease activity was significantly decreased among three groups compared with baseline. Thirty eight patients (55.1%) were in LDA at three years. A multivariate logistic regression analysis indicated that gender, the use of prednisolone (PSL) and DAS28-CRP at baseline were significant factors contributing to the achievement of LDA at three years. [Conclusions] We assessed middle-term outcome of the IGU therapy in RA. IGU was effective for monotherapy or combination therapy with MTX or Bio. The low DAS28-CRP, low usage rate of PSL, low percentage of male patients were significant factors of LDA achievement.

W35-6

Changes in serum IL-6 levels correlate with therapeutic efficacy of iguratimod in rheumatoid arthritis patients

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Conflict of interest: Yes

[Object] NFκB activation increases expression of several cytokines including IL-6 in rheumatoid arthritis (RA). The activated NFκB binding to the IL-6 promoter sites upregulates IL-6 gene expression. Iguratimod (IGU) inhibits NFκB activation *in vitro.* Thus, we investigated whether serum IL-6 levels would correlate with therapeutic efficacy of IGU in RA patients. [Methods] Forty-four RA patients treated with biologic (22 patients) or non-biologic DMARDs (22 patients) received IGU as add-on treatment. Serum IL-6 levels from these patients were measured at baseline and at 12 weeks of IGU treatment. [Results] DAS28-ESR was significantly reduced at 12 weeks compared with that at baseline in both groups (Biologic group: 2.65±0.86 at baseline, vs 2.0±0.75 at 12 weeks, $p<0.0001$, Non-biologic group: 4.0±1.8 at baseline, vs 3.5±1.5 at 12 weeks, $p = 0.02$). The changes in DA28-ESR were correlated with those in serum IL-6 levels (Spearman, Biologic group r = 0.41, Non-biologic group r = 0.45). [Conclusions] IGU treatment decreases disease activities in RA patients in either biologic or non-biologic group. The correlation of changes in serum IL-6 levels and DAS28-ESR indicates that the therapeutic efficacy of IGU would be resulted from the downregulation of IL-6 through inhibition of NFκB activity.

W36-1

Age at onset affects disease activity and response to the TNF inhibitors in early rheumatoid arthritis; An analysis from KURAMA cohort

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Conflict of interest: None

[Object] The purpose of this study was to investigate how the age at disease onset affects the prognosis in early stage of rheumatoid arthritis (RA) patients. [Methods] The analyses in the current study were performed using the Kyoto University Rheumatoid Arthritis Management Alliance (KURAMA) cohort database. [Results] From 2011 to 2015, a total of 2182 patients with RA were enrolled in the cohort, 260 patients were newly diagnosed as RA and followed for 2 years. Young-onset RA (YORA, n=127) and late-onset RA (LORA, n=133) were defined as being below or above 60 years old at the disease onset. At baseline, the titer of ACPA, CRP, ESR, tender joint counts, swollen joint counts and disease activity including DAS28 (ESR), CDAI, SDAI, mHAQ were higher in LORA patients than YORA patients. However, higher disease activity in LORA did not remain and similar number of patients achieved low disease activity or remission at 1 or 2 years after onset. Less LORA patients used less methotrexate, more LORA used corticosteroids, but bDMARDs were used in the same percentage of patients. Response to TNF inhibitors as 1st bDMARDs was better in LORA than YORA. [Conclusions] LORA patients had higher disease activity at onset but it didn't remain at 1 or 2 years after onset.

W36-2

SNPs analysys is able to be predictive tool for joint destraction in rheumatoid arthritis patients

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Conflict of interest: None

Objective The purpose of this study is to test accuracy of algorism for prediction of joint destruction by SNPs analysis. Methods Two-hundred RA patients suffering within 5 years were enrolled in this study. We have selected 10 SNPs associated with joint destruction and made algorism using the 10 selected SNPs. The patients were divided into 2 groups (high destruction group; sharp score>50 or low destruction group; sharp score<10) and analyzed the accuracy of the algorism for the patients. Results In the high destruction group, the sensitivity of this algorism was 95.7% and specificity was 93.1%. One of SNPs in high destruction group was associated with membranous protein, and SNPs in low destruction group were associated with protease, transcriptional factor, and cell cycle. Conclusion SNPs analysis may be predictive tool for joint destruction in RA patients.

W36-3

Serum IgG ACPA-IgM RF immune complexes were detected in rheumatoid arthritis patients positive for IgM ACPA

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Conflict of interest: None

[Object] To identify immunologically active rheumatoid arthritis (RA) patients by detecting IgM anti-citrullinated protein antibody (ACPA) levels. [Methods] IgM ACPA levels were determined in the serum of 176 RA patients by enzyme-linked immunosorbent assay. Influence of IgM rheumatoid factor (RF) on IgM ACPA detection was examined by removing IgG, using protein G-conjugated beads, or by purifying ACPA, using citrullinated peptide-conjugated beads. [Results] Although IgM specific for citrullinated proteins was detected in some patients, IgM molecules reactive to both citrullinated and non-citrullinated peptides were detected in a substantial number of patient samples. IgM ACPA-positive reactions were associated with the presence of IgG ACPA and IgM RF. Surprisingly, protein G-mediated removal of IgG from the serum eliminated positivity for IgM ACPA, suggesting that IgG ACPA-IgM RF complex was being detected. This assumption was confirmed by the detection of IgM RF in the eluate of protein G beads and citrullinated peptide-conjugated beads. [Conclusions] In an attempt to detect IgM ACPA, we mostly revealed false positive reactions due to the presence of IgM molecules, which were not specific for citrullinated proteins, and IgG ACPA-IgM RF immune complex.

W36-4

Elevated concentration of soluble TCTA protein-derived products in peripheral blood of untreated patients with early-onset rheumatoid arthritis

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Conflict of interest: None

[Object] T-cell leukemia translocation-associated gene (TCTA) protein is expressed ubiquitously in normal human tissues. However, its function was not clarified. Since 2009, we have demonstrated that TCTA protein is essential for human osteoclastogenesis induced by RANKL, inhibits proliferation of both small-cell lung carcinoma and fibroblast-like synoviocytes of rheumatoid arthritis, and may play as a 'coupling factor' in bone metabolism. [Methods] We constructed a high sensitivity sandwich ELISA system and measured the concentration of soluble TCTA protein-derived products (sTDP), which include inhibitor of human osteoclastogenesis, in peripheral blood of untreated patients with early-onset rheumatoid arthritis (RA). [Results] The concentration of sTDP was significantly higher in RA patients than in normal volunteers (p=0.0397). The levels of C-reactive protein (CRP) in serum were not correlated with the concentrations of sTDP in RA patients. [Conclusions] sTDP levels were elevated in untreated patients with early-onset RA, which was independent of inflammation. These finidngs suggest that sTDP play an important role in the pathogenesis of RA inhibiting osteoclastogenesis and synovitis.

W36-5

A disintegrin and metalloprotease 15 is expressed on rheumatoid arthritis synovial tissue endothelial cells and mediates angiogenesis

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Conflict of interest: None

[Background] ADAM-15 is expressed in several malignancies. However, the relationship between ADAM-15 and rheumatoid arthritis (RA) is still unclear. We previously showed ADAM-15 was expressed in RA synovial tissues. In this study, we have invastegated the role of ADAM-15 in RA angiogenesis. [Methods] In order to examine the role of ADAM-15 in RA angiogenesis, we used HUVECs. To determine the expression of proangiogenic cytokines, ADAM-15 siRNA was transfected in HUVECs. In order to confirm the role of angiogenesis, we did Matrigel assays *in vitro*. Finally, to determine whether ADAM-15 mediates adhesion to ECs, we performed *in vitro* adhesion assays. [Results] ENA-78/CXCL5 and ICAM-1 in TNF-α stimulated ADAM-15 siRNA transfected HUVECs conditioned medium were decreased compared with in TNF-α stimulated control siRNA transfected HUVEC conditioned medium. ADAM-15 siRNA treated HUVECs had decreased EC line and tube formed in response to RA synovial fluids compared with HUVECs. Adhesion index of ADAM-15 siRNA transfected HUVECs was significantly decreased compared with adhesion index of control siRNA transfected HUVECs. [Conclusions] These data show ADAM-15 play a RA angiogenesis, suggesting that ADAM-15 may be a potential target in inflammatory diseases such as RA.

W36-6

A disintegrin and metalloprotease -17 is overexpressed on rheumatoid arthritis osteoblasts

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Conflict of interest: None

[Object] We have previously reported ADAM-17 is expressed in RA synovial fluids and synovial tissues. Here, we examine the expression of ADAM-17 in RA human osteoblasts (RA-HOB). [Methods] RA-HOB were stimulated with 25 ng/ml TNF-α at 4 hours, and mRNA was collected. ADAM-17 mRNA expression was examined using qPCR. To examine the expression of ADAM-17 in RA-HOB, RA-HOB were stimulated with ajusted density TNF-α at 24 hours and measured using ELISA. To determine ADAM-17 expression in RA-HOB lysate, western blotting (WB) was also performed. To confirm the presence of ADAM-17 on RA-HOB, immunostaining was performed. Finally, in order to examine the signaling in TNF-α stimulated RA-HOB, chemical inhibitor assay was performed. [Results] ADAM-17 was expressed in TNF-α stimulated RA-HOB conditioned medium. Furthermore, TNF-α was induced dose-dependent secretion of ADAM-17 levels from RA-HOB. We found that ADAM-17 mRNA in TNF-α stimulated RA-HOB was 70 times elevated compared with in non-stimulated RA-HOB. We also found that ADAM-17 expression in RA-HOB by using immunostaining and WB. NF-κB was detected in TNF-α stimulated ADAM-17 signaling in RA-HOB. [Conclusions] We showed the expression of ADAM-17 in RA-HOB, suggesting the possibility that it plays an important role in bone metobolism in RA.

W37-1

Autologous Hematopoietic Stem Cell Transplantation for Japanese Patients with Severe Systemic Sclerosis

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Conflict of interest: None

[Object] To elucidate the efficacy and safety of autologous hematopoietic stem cell transplantation (HSCT) for Japanese patients with severe systemic sclerosis (SSc). [Methods] A phase II clinical trial included SSc patients diagnosed within the last three years and having at least one of the following clinical features: rapidly progressive diffuse skin sclerosis, refractory digital ulcer or interstitial lung disease (ILD). The mobilization regimen comprised cyclophosphamide (CY: 4 g/m2) and recombinant human granulocyte colony-stimulated factor. HSCT were performed after conditioning using CY (200 mg/kg). [Results] Fourteen patients were enrolled and underwent HSCT during 2000 and 2012. Median follow-up period was 137 months. Eight patients showed dramatic improvement of skin sclerosis (more than a 50% decrease in skin score from baseline within six months). Six patients required additional immunosuppressive treatments due to progression of skin sclerosis and/or ILD. Adverse effects occurred in six patients, including fatal cardiomyopathy. Overall survival rate was 93% at 10 years. [Conclusions] Our experience raised an important suggestion that HSCT could be a treatment option for Japanese patients with severe SSc based on careful considering the risk-benefit balance.

W37-2

Investigation of interstitial pneumonia in patients with systemic sclerosis

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Conflict of interest: None

[Object] Interstitial pneumonia (IP) is one of the critical organ involvements with systemic sclerosis (SSc), but nevertheless we have no standard medication. We investigated the current status of inpatient cases with IP. [Methods] One hundred ninety SSc patients out of 290 hospitalized patients were investigated. The relationship among disease-specific antibodies, IP, and prognosis of these patients were analyzed. [Results] Positive rate of anti- topoisomerase I antibodies, anti-centromere antibodies, anti-RNA polymerase III antibodies, anti-U1 RNP antibodies were 45.7%, 16.8%, 4.7 and 12.1%. Diffuse cutaneous pattern was 44.7%, limited cutaneous pattern was 55.2% of SSc patients with IP. They were received Glucocorticoid (94.7%), Calcineurin inhibitors (20.0%) and cyclophosphamide therapy (12.1%). The prognosis of patients with IP were poor than without IP. [Conclusions] Our study suggested that SSc with anti-topoisomerase I antibodies positive cases showed close relation with IP, and they had poor prognosis. Current medications, glucocorticoid or immunosuppressive therapy had no effectiveness, so we hope to establish a new medication for SSc with IP.

W37-3

Efficacy and safety of combination therapy with prednisolone and oral tacrolimus for progressive interstitial pneumonia with systemic sclerosis: a retrospective study

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Conflict of interest: None

[Object] To evaluate the efficacy and safety of combination therapy with prednisolone (PSL) and tacrolimus (TAC) for progressive IP with SSc (SSc-PIP). [Methods] We retrospectively studied 11 patients with SSc-PIP treated with the therapy. [Results] They included 7 patients with dc-SSc [median age; 59 (42-77) years, disease duration; 94 (8-373) weeks]. IP progression was subacute in 6 and chronic in 5 patients. At baseline, KL-6 was 914 (300-2614) U/ml, H-J classification I/II/III/IV were 2/6/2/1, SpO2 (room air) 97 (95-98%), %FVC 82.9 (55.2-110.1)%, %DLco 47.4 (9.7-64.4)%, respectively. One year after, all patients survived. Respiratory symptoms were improved in 3, stable in 7, and deteriorated in 1 patient. Total GGO score (TGS) was improved (P=0.005) and total fibrosis score (TFS) tended to decline (P=0.084). There were no significant changes of KL-6, %FVC, and %DLco. At the present, all 7 patients, who could be followed, were alive. Respiratory symptoms were improved in 3, and stable in 4 patients. TGS was improved (P=0.016) without altering TFS. There were no changes of KL-6, %FVC, and %DLco. As adverse events, mild infection was seen in 2 patients. Grade I renal injuries were observed in 3 and 1 patients at 1 year and the present, respectively. [Conclusions] These results suggest.

W37-4

Non-randomized Controlled Trial to Evaluate the Effect of Extracorporeal Shock Wave Therapy on Digital Ulcers in Systemic Sclerosis

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Conflict of interest: Yes

[Object] Extracorporeal shock wave therapy (ESWT) at low energy is shown to be effective in healing of injuries and wounds. This study evaluated ESWT for treatment of refractory skin ulcers caused by SSc. [Methods] We enrolled 60 patients with refractory digital ulcers. 30 were treated with ESWT and 30 received conventional treatment. Patients in the conventional treatment group were permitted to use any currently available therapies. Patients in the ESWT group continued pre-study treatments. One ESWT session applied to 20 areas on both hands. Treatment was performed weekly for 8 weeks. Outcomes were evaluated according to the number of skin ulcers. The primary endpoint was the mean decrease in the number of skin ulcers at 8 weeks after treatment start. [Results] The mean decrease in the number of ulcers at 8 weeks was 4.47 in the ESWT group and 0.83 in the conventional treatment group and the difference was significant. The proportion of subjects whose total number of ulcers decreased by 70% or more at 8 weeks was 26.7% in the conventional treatment group and 70.0% in the ESWT group. No serious adverse events associated with ESWT were reported during the study period. [Conclusions] ESWT demonstrated clinically meaningful improvement in SSc patients with refractory digital ulcers.

W37-5

Investigation of the nailfold capillary findings by capillary microscope in systemic scleroderma

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Conflict of interest: Yes

[Object] We studied the relationship between clinical symptoms due to systemic scleroderma (SSc) and nailfold capillary findings. [Methods] We analyzed 26 patients with SSc. Nailfold video capillaroscopy (NVC) was performed and it's finding was scored (1: partial expansion of capillary, 2: giant capillaries, micro bleeding point, 3: capillary disappearance, 4: new blood vessel appearance). The correlation between NVC score and blood NT-ProBNP, KL-6, cardiac ultrasonography (systolic pulmonary artery pressure, left ventricular ejection fraction) and pulmonary function test (% vital capacity, diffusing capacity of the lung carbon monoxide) was investigated. Patients were divided into groups (with or without pulmonary fibrosis, pulmonary arterial hypertension and skin ulcer) and NVC scores were compared among these groups. [Results] The negative correlation was found between NVC score and % vital capacity ($r=-0.42$, $P<0.05$). The NVC score of the group with pulmonary arterial pulmonary hypertension was higher than those without (3.50 vs 2.31, $P<0.05$), and the NVC score of the group with skin ulcer was higher than those without (3.50 vs 2.20, $P<0.005$). [Conclusions] It was suggested that the nailfold capillary finding might be related to clinical symptoms due to SSc.

W37-6

The significance of microvascular abnormalities in mixed connective tissue disease (MCTD)

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Conflict of interest: None

[Objectives] To investigate the significances of microvascular abnormalities in patients with MCTD. [Methods] Untreated 18 patients with MCTD were enrolled. Microvascular abnormalities were evaluated by using nailfold videocapillaroscopy (NVC). The prevalence was compared with systemic lupus erythematosus (SLE, 30cases), systemic sclerosis (SSc, 60cases) and polymyositis/dermatomyositis (PM/DM, 70cases). The relationship with organ manifestations (such as interstitial pneumonia and pulmonary hypertension) was also evaluated. [Results] The presence of anti-RNP antibodies and Raynaud phenomenon (RP) were found in all cases. The clinical findings revealed SLE + SSc-like (66.7 %) in 12 cases, SSc + PM-like (22.2%) in 4 cases, SLE + SSc + PM-like (11.1%) in 2 cases. NVC changes were found in 8 cases (38.9%), that was lower than SSc (80.0%) and PM/DM (55.7%), higher than SLE (10.0%). NVC changes in MCTD were not associated with other organ manifestations but pulmonary hypertension (PH) ($p=0.017$). [Conclusion] Despite almost all MCTD patients had RP, the prevalence of microvascular abnormalities was lower than that of SSc. However, the abnormalities were related with PH, same as SSc. This result indicates microvascular abnormalities may contribute to the mechanism of PH in MCTD.

W38-1

Characteristics of Severe Intestinal Pseudo-obstruction in Systemic Sclerosis

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Conflict of interest: None

[Object] Patients with systemic sclerosis (SSc) often show diarrhea, constipation, and malabsorption due to intestinal dysmortility. Moreover, they sometimes revealed intestinal pseudo-obstruction (IPO), but the actual prevalence and the risk factors have been rarely known. We retrospectively assessed the prevalence and clinical characteristic of IPO in SSc. [Methods] Nine patients, who entered our hospital due to IPO among 124 hospitalized patients with SSc from January 2011 to December 2016, were enrolled. All data were collected from medical record, retrospectively. [Results] Among 9 patients with IPO (7.3%), 7 patients were diffuse cutaneous SSc, and median duration of disease was 4 years. Five cases revealed myositis at the onset of disease, and 5 cases had interstitial lung disease. Six cases had been treated with mild to moderate dose of prednisolone, and 5 cases received intravenous cyclophosphamide pulse therapy before occuring IPO. [Conclusions] IPO is rare, but critical complication in SSc. The patients who showed myositis tended to occur IPO, as previously reported. Patients who had several complications but had short disease duration tended to occur IPO. Immunosuppressive therapy may not be effective for IPO occurence.

W38-2

Clinical features of small intestine bacterial overgrowth (SIBO) in patients with systemic sclerosis

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Conflict of interest: None

[Object] To clarify clinical features and risk factors of small intestine bacterial overgrowth (SIBO) in patients with systemic sclerosis (SSc). [Methods] We retrospectively collected the clinical information of SSc patients who were diagnosed at our department from January 2009 to October 2017. Clinical characteristics of SIBO group and non-SIBO group were compared, using Mann-Whitney test or Fisher's exact test. [Results] 139 SSc patients were enrolled (6 with and 133 without SIBO). Age (mean±SD) were 58.7±13.5 yrs vs 61.1±11.9 yrs, rate of females 100% vs 87.2%, diffuse cutaneous (DC) type 66.7% vs 21.8% ($p=0.028$), respectively. Positive rate of SSc-related autoantibodies (anti-centromere Ab/anti-Scl70 Ab/anti-RNApolymeraseIII Ab/anti-U1-RNP Ab) were 0/0/0/16.7% vs 57.9/21.8/6.8/9.8%, and negative for all of those autoantibodies were 83.3% vs 11.3%, respectively. All of SIBO patients had pseudo-obstruction and 2 out of them had gastrointestinal amyloidosis. [Conclusions] SSc patients with SIBO tended to have DC subtype and be negative for SSc-related autoantibodies.

W38-3

Clinical role of the pericardial effusion as the onset prediction factor of the scleroderma renal crisis

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Conflict of interest: None

Background: Scleroderma renal crisis (SRC) affect renal and vital prognosis in systemic scleroderma (SSc). The present study was aimed to clarify the clinical impact of the pericardial effusion as the onset predictor in SSc. **Methods:** The object has a diagnosis of SSc between January 2003 and November 2017 with the past of the hospitalization in our hospital. We divided them into pericardial effusion group (n=19) and non-pericardial group (n=33), and retrospectively analyzed clinical features during the clinical course in the two groups. **Result:** SSc with pericardial effusion was detected 19 of 52 (36.5%) cases. Clinically, SRC, mRSS, CS's greatest dose, anti-RNA polymerase III (anti-RNAP III) antibodies positive, MPO-/PR3-ANCA positive, finger apex ulcers were significantly different between the two groups. When the pericardial effusion was a risk factor funder age, sex adjustment for the multivariate analysis (OR 14.9, 95% CI 3.2-69.6). In the Kaplan-Meier method, SRC significantly in comparison with the two groups (in 49.6% of onset rates vs. 7.6% /3

year) p<0.01). **Conclusion:** There was not the pericardial effusion despite an independent factor of the SRC onset from this study, although pericardial effusion may be a risk factor next to the anti-RNAP III antibodies positive.

W38-4

Effective Screening Procedure for Connective Tissue Disease Associated Pulmonary Arterial Hypertension Using Serum Haptoglobin Level and Cardiac MRI

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Conflict of interest: None

[Object] To establish an effective screening procedure to detect pulmonary arterial hypertension (PAH) in patients with connective tissue diseases (CTD). [Methods] We retrospectively analyzed 31 CTD patients who underwent right heart catheterization. Six following variables were assessed as conventional risk factors of having PAH; anti-U1-RNP or centromere antibodies, high BNP level, high urate level, right axis deviation, decreased DLCO/V_A, and elevated pulmonary artery systolic pressure estimated by echocardiography. In addition, decreased serum haptoglobin level and increased ratio of right to left end-diastolic volume (RVEDV/LVEDV) calculated by cardiac MRI were considered as potential risk factors. Screening performance of these variables to detect PAH was expressed as area under ROC curve (AUC). [Results] AUC obtained by combination of the six conventional risk factors was 0.76. AUC increased to 0.82 by adding haptoglobin level and further increased to 0.84 with both haptoglobin and RVEDV/LVEDV. The sensitivity and specificity of these eight risk factors for PAH detection (cut-off: 4) were 88% and 58%, respectively. [Conclusions] Our new screening procedure including serum haptoglobin level and cardiac MRI may improve accuracy and efficiency in the detection of PAH.

W38-5

Clinical characteristics and survival in CTD patients with heart disease-associated pulmonary hypertension; comparison of patients with systemic sclerosis vs. non-systemic sclerosis

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Conflict of interest: None

[Object] To determine clinical characteristics of left heart disease (LHD)-associated PH (LHD-PH) between patients with SSc and non-SSc (SLE, MCTD). [Methods] Of 39 patients diagnosed as PH by right heart catheterization (RHC) (from 2006 through 2017), 11 (5 non-SSc / 6 SSc) were classified as LHD-PH. Clinical characteristics, complete remission (CR) rate, domiciliary oxygen therapy (DOT) rate, and survival in patients with SSc-PH and non-SSc-PH were compared. [Results] The mean age (SD) was 64 (13) in SSc and 45 (16) in non-SSc patients (P=0.08). The mean follow-up period (SD) after RHC was 32 (34) months. Patients with SSc had comparable hemodynamic parameters with those with non-SSc. E/e'tended to be higher in patients with SSc than those with non-SSc [14 (6) / 9 (3), P=0.08]. Immunosuppressant (IS) was introduced in 80% and 17% of the patients with non-SSc and SSc (NS), respectively. Fourty percent of the patients with non-SSc achieved CR while none with SSc did it. No patients died or needed DOT in patients with non-SSc while 50% needed DOTand another 50% died within 29 months. [Conclusions] LHD-PH with non-SSc could achieve remission with an appropriate use of IS. Establishment of therapeutic strategy for LHD-PH is needed in patients with SSc.

W38-6

Clinical characteristics of symptomatic subcutaneous calcinosis in systemic sclerosis (SSc)

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Conflict of interest: None

[Object] To assess clinical characteristics of symptomatic subcutaneous calcinosis in SSc. [Methods] This single-center, cross-sectional study enrolled 157 SSc patients. Demographic and clinical characteristics were retrospectively collected by medical chart review. In a case-control study, clinical features were compared between patients with and without calcinosis (1:2), in whom sex, disease subset, age at onset, and SSc-related antibodies (abs) were matched. [Results] Fourteen patients had symptomatic subcutaneous calcinosis: including 6 with diffuse cutaneous SSc (dcSSc) and anti-topoisomerase I ab and 8 with limited cutaneous SSc (lcSSc) and anticentromere. Calcinosis was detected in fingers (n = 10), trunk (n = 5), hands/foot (n = 4), extremities (n = 3), and face (n = 1) and was more frequently found in areas beyond fingers in dcSSc than in lcSSc (P = 0.01). When compared with controls, patients with calcinosis showed higher prevalence of digital ulcers (P = 0.02) and beraprost use (P = 0.02), but were less frequently treated with Ca blocker (P = 0.048). [Conclusions] Symptomatic subcutaneous calcinosis is observed in both dcSSc and lcSSc patients, but dcSSc patients had more extensive calcinosis deposition. Calcinosis may be associated with underlying peripheral vasculopathy.

W39-1

The relationship between YKL-40 and angiogenesis in systemic sclerosis

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Conflict of interest: None

[Object] Systemic sclerosis (SSc) is an intractable connective tissue disease that causes fibrosis of the skin and organs, with Raynaud's phenomenon as the initial symptom and often accompanied by nailfold capillary abnormality. SSc is thought to cause microvascular disorder from the early stage. We examined by YKL-40 which is a chitinase-like protein increasing in the serum due to inflammatory disease and angiogenesis of malignant tumors, and vascular endothelial growth factor (VEGF) which has an important role in angiogenesis. [Methods] We conducted a retrospective analysis of 78 SSc patients. We measured serum YKL-40 and VEGF levels and examined the correlation between YKL-40 age percentile which was age-corrected for serum YKL-40 levels and VEGF levels. And, skin biopsy tissues from 7 SSc patients were also subjected to immunohistochemistry (IHC) with anti YKL-40 antibody. [Results] YKL-40 age percentile was 53.4±29.3, VEGF levels was 352.9±220.1pg/ml. The correlation coefficient was a mild correlation as 0.27 between YKL-40 and VEGF. And, staining of the blood vessel wall of the superficial dermis was found in specimens obtained from all patients. [Conclusions] YKL-40 suggested to reflect regeneration after capillary injury in SSc from the results of YKL-40, VEGF, and IHC.

W39-2

Molecular Mechanism for the Therapeutic Effect of Extracorporeal Shock Wave Therapy on Digital Ulcers of Systemic Sclerosis

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Conflict of interest: None

(Object) Previously, our group reported, for the first time, the dramatic effect of Extracorporeal shock wave therapy (ESWT) on digital ulcers of SSc. To develop more effective therapeutic strategy, we designed in vitro and in vivo shock wave (SW) irradiation system to identify a

master regulator for early gene response to SW treatment. **(Methods)** SW was irradiated to human dermal microvascular endothelial cells (HDMECs) in vitro, and to rat skin in vivo. The gene expression changes were analyzed by microarray, in vitro and in vivo respectively, and the identified genes were quantified by RT-PCR. **(Results)** In vitro microarray analysis revealed that FosB, a component of transcriptional factor, AP-1, was reproducibly increased. In vivo microarray analysis revealed that FosB, angiogenic CXCL2 and PMA inducible gene population were significantly increased. In vitro, expression levels of CXCL2 and VEGFA were increased by both SW treatment and overexpression of FosB under PMA stimulation. (**Conclusion)** Early gene induction of FosB with SW irradiation may function as a master regulator for gene response to SW treatment. This finding may provide a clue for developing a more effective ESWT for DUs in SSc.

W39-3

Activation status of circulating platelets in patients with systemic sclerosis and association with clinical characteristics

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Conflict of interest: None

[Background] Systemic sclerosis (SSc) is characterized by excessive fibrosis, microvascular injury and autoantibody production. Platelet plays a significant role in hemostasis physiologically, but can systemically distribute and contribute to the disease process through activation and release of humoral factors. The aim of this study is to elucidate the activation status of platelets in patients with SSc and the association with clinical characteristics. [Methods] Twenty-one patients with SSc and 16 healthy controls were involved. Activation status of platelets was examined by the expression of CD62P or activated glycoprotein IIb/IIIa (PAC1), and production of microparticles (MP). Association with clinical characteristics was also examined. [Results] In SSc, proportion of $CD62^+$ or $PAC1^+$ platelets (P<0.05, P<0.05, respectively) and production of MP were higher (P<0.05) compared to those in controls. Of these, proportion of $CD62P^+$ platelets and MP production correlate each other (r=0.88, P<0.05). Moreover, both are higher in diffuse cutaneous SSc (P<0.05, P<0.05) and correlated with modified Rodnan skin score (P< 0.05, P<0.05). [Conclusion] In SSc, circulating platelets are activated and associated with skin sclerosis, suggesting the involvement in the pathogenesis of SSc.

W39-4

Exercise-induced pulmonary hypertension at early stage of systemic sclerosis: Changes in gene expression of peripheral blood cells

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Conflict of interest: None

Purpose: To detect a gene co-expression network involved in the pathogenesis of exercise-induced pulmonary hypertension (exPH) at early stage of SSc. **Methods:** Total of 93 cases without PH symptoms with either Raynaud phenomenon (n=80), skin sclerosis (n=51) or SSc-related autoantibody positive (n=68) were enrolled. To segregate the exPH from normal response (N) group, exercise Doppler echocardiography (DE) was carried out. Meanwhile, genome-wide gene expression analysis was performed with using whole peripheral blood (n=74). After quantifying the expressions of transcripts, differentially expressed genes (DEGs) between exPH and N were analyzed by WGCNA and pathway enrichment analysis. **Results:** 20 of exPH and 73 of N group were identified. The anti-RNP Ab positive seems to be a risk factor and the level of BNP was high in exPH. Based on the gene expression analysis, 817 genes were differentially expressed between two groups and 6 co-expression modules were identified by WGCNA. Pathway analysis revealed that modules positively related with TRPG by DE were enriched with genes of Wnt or Toll-like receptor signaling pathway. **Conclusion:** The results by our study may show a hint for therapeutic intervention at the latent PAH stage of the disease to prevent the aggravation of PVD.

W39-5

Enhanced High Mobility Group Box 1 pathways in monocytes from systemic sclerosis patients

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Conflict of interest: Yes

[Object] To elucidate the characteristic transcriptome patterns of peripheral blood immune cells in systemic sclerosis (SSc) and to reveal the crucial factors of SSc pathogenesis. [Methods] We sorted peripheral blood immune cells into 20 subsets using flow cytometer, and performed transcriptome analysis of sorted cells using next-generation sequencing. Nine SSc patients (anti-topoisomerase-I antibody positive 4 cases, anti-centromere antibody positive 5 cases) and 14 healthy controls (HCs) were included. Differentially expressed genes (DEGs) were detected between SSc and HCs, and were subsequently analyzed by Ingenuity Pathway Analysis (IPA). [Results] Canonical pathway analysis revealed that High Mobility Group Box 1 (HMGB1) pathways were enhanced in CD16 negative monocytes from SSc (Z score = 2.49, p = 0.0001). HMGB1 is known to serve as damage-associated molecular pattern molecules and to bind to toll-like receptor (TLR). Upstream regulator analysis showed that not only TLR, but also growth factors and IFN-related genes were predicted as upstream regulators activated in this subset. [Conclusions] The enhanced HMGB1 pathways in CD16 negative monocytes can play an important role in SSc pathogenesis.

W39-6

Anti-inflammatory and anti-fibrotic effects of intravenous adipose-derived stem cell transplantation in a mouse model of bleomycin-induced scleroderma

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Conflict of interest: None

[Object] Adipose-derived stem cells (AdSCs) have recently been considered a useful treatment tool for autoimmune disease because of their anti-inflammatory and immunosuppressive effects. We investigated the therapeutic effect of intravenous AdSC transplantation in a mouse model of bleomycin-induced scleroderma (BLM-SSC). [Methods] Balb/c mouse of 8 weeks of age was given BLM 100 ug subcutaneously everyday for 21 days. mAdSC was administered from tail vein one week after BLM start. Thickening of skin, infiltrationin of flammatory cells, gene expression of inflammatory cytokines, and fibrotic factors were evaluated. [Results] After the initiation, AdSCs accumulated in thymus and spleen, without accumulation in skin. In a group of BLM-SSC mice treated with 1.0×10^5 AdSCs, thickening of skin, infiltration of inflammatory cells, gene expression of inflammatory cytokines, and fibrotic factors were significantly reduced compared with a non-treatment group. But in a group treated with 1.0×10^4 AdSCs, there was no reduction of them. [Conclusions] AdSCs inhibited both inflammation and fibrosis of BLM-SSC mice skin in a cell number-dependent manner.

W40-1

Continuation Rates of Six Biological Agents in Senile Patients with Rheumatoid Arthritis

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Conflict of interest: Yes

[Object] To investigate continuation rates of six biological agents in senile patients with rheumatoid arthritis (RA) in comparison to younger patients with RA. [Methods] Toyohashi RA Database (TRAD) was used. Continuation rates of six biological agents (IFX, ETN, ADA, TCZ, ABT, GLM) in younger RA patients (Y group: age≦64 years) and older RA patients (O group: age≧65 years). Continuation rates were calculated using Kaplan-Meier method and statistical significance was evaluated using Log-Rank analysis. [Results] IFX (n=97), ETN (n=144), ADA (n=81), TCZ (n=68), ABT (n=50), GLM (n=64). Mean age and %older patients were 55 years (26.8%) in IFX group, 57 years (35.4%) in ETN group, 60 years (38.3%) in ADA group, 59 years (39.7%) in TCZ group, 68 years (72.0%) in ABT group and 60 years (39.3%) in GLM group. Continuation rates at five years were as below. IFX (Y: 33.7%, O: 33.3%, p=0.79), ETN (Y: 67.3%, O: 44.7%, p=0.02), ADA (Y: 33.1%, O: 29.6%, p=0.59), TCZ (Y: 72.0%, O: 53.4%, p=0.06), ABT (Y: 45.0%, O: 49.7%, p=0.90), GLM (Y: 68.1%, O: 61.6%, p=0.47). [Conclusions] %older patients in ABT group was highest among 6 groups. There was a significant difference in drug continuation rates in only ETN-treated group. Continuation rates in older RA patients in GLM, TCZ and ABT groups were comparatively good.

W40-2

The retention rate of abatacept or tocilizumab is higher than that of TNF inhibitor when used as 2nd biologics-Data from ANSWER cohort-

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Conflict of interest: None

[Object] Approximately one-third of rheumatoid arthritis patients show inadequate response to TNF inhibitors (TNF-i). Most of them need switch of biologics (bio) to 2nd agent. We analyzed the efficacy of TNF-i and non-TNF-i as the 2nd bio after TNF-i as 1st bio. [Methods] We recruited the cases who were switched to 2nd bio from TNF-i for 1st bio from Kansai Consortium for well-being for rheumatic disease patients (ANSWER) cohort. The cases were categorized into two groups; 2nd bio TNF-i (2nd TNF) group and non-TNF-i (2nd non-TNF). We compared disease activity and retention rate between the two groups. [Results] 92 cases were recruited in 2nd TNF group and 101 in 2nd non-TNF group. Age, sex and CDAI at baseline were similar in the two groups, except the ratio of glucocorticoid usage that was higher in 2nd non-TNF group than 2nd TNF (2nd TNF 27.1%, 2nd non-TNF 47.5%, p=0.0057). No significant differences were observed between CDAI after switch in 2nd TNF and that in 2nd non-TNF. The retention rate of 2nd non-TNF was higher than 2nd TNF group (p=0.017, Log-rank test). Similar results were obtained with analyses using propensity score matched data. [Conclusion] These results indicate that the retention rate might be higher when non-TNF-i is chosen as 2nd bio after TNF-i inadequate response.

W40-3

Efficacy of Infliximab for suppressing radiographic progression of cervical lesions in patients with rheumatoid arthritis comparison with methotrexate therapy; three years of follow-up ~a Multicenter Registry Study ~

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Conflict of interest: None

[Objectives] To evaluate the efficacy of Infliximab (IFX) for suppressing the radiographic progression of RA cervical lesions comparison with methotrexate (MTX) for 3 years. [Methods] We used IFX and MTX for treating each 70 and 64 Japanese patients with active RA for at least 3 years. For evaluation of cervical lesions ADI, SAC and the Ranawat value were measured at initiation and Year 1,2,3. [Results] In the patients receiving IFX (n=70) and MTX (n=64), the mean age was 54.2 vs 63.4 years old (p<0.001), disease duration was 10.5 vs 8.5 years (p=0.027). The respective changes in cervical lesion parameters after 1 year were as follows: ADI: 0.21 vs 0.27mm (p=0.399), SAC: -0.17 vs -0.17mm (p=0.849) and Ranawat value: -0.16 vs -0.10mm (p=0.273). The respective changes in cervical lesion parameters after 2 years were as follows: ADI: 0.36 vs 0.55mm (p=0.088), SAC: -0.30 vs -0.47mm (p=0.058) and Ranawat value: -0.27 vs -0.36mm (p=0.497). The respective changes in cervical lesion parameters after 3 years were as follows: ADI: 0.47 vs 0.70mm (p=0.042), SAC: -0.44 vs -0.69mm (p=0.043) and Ranawat value: -0.34 vs -0.48mm (p=0.359). [Conclusions] This study suggested that IFX treatment can be used to suppress the progression of RA cervical lesions.

W40-4

Efficacy of Abatacept in Rheumatoid Arthritis with or without MTX

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Conflict of interest: None

[Objective] To compare the efficacy of Abatacept with or without MTX and Tacrolimus. [Methods] Using the EULAR improvement criteria, we investigated efficacy at 24 weeks in 89 RA patients who started treatment with abatacept, 17 patients who started treatment without MTX/tacrolimus (non-MTX/non-TAC group), 15 patients who started treatment with TAC (non-MTX/TAC group), 38 patients who started treatment with low dose MTX (< 10mg/w (low-MTX group), 19 patients who started treatment with high dose MTX (> 10mg/w (high-MTX group). [Results] The rates of low disease activity defined as “DAS28-CRP<2.7” were 47.0%, 20.0%, 57.9%, and 63.1% in the non-MTX/non-TAC, non-MTX/TAC, low MTX, and high MTX groups respectively, The rates of remission defined as “DAS28-CRP<2.3” were 29.4%, 13.3%, 36.8%, and 42.1% in the non-MTX/non-TAC, non-MTX/TAC, low MTX, and high MTX groups respectively. On the other hand, the percentage of no response were 29.4%, 13.3%, 13.2%, and 15.8%. [Conclusion] The results of this analysis at our hospital suggest that Abatacept with high dose MTX can induce remission of active RA at high rate. Abatacept with MTX is more effective than ABT with tacrolimus, so the use of abatacept with tacrolimus as the second-line treatment for these patients should be considered.

W40-5

The effectiveness and safety of treatment strategy targeting low disease activity with biological and non-biological DMARDs for elderly-onset rheumatoid arthritis complicated with interstitial lung disease

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Conflict of interest: None

[Object] The aim of this study is to evaluate effectiveness and safety of treatment targeting low disease activity (LDA) for elderly onset rheumatoid arthritis (EORA) with ILD (ILD+) or without ILD (ILD-). [Methods] Data from 198 MTX-naïve patients (mean 74 years-old, median symptom duration 0.5 years, and mean observation period 175 weeks) with EORA from a prospective registry were analyzed. [Results] Baseline DAS28-ESR, SDAI and HAQ were 6.1±1.2,36.0±16.3, and 1 (0.5-1.75). Twenty-nine ILD+ were identified at baseline. Clinical findings were same between the ILD+ and the ILD-. MTX was started less frequently in the ILD+, and frequency of switching to biological DMARDs was not different. LDA at week 104 and 156 was achieved in 69% and 77% of the ILD+, and these were same as ILD-. Achievement rate at week 104 of HAQ-DI≦0.5 was significantly lower in the ILD+, however the difference was disappeared at week 156. Liner mixed model analysis showed SDAI and HAQ were improved in the ILD+ as well as the ILD-. Kaplan-Meier method showed cumulative rate of serious infection and exacerbation of ILD were significantly higher in the ILD+. [Conclusions] Treatment targeting LDA is an effective treatment strategy of EORA with ILD. Safety profile was quite different between the two groups.

W40-6

Predictive factors for achievement of low disease activity at 52 weeks are different between elderly and young rheumatoid arthritis patients treated with abatacept

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Conflict of interest: Yes

[Object] Japanese PMS reported that clinical response of abatacept in elderly was similar to that in young patients despite their quite different characteristics. Thus, we hypothesized that predictive factors for clinical results were different between elderly and young patients treated with abatacept. [Methods] Participants were consecutive 464 RA patients treated with abatacept and observed for longer than 52 weeks, in the TBC Registry system. Multivariate logistic regression analysis was used to study predictive factors at baseline for achievement of low disease activity (LDA) at 52 weeks, separately in elderly (> 65 years) and young (< 65 years) group. [Results] In the young group, concomitant MTX used (OR: 3.2, p=0.033), DAS8-CRP score (OR: 0.53, p=0.017), mHAQ score (OR: 0.29, p=0.007), and positivity for anti-CCP antibody (OR: 4.4, p=0.041) were determined as independent predictors. In the elderly group, only DAS28-CRP score (OR: 0.53, p=0.017) and bio-naïve (OR: 3.8, p=0.004) were determined. [Conclusions] Our results suggested that the effect of concomitant MTX and anti-CCP antibody on the clinical result of abatacept treatment could be different between ages, and then we could expect adequate response to abatacept in the elderly patients similarly in the young patients.

W41-1

Comparison of effects of IL-6 inhibitor and TNF inhibitors on arteriosclerosis-related factors in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] TNF inhibitors have been reported to inhibit the progression of arteriosclerosis in patients with rheumatoid arthritis (RA). We compared the effects of IL-6 inhibitor on arteriosclerosis-related factors concerning the promotion of arteriosclerosis due to lipid abnormalities with those of TNF inhibitors. [Methods] Female bio-naïve 19 RA patients aged 40 to 79 years old were randomly assigned to 2 groups of TNF inhibitors and IL-6 inhibitor. We measured Flow-Mediated Dilation (FMD), Pulse Wave Velocity (PWV), Ankle Brachial Index (ABI) before administration and after a year. The values before and after administration of the 2 groups were compared, and the changes were compared between 2 drugs. [Results] There were no significant differences in the background of DAS28 before and after administration of the 2 groups of TNF inhibitors and IL-6 inhibitor, and the DAS28 was significantly decreased one year after administration. There were no significant differences in FMD, PWV and ABI before and after administration of 2 groups, and no significant differences were observed between two drugs before and after administration. [Conclusion] This study suggested that the effects of IL-6 inhibitor on arteriosclerosis of RA patient might not be different from those of TNF inhibitors.

W41-2

Current status and problems of Rheumatoid arthritis with Chronic Kidney Disease

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Conflict of interest: None

[Object] To clarify the problem in treatment of patients with rheumatoid arthritis complicated with chronic kidney disease. [Methods] Patients with chronic kidney disease were extracted from 835 patients with rheumatoid arthritis who visited Akita University hospital from January 2017 to March, and the cause of the clinical practice, coexisting disease, renal function deterioration was investigated. [Results] 28% was a chronic kidney disease. 3% for abnormal urinalysis, 22% for grade 3 (GFR 30-59), 2% for grade 4 (GFR 15-29), and 1% for grade 5 (GFR 0-14). NSAIDs, tacrolimus, hypertension, dyslipidemia, diabetes, and existing chronic kidney disease were mentioned as factors related to renal function of 189 grade 3 patients. NSAIDs was given in 58 people, with GFR averaging 10 lower in 3 years. A similar trend was also observed in tacrolimus. The GFR decline of patients with rheumatism with hypertension, dyslipidemia, diabetes mellitus was more than 3 to 4 / year average drop. The GFR decline of rheumatism patients with existing chronic kidney disease was relatively moderate. Grade 4 patients were various. In grade 5, rheumatoid arthritis is no longer the main disease. [Conclusions] Intervention for chronic kidney disease should start with grade 2.

W41-3

Usefulness of CT screening, safety and efficacy of bDMARDs therapy in RA patients with nontuberculous mycobacteria pulmonary disease (NTM-PD): FIRST registry

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Conflict of interest: None

[Objectives] The aims of our study were to assess the usefulness of CT screening, safety and efficacy of bDMARDs in RA pts (pts) with NTM-PD. [Methods & Results] 2978 RA pts were screened using CT scan before starting bDMARDs in our hospital from April 2005 to April 2017. 31 pts were suspected of having NTM-PD from CT findings. After further examination, NTM infection was diagnosed in 16 pts (definite 6, past history 4, PCR and/or MAC-GPL IgA antibody positive 6; Species, *M. avium* 8, *M. intracellulare* 2, *M. Kansasii* 2). When typical CT findings of NTM-PD were shown, CT has a sensitivity of 91% and a specificity of 67%. Clinical characteristics of 16 pts (mean age 66.7 years; disease duration 148 months; DAS28-ESR 6.15) were not significantly different from those of 2978 RA pts. Nine pts were treated with chemotherapy for NTM before bDMARDs were started. Although ETN was discontinued in 2 pts due to LPD and scabies, the other 14 pts (ETN 4, ABT 10) had no adverse events. A year after starting bDMARDs, SDAI scores were not significantly different between RA pts with and without NTM-PD. [Conclusion] CT Screening before starting bDMARDs was useful to detect NTM-PD with high sensitivity. Adequate diagnosis and treatment for NTM-PD could enable disease control of RA with bDMARDs.

W41-4

A prospective study of the influence of therapeutic agents on the standardized incidence ratio (SIR) of tuberculosis (TB) in patients with RA by NinJa cohort data for 14 years

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Conflict of interest: None

[Object] To evaluate the incidence of therapeutic agents on the standardized incidence ratio (SIR) of tuberculosis (TB) in patients with rheumatoid arthritis (RA) prospectively. [Methods] We calculated the standardized incidence ratio (SIR) of TB from the clinical data on National Database of Rheumatic Disease by iR-net in Japan (***NinJa***) prospectively from 59 facilities for 14 years. [Results] Among 125,862 RA patients registered from 2003 to 2016, 69 patients developed TB and the SIR of TB was 2.28 (95%CI:1.74-2.82). 25 patients (36.2%) and 9 patients (13.0%) were treated with MTX and biologic agents, respectively. The SIR of TB in RA patients treated with biologic agents was 1.29 (0.16-2.42), and the SIR of TB in patients treated without biologic agents was 2.72 (1.98-3.46). [Conclusions] The SIR of TB of RA patients tended to decrease, and it was reconfirmed by prospective studies that there was no increase due to administration of biologic agents.

W41-5

Analysis of DMARDs selection in rheumatoid arthritis patients with malignancies

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Conflict of interest: None

[Object] The associations of malignancy with RA have been well established, however there is little information comparing the potential risk of cancer across conventional and biologic disease-modifying anti-rheumatic drugs (DMARDs) in patients with rheumatoid arthritis (RA). According to 2015 update of ACR recommendation for the use of DMARD, the panel recommends starting or resuming any biologic DMARDs for patients who have been finished to treat for solid malignancies. This study analyzed the DMARDs selection in rheumatoid arthritis patients with malignancies. [Methods] 2058 patients was seen in our clinic whose records were reviewed retrospectively and analyzed. [Results] Of the 2058 patients, 59 developed solid tumors. Of 59 patients, 43 patients were treated with methotrexate (MTX), and no patient was treated with biologic DMARDs. 27l of 43 patients treated with MTX were discontinuation of treatment with MTX. After diagnosis of malignancies, 14 patients showed relapse of RA (23.7%). After treatment of malignancies, 14 patients were restart to given for the treatment of RA. [Conclusions] Further study is needed to evaluate the safety for using DMARDs in RA with malignancies.

W41-6

Usefulness of long-term administration of abatacept for secondary Sjögren's syndrome associated with rheumatoid arthritis

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Conflict of interest: None

[Object] To clarify the efficacy and safety of long-term administration of abatacept (ABT) for secondary Sjögren's syndrome (sSS) associated with rheumatoid arthritis (RA). [Methods] 20 patients with sSS with RA followed up at our hospital, who were enrolled into an open-labeled, prospective, observational, and multicenter study (ROSE trial), were examined for 260 weeks (W) of long term observation after 52W of the study period. We analyzed 1) continuation rate of ABT for 260W and reason for cessation, 2) SDAI, 3) saliva volume, and 4) adverse events (AEs), retrospectively. [Results] 1) The continuation rate for 260W was 65% (13/20 cases). The reasons for cessation were insufficient response in 3, AEs in 1, cost in 1, and hospital transfer in 2 cases. 2) In 13 patients who continued ABT, SDAI significantly decreased from 18.4±11.8 (0W, baseline) to 7.0±5.3 (52W) ($P<0.05$), and the response was maintained at 156W (6.0±4.2). 3) Saliva volume by Saxson's test significantly increased from 3.0±1.9 (0W) to 4.2±2.3 g/2min (52W) ($P<0.05$), and was comparable between 0W and last observation (295±34W, 2.4±1.2 g/2min) in 6 cases. 4) For 260W, 32 AEs occurred in 15 out of 20 cases (75%), and 20 of AEs were infections. [Conclusions] Long-term administration of ABT might be useful for sSS with RA.

W42-1

Safety and effectiveness of abatacept in Japanese elderly and non-elderly patients with rheumatoid arthritis in all cases postmarketing surveillance

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Conflict of interest: Yes

Objectives: To investigate the safety, effectiveness and risk/benefit (R/B) balance of intravenous abatacept (ABT) in elderly/non-elderly patients with rheumatoid arthritis (RA) in all-case post-marketing surveillance in Japan. Methods: Patients were divided into non-elderly (<65 yrs) (NEG) and elderly (≧65 yrs) (EG) groups. Safety analysis was performed for all 3,882 enrolled patients. Effectiveness analysis was performed on 2,544 patients with at least two DAS28-CRP. The R/B was evaluated based on the incidence rate of infection and DAS28-CRP improvement >1.2 in 2,345 patients with relevant data. Results: There were 2,170 patients in NEG and 1,712 in EG. The ABT retention rate was 80.2% in NEG and 77.1% in EG. NEG had fewer adverse drug reactions (14.5% vs. 17.2%, p=.021) and infections (4.8% vs. 7.2%, p=.002) than EG. The changes in DAS28-CRP were similar between groups. Low-R/High-B and High-R/Low-B patients were 33.1 and 6.9% in NEG and 29.7 and 9.0% in EG. The parameters with a higher percentage/value in High-R/Low-B were age, disease duration, comorbidities, concomitant oral glucocorticoid use, prior use of biologics, and concomitant MTX non-use. Conclusion: Evaluation of Low-R/High-B factors may aid in determining the most appropriate medication for individual patients.

W42-2

Comparison for the response to abatacept for long term efficacy and safety in anti-Ro/SSA-antibody positive 30 patients and antibody negative 76 patients with RA

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Conflict of interest: None

Objective: Anti-Ro/SSA antibody is the most important autoantibody used as diagnostic markers for Sjögren's syndrome (SS). It was reported that RA patients with secondary SS had worse joint damage than RA without SS. And there is a difference in the clinical results of response to TNF inhibitors and non-TNF inhibitors in anti-Ro/SSA-antibody positive and antibody negative patients with RA. The aim of the present study

was to compare the response to abatacept for long term efficacy and safety in anti-Ro/SSA-antibody positive and antibody negative patients with RA. Methods: We examined 106 patients with RA (30 were positive and 76 were negative for anti-Ro/SSA antibody) who passed after initiation of treatment with abatacept for three years between January 2008 and October 2014. we compared the clinical characteristics and changes in composite disease activity index, such as DAS28, SDAI, and CDAI, for 3 years in anti-Ro/SSA antibody-positive and antibody-negative patients. Results: Disease activity was significantly decreased, relative to baseline, in both anti-Ro/SSA antibody-positive and antibody-negative patients by treatment with abatacept. Conclusion: Abatacept is effective in anti-Ro/SSA antibody-positive RA patients as well as other RA patients.

W42-3

The Comparative Observational Study about Efficacy, Safety and Continuation Rate between Infliximab and Tocilizumab in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Object] There have been few reports about head to head comparison of TNF inhibitors and IL-6 inhibitor in patients with RA. We investigated the efficacy, safety, and continuation rate of patients treated with infliximab (IFX) or tocilizumab (TCZ). [Methods] 167 patients with RA treated with IFX or TCZ retrospectively observed for 12 months. We compared the baseline characteristics, disease activity, physical disability, continuation rate, and safety. [Results] In IFX group (n=73) compared with TCZ group (n=94), we found shorter disease duration (IFX vs. TCZ:6.4 vs. 9.8years), higher naïve rate (93.2% vs. 29.8%), higher MTX users (100% vs. 64.9%), and higher MTX dose (8.5 vs. 5.7mg/week). Age of onset, rate of female, DAS28-ESR4, HAQ-DI, RF, MMP-3, and dose of PSL were similar. DAS28-ESR4 and HAQ-DI significantly decreased for one year in both groups. The patients who achieved remission or low disease activity were more in TCZ group (47.1% vs. 62.5%). There was no significant difference in the continuation rate (74.0% vs. 76.6%) and adverse events (11.0% vs. 12.8%), but inefficacy rate was higher in IFX group (13.7% vs. 5.3%) [Conclusion] TCZ-treated patients, who were less bio-naïve, showed equivalent or grater efficacy, continuation rate, and safety comparing with IFX.

W42-4

The limited usefulness of golimumab 100 mg under the Treat-to-Target strategy -Go-Go study-

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Conflict of interest: Yes

[Object] To examine the usefulness of GLM100 in T2T strategy. [Methods] 135 patients were randomized into G1: Use only GLM50, G2: Start with GLM50, increase after 12w to GLM100 with DAS28ESR>3.2, G3: Start with GLM100 and after 12w DAS≦3.2 to reduce to GLM50. In all groups, the increase/decrease of csDMARDs was allowed with the concept of T2T. Primary end point was RRP (ΔmTSS≧5) and CRRP (ΔmTSS≧3) patient proportion. [Results] In FAS analysis. There was no significant difference in the number of patients showing RRP and CRRP among G1 (n=44), G2 (n=40) and G3 (n=45) (P=0.167, 0.937). There was no significant difference in DAS28ESR/CRP, SDAI, CDAI and mHAQ (G1:5.51→3.64, G2:5.77→3.26, G3:5.67→3.53, median change in DAS28ESR over 48w). No difference was observed in the change of ESR or MMP-3. The persistence rate by Log-rank test was good in the order of G3> G2> G1, but no significant difference was observed (P=0.072). There was no difference for adverse event occurrence. The GLM cost was significantly different between G1 (1,520,000 yen), G2 (1,650,000) and G3 (2.780,000) (P<0.001). In PPS analysis, the bone erosion score was significantly suppressed by G2 compared to G1 (P=0.013). [Conclusions] Under the T2T strategy, the usefulness of GLM100 was limited.

W42-5

The long-term results of infliximab and etanercept in Bio-naive RA paitents by Kaplan-Meier survaivalship analysis

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Conflict of interest: None

[Object] To evaluate the 10-year survival of the first tumor necrosis factor inhibitor (TNFi) treatment in a cohort of rheumatoid arthritis (RA) patients, comparing the between-groups discontinuation rates for infliximab, and etanercept. [Methods] RA patients treated with their first TNFi were investigated from Nagoya Medical Center. Overall and by individual TNFi 10-year drug retention was evaluated. Drug survival rates were calculated using the Kaplan-Meier method and compared by the Cox extended model. Subanalyses were performed according to discontinuation reasons for insufficiency or adverse events. [Results] Of 190 patients, 80 were treated with infliximab, 102 were treated with etanercept. The 10-year drug survival rate for the unmatched population was 53.8% in ETN, 19.9% in IFX.26.6% and 13.7% discontinued the first TNFi because of adverse events, 54.1% and 37.7% discontinued the first TNFi because of insufficiency, respectively. The major incidence of withdrawal due to adverse event was malignancy, infection, drug allergy. [Conclusions] The overall 10-year drug survival rate was significantly higher for etanercept than infliximab. The reason are the incidence for anti-drug antibody, insufficient dose of IFX, MTX induced adverse event (ex. MTX-LPD) and so on.

W42-6

Real-world experience of effectiveness and safety of celtolizumab pegol for rheumatoid arthritis from the IORRA cohort study

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Conflict of interest: None

[Object] To investigate the effectiveness and safety of celtolizumab-pegol (CZP) for rheumatoid arthritis (RA). [Methods] We retrospectively investigated retention rate, change in disease activity and safety of CZP through medical records and the Institute of Rheumatology, Rheumatoid Arthritis (IORRA) cohort data, and factors associated with therapeutic re-

sponse at 12 weeks with CZP by using logistic regression analysis. [Results] Consecutive 143 RA patients who started CZP at our institute from April 2013 to July 2017 were enrolled (Female 93%; average age 48.3 y.o; disease duration 7 years; DAS28 3.7). Bio-naive patients were 42%. Methotrexate (MTX) was used in 68%. Patients discontinued CZP because of lack of effectiveness (n=51), marked effective (n=2), pregnancy (n=5) and side effects (n=13). The retention rate was 80% at 12 weeks. Patients in bio-naive and with MTX continued to use CZP than those in bio-switch (p=0.04) and without MTX (p=0.03), respectively. DAS28 at 12 weeks was significantly decreased in bio-naive (p<0.01) and with MTX (p<0.01), respectively. Bio-naive might be the factor for achieving good response at 12 weeks (p=0.08). [Conclusions] CZP therapy used as first bDMARD or in combination with MTX is associated with effectiveness.

W43-1

Analysis of renal functional change in elder patients with rheumatoid arthritis between 2012 and 2017

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Conflict of interest: None

[Objective] To analyze renal function evaluation and related factors of elder rheumatoid arthritis (RA) patients. [Method] Registered in the database for Ninja of our department for all 5 years from 2012 to 2017, fifty-two RA patients were enrolled, who were 75 years old and over when registered, and whose estimating glomerular filtration amount (eGFR) was obtained in both 2012 and 2017. These patients were divided into tertiles based on ΔeGFR. Factors related to ΔeGFR and changes in disease activity index (DAS28-CRP) between 2012 and 2017 were evaluated by uni- and multivariate analysis. [Results] There was a significant decrease in eGFR in 2017 from 2012 (P = 0.00606). As a dependent variable, DAS28-CRP, diabetes mellitus, MTX use and Tac use were extracted in 2012 (P = 0.003, <0.005, <0.02, <0.04, multiple regression analysis). Among the 3 groups, there were no significant differences in DAS 28-CRP in 2017 (P = 0.678), Δ DAS28-CRP (P = 0.342) and treatment except for Iguratimod (IGU) use. As a dependent variable, IGU use was extracted (P <0.04, multiple regression analysis). [Conclusions] In elder RA patients, eGFR was significantly reduced from 2012 to 2017. Significant factors associated with eGFR lowering were DAS28-CRP, diabetes mellitus, MTX use and Tac use.

W43-2

Nationwide survey of 199 patients with reactive amyloid A amyloidosis in Japan

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Conflict of interest: None

[Object] To retrospectively investigate the clinical features of amyloid A (AA) amyloidosis in Japanese patients. [Methods] We conducted a survey of Japanese AA patients. [Results] A total of 199 AA patients were included in this study. Underlying diseases of AA were rheumatic diseases (67%), uncharacterized inflammatory disorders (UID,11%), malignancy (7%), inflammatory bowel diseases (5%), chronic infection (5%) and Castleman's disease (4%), respectively. Clinical manifestations at diagnosis in AA patients were moderate to severe renal dysfunction (46%) and proteinuria (31%), severe GI manifestations (40%), heart failure (12%), arrhythmia (10%), respectively. Biologics was used in 49%. Tocilizumab (TCZ) was administered to about 70% and good responses were obtained in 96%. anti-TNF agents were administered in about 30% and good responses were seen in 74%. [Conclusions] Most frequent underling diseases of AA were rheumatic diseases. Meanwhile, UID and malignancy were frequent underling diseases of AA. Renal and GI manifestations were common and important pathological conditions in AA. Similarly, cardiac involvements were significant manifestations to remember. In the treatment regimens, biologics, especially TCZ, were effective therapeutic modalities.

W43-3

Comparison of renal function and treatments in patients with rheumaotid arthritis between NinJa 2012 and NinJa 2016

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Conflict of interest: None

[Object] To compare renal function and treatments in Japanese rheumaotid arthritis (RA) patients between NinJa 2012 and NinJa 2016. [Methods] Retrospective observational study was conducted. Studied were 8126 of 11940 RA patients from NinJa 2012 and 10672 of 15341 RA patients from NinJa 2016, whose eGFR were estimated using serum creatinine values. Age, sex, eGFR, serum CRP levels, erythrocyte sediments rates, DAS28, NSAIDs, steroids, csDMARDs, and bDMARDs were compared. Mann-Whitney U test and Chi-square test were employed for statistical analysis, and P<0.05 was regarded as statistical significance. [Results] Median of age was significantly older in NinJa 2016 (65 years old in NinJa 2012, and 68 years old in NinJa 2016). No difference was seen in sex ratio. eGFR, serum CRP levels, ESR, DAS28 were significantly lower in NinJa 2016. In NinJa 2016 patients with eGFR less than 60, daily NSAIDs, steroid, methotrexate, and TNF inhibitors were significantly less prescribed, and salazosulfapyridine, tacrolimus and non-TNFi biologics were more prescribed. [Conclusions] Japanese RA patients aged more with deterioration of renal function in four years from 2012, resulting in alteration of drug prescription.

W43-4

The causes of death in deceased patients with RA by NinJa 2016 cohort

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Conflict of interest: None

[Object] 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 NinJa 2016. [Methods] 114 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 76.3 years old. The major cause of death in deceased patients was malignancy in 31 patients. Next was infection in 21 patients involving in pneumonia in 16 patients, respiratory dysfunction involving intestinal pneumonia in 14 patients, cardiovascular disease in 12 patients, unknown sudden death in 5 patinets. [Conclusions] 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 since NinJa 2015.

W43-5

Descriptive analysis of pregnancy, delivery and lactation in patients with rheumatoid arthritis from the IORRA cohort

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Conflict of interest: None

[Object] To evaluate pregnancy, delivery, lactation and treatments during pregnancy in rheumatoid arthritis (RA) patients. [Methods] Among RA patients who enrolled in the IORRA cohort between 2010 and 2016, and those between 20 and 50 years who responded that they were "pregnant" or "delivered", we extracted the patients whom pregnancy was confirmed in medical records. [Results] Among 136 confirmed pregnancy cases, there were 106 births and 30 miscarriages. The average age at pregnancy was 34.2 years and 36.1 years in delivered and miscarried cases, respectively. Miscarried cases were significantly older pregnancies ($p<0.05$). Of the 106 births, 65 cases were confirmed birth weeks and the average was 37.9. The number of preterm delivery was 11 cases. The average birth weight of 59 babies whose birth weight could be confirmed was 2699 g. Drugs used before pregnancy were PSL (48.8%), NSAIDs (14.2%), csDMARDs (24.8%), and bDMARDs (48.0%). Of bDMARDs user, 73.8% were discontinued after the pregnancy, and 26.2% were continued during pregnancy. In some patients, bDMARD was used during lactation. [Conclusions] The actual situation of pregnancy, delivery and lactation in RA patients was revealed. Especially, bDMARDs were used at relatively high rates in RA patients who wish to have a child.

W43-6

Cost-effectiveness of biologics for the treatment of patients with rheumatoid arthritis analyzed using number needed to treat (NNT) method

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Conflict of interest: None

[Object] This study evaluated the cost-effectiveness of biologics for rheumatoid arthritis (RA) using number needed to treat (NNT) method. NNT is an index for determining the number of patients who need to be treated in order to achieve the clinical goal when a new treatment is introduced. [Methods] Fifty-four patients with RA was included in this study who were introduced biologic agents between September 2012 to March 2017 and continued same agent up to 24 weeks after. NNT was calculated based on disease activity score (DAS28-ESR) at 24 weeks. Ninety-four patients were investigated as a control group who treated with conventional DMARDs (csDMARDS). [Results] Forty-two patients (77.8%) achieved remission in DAS28-ESR, and NNT was 1.29 in biologic group, on the other hand, the rate of remission was 61.7% and NNT was 1.62 in control group. The actual health care cost in the study period was 1044066 JPY in biologic group and 78020 JPY in control group. [Conclusions] The actual health care cost of biologic group was more than10 times higher compared with csDMARDs group, however the cost-effectiveness of biologics was superior to csDMARDs in terms of NNT.

W44-1

Transition of the discordance of global assessment (GA) of rheumatoid arthritis (RA) disease activity between RA patients (PGA) and their physicians (PhGA) - Analysis based on NinJa 2011-2016 database

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Conflict of interest: None

[Object] In previous JCR meetings, we reported that PGA-PhGA discordance was significantly related to pain, functional impairment, and large-joint involvement. The aim of the present study is to investigate the factors causing persistent PGA-PhGA discordance. [Methods] The number of RA patients whose VAS were available and registered in both *NinJa* 2011 and 2016 was 4484. Positive discordance was defined as PGA-PhGA (PGA minus PhGA) ≧3 cm (n=3688), and concordance between -3 and 3 cm (n=775). The association of PGA-PhGA discordance in *NinJa* 2016 with clinical manifestations of *NinJa* 2011, including age, sex, age at onset, disease duration, TJC, SJC, mHAQ, stage, class, DAS28, and PGA-PhGA, were examined. [Results] It was demonstrated that 35 % of RA patients in the positive discordance group in 2011 remained in the same group in 2016, while 10% of RA patients in the concordance group were classified in the positive discordance group in 2011 ($p<0.01$). Multivariate logistic regression identified age, pain, mHAQ, and positive discordance as risk factors for positive discordance 5 years later. [Conclusions] Since PGA-PhGA discordance can be persistent, RA care providers should pay attention to pain and functional impairment to share common disease recognition with their RA patient.

W44-2

Comparison of QOL evaluation using EQ-5D-3L and EQ-5D-5L in patient with japanese rheumatoid arthritis ~Research using IORRA cohort~

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Conflict of interest: None

[Object] EQ-5D-3L is frequently used for QOL evaluation. Recently EQ-5D-5L is developed due to problems such as sensitivity and ceiling effect.A comparison study was conducted between EQ-5D-3L and EQ-5D-5L in RA patients. [Methods] The subjects were Japanese RA patients who participated in the IORRA survey in October 2016. We examined the difference in QOL value distribution between EQ-5D-3L and EQ-5D-5L across the board. We compared QOL values by EQ-5D-3L and EQ-5D-5L for each sex, duration, disease activity and dysfunction, and used medicine. We examined whether EQ-5D-5L was more useful in patient background or EQ-5D-5L which was completely healthy at EQ-5D-3L and was not completely healthy by using EQ-5D-5L. [Results] 5,023 subjects were targeted, overall EQ-5D-3L is 0.823±0.1789, EQ-5D-5L is 0.848±0.158. For whole and all patient backgrouds and with or without medicine, the numerical value was larger for EQ-5D-5L than for EQ-5D-3L was larger and QOL value was higher. In EQ-5D-3L, 2,264 patients in perfect healh state, 28.2% of these who lost complete health by EQ-5D-3L to EQ-5D-5L, the problem of ceiling effect was improved. [Conclusions] In Japanese RA patients, the problem of ceiling effect was improved by using EQ-5D-5L, suggested that it is a question reflecting more health condition.

W44-3

Importance of affected joint sites in the clinical practice of rheumatoid arthritis

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Conflict of interest: None

Objective: The aim of our study was to assess the importance of the affected joint sites in the clinical practiceof 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 joint sites, patient's and physician's global assessments, and RA treatments received. Results: SDAI remission rate was 49.7%. The joint pain in the shoulder and knee joints were observed in 17% and 18%, respectively, of the patients, while tenderness (4% and 6%) and swelling (2% and 9%) were less frequent. Patient global assessment, HAQ-DI, CRP and MMP-3 were dependent on the swelling of large joints, while physician's global assessment was based on the swelling of both large and small joints. In addition, SDAI remission rate was significantly lower in large joint-dominant group (23%) than the small joint-dominant group (17% vs. 59%, P<0.0001). Conclusion: Affected joint sites, especially large joints, should be taken into consideration in the clinical practice of RA.

W44-4

Analysis of factor for elbow destruction of rheumatoid arthritis

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Conflict of interest: None

[Object] Patients with rheumatoid arthritis (RA) suffer from elbow destruction. We investigated factors that affect Larsen grade of elbow. [Methods] We recruited 260 RA patients treated at Kyoto University Hospital (KURAMA cohort). We checked Patient-Related Elbow Evaluation (PREE), power doppler (PD) signal of elbow, dose of MTX, DAS28-ESR, TJC28, SJC28, RF, ACPA, stage, class, steroid-use, HAQ. We adopted Spearman rank correlation analysis between Larsen Grade and Stage, PREE and HAQ. Larsen Grade was adopted as the objective variable. Further, each parameter was used as an explanatory variable. First, univariate analysis was performed and we got statistically significant paremeters. Second, stepwise multiple regression analysis was performed with the same explanatory variables. [Results] We found a moderate positive correlation between Larsen Grade and Stage. Further, strong positive correlation were existed between PREE and HAQ. With multiple regression analysis, PREE, PD signal of elbow, Stage and age were statiscally significant pridictors for Larsen Grade. [Conclusions] Larsen Grade had a moderate association with Stage. PREE related to the HAQ strongly. PREE, PD, Stage, age may be useful for predicting RA elbow joint destruction.

W44-5

Epidemiological features of Japanese patients with juvenile idiopathic arthritis - Findings at diagnose from nationwide survey for the core facilities specialized in pediatric rheumatism -

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Conflict of interest: None

[Object] We aimed to disclose the specific characteristics of juvenile idiopathic arthritis (JIA) in Japan. [Methods] This first nation-wide epidemiological research on JIA was organised by the study group of Ministry of Health, Labour and Welfare. We used the case cards on patients who regularly visit the core facilities specialized in pediatric rheumatism at January 2017. The evaluation items were onset age, subtype, family history of rheumatic disease, results of blood examination, JADAS-27 and Poznanski score at diagnose. [Results] The data of 726 patients from 15 core facilities were evaluated. The most common subtypes were oligoarthritis, systemic arthritis (sJIA) and rheumatoid factor (RF) positive polyarthritis. The onset age was the youngest in oligoarthritis. There was girl dominancy except in sJIA and enthesitis related arthritis (ERA). The family history was identified in 10.7%. ANA titer was higher in oligoarthritis and RF-negative polyarthritis. JADAS-27 was highest in RF positive polyarthritis (24.9±8.0). The Poznanski score was already lower than - 2SD in RF positive arthritis, ERA and undifferentiated arthritis. [Conclusions] The characteristics of JIA show difference between races and domestic research is important for understanstanding the pathophysiology.

W44-6

Epidemiological features of Japanese patients with juvenile idiopathic arthritis - Findings at prognosis from nationwide survey for the core facilities specialized in pediatric rheumatism -

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Conflict of interest: None

[Object] Detailed investigation on juvenile idiopathic arthritis (JIA) in Japan has not been done in the past, and it reports on the prognosis based on the nationwide epidemiological findings. [Methods] We asked 15 domestic facilities that specialize in pediatric rheumatic diseases to investigate patients on regular hospitalization. We analyzed complications

during treatment, remission rate of JIA, adult medical examination. [Results] Data of 726 patients with JIA were collected. Clinical remission rates were significantly higher in the systemic type and RF positive polyarthritis was the lowest. Infectious diseases during the course of treatment were without TB infection, no infection with hepatitis B virus, 24 cases of varicella, and 8 cases of shingles. In 2 cases of malignant tumors, one case of germinoma and malignant lymphoma was seen. Pathological fracture was observed in 11, and systemic arthritis with active arthritis (without systemic features) was significantly more than in other disease types. At the time of the last observation, there were 148 cases out of 712 adults. There were 85 cases in which there was no plan to move to adult studies. [Conclusions] The course after treatment of JIA patients was revealed.

W45-1

Usefulness of the 25-question Geriatric Locomotive Function Scale as a physical function evaluation in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] Rheumatoid arthritis (RA) is one of the diseases which causes Locomotive Syndrome (LS). HAQ is widely used as a physical evaluation in RA patients, while the 25-question Geriatric Locomotive Function Scale (GLFS-25) is rarely used in RA patients. [Methods] There were 159 RA patients examined about GLFS-25 in 2017. The correlation between HAQ-DI and GLFS-25 was analyzed using Pearson's moment correlation coefficient. In addition, the cutoff value of GLFS-25 for HAQ-DI=0.5 was calculated by ROC analysis. [Results] In 159 patients, the age was 66.2 ± 12.0 years, HAQ-DI was 0.5 ± 0.7, GLFS-25 was 17.8 ± 19.1. GLFS-25 and HAQ-DI showed a positive correlation (correlation coefficient [r]=0.869). Furthermore, the question with the highest correlation coefficient was "Walk outdoors on flat ground?" (r=0.823), the lowest question is "Carry meals with your chopsticks?" (r=0.641). The cutoff value of GLFS-25 for HAQ-DI=0.5 was 20. [Conclusions] GLFS-25 was strongly correlated with the question about the lower limb function of HAQ. In addition, the cutoff value of GLFS-25 for functional remission of RA patients was higher than the cutoff value (16, Seich et al. 2012) where intervention is required as LS. There is a possibility of LS in RA patients who achieve remission.

W45-2

Does obesity represents a risk factor for a poor remission rate to anti-tumor necrosis factor a therapy in Japanese rheumatoid arthritis?

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Conflict of interest: None

[Object] Evidence remains sparse on obesity in rheumatoid arthritis. We examined the association between obesity and a poor remission rate to anti-tumor necrosis factor a in Japanese rheumatoid arthritis. [Methods] Patients requiring anti-tumor necrosis factor a were identified from our hospital in Shizuoka, 2009-2017. Following World Health Organization guidelines, participants were classified using a appropriate body mass index: BMI (kg/m^2) for Asian populations as follows:<18.5 (underweight), 18.5-23.0 (normal weight), 23.0-27.5 (overweight) and ≧27.5 (obesity). We estimated odds ratios and their 95% confidence intervals for non-remission of SDAI and failure for anti-tumor necrosis factor a therapy, controlling for age, sex, smoking status, anti-CCP antibody, rheumatoid factor, disease duration. [Results] Compared with normal-weight participants, obese participants tended to have higher odds ratios; the multivariate odds ratios (95% confidence interval) were 2.24 (0.53-9.43) for obesity. [Conclusions] Obesity might be a risk factor for a poor remission rate to anti-tumor necrosis factor a therapy in Japanese rheumatoid arthritis. Our findings imply that weight loss interventions can be recommended for obsity.

W45-3

Prediction factors of commodities on clinical remission for rheumatoid arthritis whose onset are less than three years - Results from Kansai Consortium for Well-Being of Rheumatic Disease Patients -

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Conflict of interest: None

[Object] A part of rheumatoid arthritis (RA) patients are resistant to clinical remission (CR) irrespective of therapies. In addition to known risk factors, systemic organ complications are assumed to interfere with CR. [Methods] In Kansai consortium for well-being of rheumatic disease patients (ANSWER) cohort, RA patients within 3 years after onset were included and followed. Using logistic regression analysis, background factors at the initial visit to predict CR after 1 year (1 year-non CR) were extracted with disease activity and treatment at first visit taken into account. [Results] Of the 753 subjects included in the study, 273 (36.3%) cases were resulted in 1 year-non CR. The average scores of DAS28-CRP at the time of first visit and one year later was 3.43 and 2.18, respectively. Non CR at first visit (OR 14.5, 95% CI 2.50 - 84.5), age at onset (OR 1.02/year, 95% CI 1.01 - 1.04), ischemic heart disease (OR 10.0, 95% CI 1.26 - 79.43), lung disease (OR 2.86, 95% CI 1.24 - 6.62), obesity (OR 2.80, 95% CI 2.30 - 6.04) and allergic disease (OR 0.45, 95% CI 0.22 - 0.93) were extracted as independent predictive factors for 1 year-CR. [Conclusions] The presence of a certain organ complication may have influence on the achievement clinical remission.

W45-4

Bone erosion risk prediction: evaluation of patients with rheumatoid arthritis from the first visit

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Conflict of interest: None

[Object] The aim of this work was to retrospectively identify risk factors for the progression of bone erosion in patients with rheumatoid arthritis (RA). [Methods] Among 512 patients who visited our hospital for the first time, 214 RA patients without bone erosion were enrolled for the study. The CRP level, CDAI, HAQ score, the presence of bone erosion, and the use of prednisolone (PSL), methotrexate (MTX), or biological disease-modifying antirheumatic drugs (bDMARDs) of the patients at 3, 6, 12, 18, and 24 months after their first visit to our hospital were analyzed statistically. [Results] By the end of 24 months, CDAI remission was achieved in 40.2% of the patients and low disease activity was achieved in 26.6%. Bone erosions progressed in 13.6% of the patients. Anti-CCP antibody (ACPA) level and disease duration were associated with bone erosion progression in the Cox proportional hazards model. In landmark analyses, CRP levels of <0.3 mg/dl at 3 months were associated with no subsequent bone erosion progression in the ACPA-positive patients, but CDAI and the use of MTX or bDMARDs at 3 months showed

no association. [Conclusions] Lower CRP levels at 3 months may help prevent bone erosion progression, but the achievement of CDAI remission at 3 months could not prevent it.

W45-5

Serum metabolomic analysis for identifying biomarkers to predict response to biological treatment in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To identify serum biomarkers for prediction of the response to biological (Bio) treatment in patients with rheumatoid arthritis (RA). [Methods] We measured 120 metabolites of RA patients with moderate and high disease activity prior to Bio treatment using a Capillary Electrophoresis-Mass Spectrometry. The patients' response was determined 12 weeks after Bio treatment, based on the EULAR response criteria. We compared the metabolites between the response and the non-response group and analyzed discriminative ability. [Results] Among 43 patients, responders were 14 of 26 patients in TNF-α inhibitors (TNFi) group and 6 of 17 patients in abatacept (ABT) group. By using the orthogonal partial least-squares discriminant analysis, we have identified 5 metabolites for prediction of the response to TNFi and 3 metabolites for that to ABT. The receiver operating characteristic (ROC) analyses for multi-biomarkers revealed an area under the curve (AUC) of 0.781 for TNFi, and that of 0.908 for ABT. The ROC analyses for multi-biomarkers with clinical factors revealed AUC of 0.941 for TNFi, and that of 0.940 for ABT. [Conclusions] We identified serum biomarkers with high discriminative ability for the response to TNFi and ABT treatment in patients with RA by using metabolomic analysis.

W45-6

Influence of dose titration of concomitant steroid and methotrexate during biologic therapy on remission rates in patients with rheumatoid arthritis in daily practice based on the IORRA cohort

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Conflict of interest: None

[Objectives] To examine remission rate and concomitant use of MTX and steroid in RA patients receiving bDMARDs. [Methods] RA patients who commenced bDMARDs from 2012 to 2016 were extracted from the IORRA cohort. DAS28, DAS28 remission rate, and the proportion of patients taking concomitant MTX and steroid and doses of these drugs were evaluated before and 2 years after initiation of each bDMARD. [Results] DAS28 before and after infliximab (IFX: n=39), etanercept (ETN: n=199), adalimumab (ADA: n=101), tocilizumab (TCZ: n=261), abatacept (ABT: n=123), golimumab (GLM: n=128) and certolizumab pegol (CZP: n=87) were 3.5/2.7, 3.4/2.7, 3.5/2.8, 3.8/2.4, 3.8/3.3, 3.7/2.8, and 3.6/2.9, respectively. The DAS28 remission rates were 56.4%, 57.3%, 53.3%, 64.0%, 23.6%, 50.1%, and 46.0%, respectively. The proportion of patients taking MTX decreased among ABT, ETN and TCZ users, while that and MTX dose increased among ADA and IFX users. The proportion of patients taking steroid did not change over time except for ETN user, and 42.0% of bDMARD users were still treated with steroid. [Conclusion] MTX and glucocorticoid use and doses in daily practice were commonly titrated after the initiation of bDMARDs.

W46-1

The analysis of factors affecting well-controlled RA patient VAS

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Conflict of interest: None

[Object] Among the elements of composite measure to evaluate the disease activity of RA, patient VAS is thought to be the most difficult to improve. We now examined factors influencing it with be well-controlled arthritis by multivariate analysis. [Methods] Of the RA patients registered in the ANSWER cohort, we focused on the first visit day in 2016 of 935 cases with swollen joint number 1 or less and CRP 1.0 mg/dl or less. With an objective variable that the patient VAS was 1cm or less (0-10), explanatory variables such as age, sex, duration of RA, presence or absence of autoantibodies, number of tender joints, presence or absence of corticosteroid/ sDMARDs / bDMARDs were established. [Results] The number of tender joints, stage and use of corticosteroid were significantly correlated with patient VAS. If the number of pain joints was 1 or less, OR was 5.58 (95% CI 2.99 - 10.40: $p = 6.1\times10^{-8}$). Stage 1 or 2, OR was 1.79 (95% CI 1.21 - 2.65: $p = 3.4\times10^{-3}$). On the other hand, the use of corticosteroids was a risk and OR was 0.52 (95% CI 0.34 - 0.79: $p = 2.3\times10^{-3}$). [Conclusions] In this analysis, we found that not only suppressing arthritis, but also reducing tender joints and suppressing joint destruction without using corticosteroid are important to achieve good patient VAS.

W46-2

The effect of large joint involvement on the efficacy of MTX-based non-biologic DMARDs treatment -Data from Kansai consortium for well-being of rheumatic disease patients (ANSWER Cohort)-

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Conflict of interest: None

[Object] To verify the effect of large joint involvement (LJI) on the efficacy of MTX-based non-biologic DMARDs (non-bDMARDs) treatment in patients with rheumatoid arthritis (RA). [Methods] Among 618 cases with affected joint information in the ANSWER Cohort, 424 cases who were not in clinical remission (CR) and did not use biologic DMARDs (bDMARDs) at the start of MTX were analyzed. Regarding the initiation of bDMARDs after starting MTX as competing risk for

achieving CR (DAS28-ESR<2.6), we compared the cumulative incidence of CR achievement after 1 year using Gray test, and calculated sub-hazard ratio (adjSHR) (95% CI) adjusted with potential confounders at baseline using Fine-Gray competing risk model. [Results] The median was significantly higher in LJI group at age 64.6 vs 59.1 years, BMI 21.9 vs 21.2kg/m^2, CRP 1.70 vs 0.20mg/dl, MMP-3 206.8 vs 66.6ng/ml, DAS28-ESR 4.96 vs 4.17, HAQ-DI 1.00 vs 0.62. The cumulative CR achievement rate at 1 year was significantly lower in LJI 43.0% than in non-LJI 55.1% (p = 0.03). The adjSHR of LJI was 0.63 (0.42 - 0.95). The adjSHR of the shoulder, elbow and knee was 0.94 (0.43 - 2.10), 0.67 (0.37 - 1.23), and 0.62 (0.40 - 0.98). [Conclusions] LJI, especially knee joint involvement, inhibits achievement of CR in MTX-based non-bDMARDs treatmemt.

W46-3

Association between distribution of affected joints and disease activity score in rheumatoid arthritis patients

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Conflict of interest: None

[Object] It is unknown which part of the joints strongly contributes to increased levels of ESR and CRP in rheumatoid arthritis (RA) patients. [Methods] We analyzed retrospectively 3685 clinical data (1148 RA patients) who visited our hospital on January to July in 2017. We divided the joints into 6 sites (shoulders, knees, hands, elbows, MCPs, PIPs) for further analysis. We investigated the correlation between swollen, tender joints and the disease activity-related scores such as ESR, CRP, PtVAS and Dr VAS. [Results] Interestingly, among the 6 sites, knees are the strongest factors which induce increased levels of ESR and CRP. By contrast, elbows are the weakest factors which contribute to elevated levels of ESR and CRP. PtVAS strongly correlated with increased affected joints of hands, shoulders and MCPs. By contrast, DrVAS related to swollen, tender joints of hands, MCPs, shoulders and knees. Elbows are the weakest factors which contribute to increased levels of PtVAS and DrVAS. [Conclusions] Thus, these findings suggest that different joint distribution in RA patients leads to different results of disease activity score.

W46-4

Radiographic progression of large joint damage during treatment with biologic agents and its predictive factors: 3-years follow-up results

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Conflict of interest: None

[Objectives] A little information is available regarding radiographic progression of large joint damage (RPD) during treatment with biologic agents (BAs) for more than 3 years. We investigated the 3-years follow-up results and association between RPD and patient backgrounds or Larsen grades of joints. [Methods] Seventy patients receiving BAs for more than 3 years or achieving BAs-free status were included in this study. The mean age at the start of BAs was 62.4 year-old, and the mean disease duration was 10.9 years. A total of 321 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 22 patients (31.4%) and 32 joints (10.0%). Joints with LG: 3 or more had significantly higher rates of RPD than those with LG: 2 or less. A multivariate logistic regression analysis revealed that HAQ was an independent risk factor for RPD (odds ratio: 7.075, 95% CI: 1.363-36.735). AUC of the ROC curve was 0.727 and the cut-off value was 1.4375 (sensitivity: 0.538, specificity: 0.903). [Conclusion] LG and HAQ at the start of BAs were predictive of RPD after 3 years. BAs should be started before LG and HAQ exceed 3 and 1.5, respectively.

W46-5

Target of joint surgery in patients with rheumatoid arthritis based on index of activity speed (Timed up and Go test)

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Conflict of interest: None

[Object] The purpose of this study is to examine the target value for the operation speed Timed Up & Go test (TUG) from the effect of lower leg joint operation. [Methods] This is a multicenter study conducted as a research by the Ministry of Health, Labor and Welfare. We examined the numerical targets for joint surgery of lower limbs in RA patients based on the relation between achievement of functional remission (HAQ<0.5) and TUG before and after operation and its change. Logistic regression model, GML model adjusted and analyzed age and gender. Cut-off value was calculated based on ROC analysis. [Results] 139 patients with lower extremity surgery were included. Average age 65.4 years, disease duration 17.5 years, female 92.1%, DAS 28 2.95, the main operation was THA 10.1%, TKA 33.8%, forefoot arthroplasty 46%. TUG was significantly improved by surgery. Postoperative TUG was significantly related to postoperative HAQ remission. TUG / 1 second was OR 1.36 (1.02 - 1.79). Postoperative TUG cut-off from ROC analysis was 9.2 seconds. [Conclusions] TUG is considered to be a useful objective indicator that quantifies the effect of surgery with high sensitivity. The TUG target value of the lower limb surgery is 9 to 10 seconds.

W46-6

Treatment target considering quality of life in patients with elderly rheumatoid arthritis

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Conflict of interest: None

[Object] To determine the target DAS28 value in patients with elderly rheumatoid arthritis (RA) considering Health Assessment Questionnaire (HAQ). [Methods] In WakaURA cohort, 261 patients with RA (female = 78.9%, age = 61.3 years old, disease duration = 9.2 years) were divided into elderly (>=65 years old) and non-elderly (<65 years old) patients. Patients' background, treatment and HAQ were examined retrospectively, and DAS28 value for well-controlled HAQ was determined. [Results] 1) Disease duration was longer (11.4 vs. 7.6 years), stage III+IV (40.4 vs. 20.3%) were more frequent and DAS28 was higher (3.44 vs. 2.89) in elderly than in non-elderly RA. 2) Methotrexate (45.0 vs. 76.3%) and biological disease-modifying antirheumatic drug use (34.9 vs. 40.1%) were different between in elderly and non-elderly RA. 3) Among elderly RA, a significant lower HAQ was observed in patients with than without low disease activity (0.71 vs. 1.15), whereas HAQ levels were equal between with and without clinical remission (0.91 vs. 0.89). Among non-elderly RA, however, patients with clinical remission had the lowest HAQ level

(0.20). [Conclusion] Different from non-elderly RA, more decreased HAQ level was not observed in patients with than without clinical remission in elderly RA.

W47-1

Clinical features of rheumatoid arthritis in patients within one year after diagnosis who have renal dysfunction

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Conflict of interest: None

[Object] We aimed to determine the clinical features of patients with rheumatoid arthritis (RA) within one year after diagnosis who have renal dysfunction. [Methods] The retrospective study analyzed data from 381 patients with RA at our institution who were diagnosed with renal dysfunction between April 2011 and July 2016. [Results] Among the patients, 325 had renal dysfunction (Group A) and 56 did not (Group B). Groups C (n=48) and D (n=7) comprised patients with eGFR 30-60 and <30, respectively. Group A had a younger mean age than Groups B, C, and D. Methotrexate and biologic DMARD were less frequently administered to Group B than Group A, whereas salazosulfapyridine was more frequently administered to Group B than Group A. Among patients treated with prednisolone, the doses were the same in Groups A and B. Disease activity (determined by DAS28, SDAI, and CDAI) of RA at the time of diagnosis and at one year later was the same in Groups A and B. Nineteen patients in Group C were treated with MTX and the proportion of those who discontinued MTX was equal to that in Group A. Both groups received the same dose of MTX. [Conclusions] Contrary to previous findings, renal dysfunction seems to have little effect on RA.

W47-2

Discrepancy between the population of biological RCT and daily practice based on the IORRA cohort

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Conflict of interest: None

[Object] By increasing the importance of real world evidence, the discrepancy between the evidence based on the randomized controlled study (RCT) and on the daily practice has been recognized. We investigated the percentage of patients in daily practice who fulfill the entry criteria of RCTs conducted in Japan. [Methods] Percentage of patients in the IORRA who fulfill the entry criteria of phase 2 or 3 RCTs of infliximab (IFX), etanercept (ETN), adalimumab (ADA), golimumab (GLM), certolizumab (CZP), abatacept (ABT), tocilizumab (TCZ), infliximab-BS (IFX-BS)] conducted in Japan has been investigated. [Results] Percentage of patients in the IORRA who met the inclusion criteria of 19 RCTs of biologics (IFX: 2, ETN: 1, ADA: 2, GLM: 2, CZP: 3, ABT: 2, TCZ: 6, IFX-BS: 1) was 2.3% in average (0.0%-16.2%). Percentages of patients who had 6 or 8 swollen joints were 17.3% [3.7%-33.9%] in mean [min-max], tender joints were 16.1% [4.5%-33.0%] and CRP ≥1 or 2mg/dl were 33.9% [20.2%-49.9%] in the IORRA cohort. [Conclusions] We should recognize that the evidence of biologics from RCT is based on the limited patients in the daily practice.

W47-3

Concerns about the evaluation of disease activity by composite measures in elderly patients with rheumatoid arthritis

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Conflict of interest: Yes

[Object] To examine the concerns about the evaluation of disease activity by composite measures in elderly patients with rheumatoid arthritis (RA). [Methods] Female RA patients, who had no tender and swollen joints (28 joints evaluation) and whose physician's VAS≦5/100 (defined as "doctor's remission"), were extracted from the National Database of Rheumatic Diseases in Japan (NinJa) 2015, and the components of composite measures (DAS28-ESR, DAS28-CRP, SDAI and CDA), rates of remission, tender and swollen joints (68 joints evaluation), ADL, QOL and their treatments were evaluated. [Results] Doctor's remission achievement rate gradually decreased from 24.8% (under the age 40) to 10.4% (over the age 80). If the average value of composite measure under the age 40 is 100, it rises to 140 in DAS 28-ESR, 121 in DAS 28-CRP, 203 in SDAI, and 189 in CDAI over the age 80, and the remission rate also increased; 92.3 (under the age 40) to 62.1% (over the age 80), 99.4 to 93.9%, 96.8 to 80.3%, and 95.5 to 76.5%, respectively. Many factors worsened by aging except tender and swollen joint count (68 joints evaluation). [Conclusions] Composite measure is influenced by various factors due to aging, and there is concern about overestimation of disease in elderly RA patients.

W47-4

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

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Conflict of interest: None

[Objective] To determine whether dose redaction of MTX in rheumatoid arthritis patient who achieved clinical remission is possible without relapse. [methods] Patients had to have been receiving stable dose of MTX and in remission as defined by DAS28-CRP at least 12 weeks were included in this study. MRIs of dominant hands at baseline were obtained and scored using the RAMRIS system. MTX dose was reduced by half from baseline. Clinical disease activity was evaluated from baseline to every 4 weeks. [Result] Thirteen patients were enrolled in this study (8 female). The mean (±SD) age, disease duration, MTX dose before including study and DAS28-CRP at baseline was 66.6±9.8y, 6.4±4.0y, 8.5±2.9 mg/w and 1.35±0.26. Eleven patients were seropositive. Low grade subclinical MRI inflammation was detected in all patients. The median (range) synovitis, bone edema and bone erosion sore were 1 (0-7), 0 (0-4) and 6 (1-22). There was a significant correlation between DAS28-CRP and synovitis score at baseline ($r=0.64$, $p<0.05$). At 8 weeks, all patients stayed in clinical remission (8w:DAS28-CRP1.55±0.38). [Conclusion] We conclude that half dose redaction of MTX for the RA patient who achieved clinical remission and had low grade MRI subclinical inflammation might be a beneficial option of tapering MTX.

W47-5

Th1/17 cells and RF as novel predictive markers for clinical response to abatacept treatment in patients with rheumatoid arthritis: the 52-week analysis

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Conflict of interest: None

[Introduction] Presence of autoantibodies is reported to predict response to abatatacept (ABA) treatment. Here, we have determined the temporal effects of ABA on lymphocyte subsets, autoantibody titers and disease activity, and also tested whether the abnormalities of these subsets at baseline could be a predictor of ABA treatment. [Methods] Twenty-five of bio-naive patients with RA were treated with ABA and subject to sequential analysis of lymphocyte subsets and the titers of autoantibodies, along with the assessment of disease activity. [Results] After commencing ABA treatment, disease activity and activation of Th subsets were both gradually decreased. The proportion of central and effector memory $CD4^+$T cells, Th17, Tfh and Treg cells was sequentially decreased, while that of naive $CD4^+$T cells was increased. On the other hand, changes in $CD8^+$T cells, B cell subsets and autoantibody titers were minimally affected. Notably, higher RF titers and lower proportion of Th1/17 cells at baseline were significantly noted in the good EULAR response group. [Conclusions] These findings suggest that ABA corrects the abnormalities of $CD4^+$T cell subsets, along with inhibition of disease activity, and Th1/17 cells and RF at baseline are good predictors of clinical response to ABA treatment.

W47-6

The achievement and maintenance of bio holiday of Infliximab and Adalimumab started after 2012 for Rheumatoid Arthritis

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Conflict of interest: Yes

[Object] To explore factors that can achieve and maintain bio holiday in cases of Infliximab (IFX) and Adalimumab (ADA) started after 2013. [Methods] 28 IFX and 55 ADA were started after 2013, 12 and 22 cases achieved bio holiday. Differences between achieved bio holiday and not were examined by logistic regression analysis using variables including age, sex, etc. The definition of relapse after drug withdrawal was SDAI> 3.3, and factors of relapsed cases were also examined. [Results] For achievement of bio holiday, age ($p < 0.01$), baseline prednisolone dose ($p < 0.01$) and prior use of biological agent ($p = 0.01$) was extracted as significant factors by logistic regression analysis. The probability of maintenance of bio holiday was 89% and 77% at 12 and 24 months, respectively. As factors predicting relapse after withdrawal, DAS28-CRP at discontinuation ($p < 0.01$), ACPA titer ($p = 0.02$), baseline MTX dose ($p = 0.04$), RF titer at discontinuation ($p = 0.02$) were identified. In patients with DAS28-CRP$\leqq$1.02 at discontinuation, the probability of maintenance of bio holiday were 100% and 93% at 12 and 24 months, respectively. [Conclusions] When disease activity was strictly controlled and RF was low, there was less relapse after withdrawal.

W48-1

Rituximab or cyclophosphamide for remission induction of ANCA associated vasculitis: a clinical observational study

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Conflict of interest: None

Objective: Rituximab (RTX) is recommended for remission-induction in ANCA-associated vasculitis (AAV) as well as cyclophosphamide (CYC). However, the efficacy and safety of RTX in Japanese patients is not established. The aim of our study is to clarify the efficacy and safety of RTX and those of CYC for remission-induction in AAV patients. Methods: This retrospective observational study includes 60 AAV patients treated with CYC or RTX. Complete remission was defined as Birmingham Vasculitis Activity Score version 3 of 0. Results: Of 60 AAV patients, 41 cases and 19 cases received CYC and RTX as induction therapy, respectively. Thirty-eight cases (93.5%) of those received CYC and 8 cases (43.1%) of RTX were newly diagnosed. RTX included 8 cases that relapsed after CYC. Induction rate at 3 months after drug administration were similar in both groups (CYC: 58.5%, RTX: 57.9%). During the first 6 months, the incidence rates of adverse events were 36.6% in CYC and 63.2% in RTX, and infection rates were 17.4% and 36.8% respectively. Conclusion: RTX was comparable to CYC in remission-induction for Japanese AAV patients in terms of efficacy and safety. RTX was effective even in relapsing disease after induction with CYC.

W48-2

Comparison between rituximab and intravenous cyclophosphamide for induction therapy of microscopic polyangiitis associated interstitial lung disease: a single-center retrospective study

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Conflict of interest: None

[Objectives] To investigate the efficacy and safety of rituximab (RTX) and intravenous-cyclophosphamide (IVCY) for microscopic polyangiitis (MPA) associated interstitial lung disease (ILD). [Methods] We retrospectively examined the patients who met the MPA diagnostic criteria from 2003 to 2017 and received induction therapy of RTX or IVCY for ILD. We divided them into 2 groups, those treated with RTX and IVCY, and evaluated the efficacy and safety for 2 years. We compared the percent improvement of %FVC from baseline, the rate of hospitalization by the ILD deterioration, a home oxygen therapy (HOT) requirement rate, and safety profiles. [Result] We evaluated 14 patients with RTX group and 22 with IVCY group. A higher value of serum KL-6 and a lower percentage of patients treated with methylprednisolone pulse therapy were observed in IVCY group comparing with RTX group ($p=0.02$ and 0.02, respectively). No significant difference was found in rate of deterioration of ILD, hospitalization, HOT requirement, and adverse events ($p=0.30$, 0.11, 0.18 and o.24, respectively). However a greater improvement of %FVC was seen in IVCY group than RTX group ($p=0.02$). [Conclusions] Additional therapeutic effect may be seen in %FVC improvement for IVCY comparing with RTX in MPA-associated ILD.

W48-3

Rituximab in initial remission induction therapy for ANCA-associated vasculitis

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Conflict of interest: None

[Object] To evaluate the efficacy and safety of rituximab (RTX) in

the initial remission induction therapy for ANCA-associated vasculitis (AAV). [Methods] 18 patients who received CY or RTX from April 2014 to November 2017 were evaluated retrospectively. [Results] Among 18 patients,11 CY and 8 RTX were administered as initial treatment. One patient who changed to RTX because of CY resistance was included in both groups. We compared 11 cases of CY group with 8 cases of RTX group. The mean ages were 71.4 years old and 71 years old, and male were seven and three respectively. CY group had 5 MPA, 5 GPA and 1 unclassified AAV. RTX group had 3 MPA and 5 GPA. The mean BVAS were 13.4 in CY group and 17.5 in RTX group. Remission rates after six months were 6/11 (55%) and 7/7 (100%), and PSL doses after six months were 15.6 mg/day and 6.7 mg/day respectively. Serious adverse events during first six months were 1 pneumonia, 1 heart failure,1 depression and 2 CMV antigenemia in CY group, and 1 bronchitis, 1 heart failure and 1 CMV antigenemia in RTX group. There were no death due to adverse events, but one patient in CY group died due to the progression of AAV. [Conclusions] RTX for the initial induction therapy of AAV could achieve high remission rates, and reduce corticosteroid dose at an early stage.

W48-4

Clinical and adverse effects of rituximab treatment of microscopic polyangiitis and granulomatosis with polyangiitis

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Conflict of interest: None

[Background] Rituximab (RTX) was approved in Japan in 2013 to treat microscopic polyangiitis (MPA) and granulomatosis with polyangiitis (GPA). However, the clinical efficacy and side effects of rituximab have not been established. [Object] This study aimed to determine the effects of RTX compared with cyclophosphamide. [Methods] We analyzed the clinical records of patients who were treated for one year to induce MPA and GPA remission at our hospital between April 2008 and March 2017. [Results] Fifteen, 17, and 13 patients were treated with RTX and corticosteroid (CS), cyclophosphamide (CY) and CS, and CS alone, respectively. The BWAS before treatment were 9.1±7, 11.9±8.8, and 11.8±7 (not significant, NS), respectively; rates of complete remission after treatment were 78%, 82%, and 62% (NS), respectively; doses of CS at one year of treatment were 8.1±1.9, 8.2±2.9, and 12.9±10.2 mg (RTX and CY < CS, p=0.05), respectively. The rates of death from infection were 40%, 0%, and 13% (RTX > CY, p=0.05), respectively. Patients in the RTX group who died ofinfection had worse renal function, more infectious episodes, and more lung lesions than those who did not (p<0.05). [Conclusions] Rituximab was as clinically effective as CY, but the rate of fatal infections was higher.

W48-5

Change in the treatment and outcome of ANCA-associated vasculitis

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Conflict of interest: None

[Objective] To examine the possibility of treatment for ANCA-associated vasculitis (AAV), we investigated the treatment and outcome in our hospital. [Methods] We extracted 58 patients with AAV (MPA 28, GPA 29) who were started remission induction therapy between January 2013 and September 2017 in our hospital. We divided them into two groups A (before) and B (after) through June 2014. We retrospectively analyzed clinical background, treatment, relapse rate, incidence rate of infection by comparing two groups. [Results] There was no difference in the clinical background between two groups. In group B compared with group A, the dose of prednisolone (PSL) (mg/kg) decreased (p<0.004) and the total dose of intravenous cyclophosphamide (IVCY) tended to increase (p=0.061). There was no significant difference in the combination with other immunosuppressant, the period until the first remission, the change of ANCA. Relapse rate and incidence rate of opportunistic infection decreased in group B as compared with A (p=0.003, p<0.00001). [Conclusion] Both relapse rate and incidence rate of infection decreased in our hospital. We suggested the change of IVCY dose and the decrease of PSL dose were associated. We will need to make a continuous effort for the improvement of outcome in AAV.

W48-6

Potential risk of conventional immunosuppressive therapy for elderly onset ANCA-associated vasculitis patients

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Conflict of interest: None

[Object] Past several cohort studies indicated that age, renal impairment, severe vasculitis score and severe infection were associated with mortality, but there were only a few cohort studies focus on the elderly onset ANCA-associated vasculitis (AAV) patients. We retrospectively investigated the risk of mortality and severe infection among elderly (≧75 years) onset AAV (EOAAV) patients in our hospital. [Methods] A total of 182 consecutive patients with AAV from January 2000 to June 2017 in our hospital were recruited, and 83 patients were categorized into EOAAV group. We compared clinical characteristics, all-cause mortality, first relapse and early severe infection (≦ 6 months) in EOAAV group with those in younger group. [Results] EOAAV group had worse survival than younger group (p<0.001) and independent risk factors of all-cause mortality were age (p=0.032), and early severe infection (p=0.026). Renal impairment (Cre≧1.5mg/dl) subgroup of EOAAV patients with conventional immunosuppressive therapy (corticosteroid + Cyclophosphamide or Rituximab) had more severe vasculitis (p=0.011), and early severe infection (p=0.027). [Conclusions] Conventional immunosuppressive therapy for EOAAV patients has potential risk of early severe infection, and that may contribute to early mortality.

W49-1

Three cases of ANCA - positive eosinophilic granulomatosis with polyangiitis with severe thrombosis

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Conflict of interest: None

[Case 1] 63-year-old woman was afflicted with bronchial asthma 4 years ago, sinusitis and weight loss 1 year ago, and a left retinal artery occlusion two months ago. Since numbness and pain of limbs, eosinophilia, rapidly progressive kidney dysfunction, positivity of MPO-ANCA appeared, she was admitted to our hospital. Kidney biopsy revealed 4 crescents of the 33 glomeruli and severe intrarenal artery thromboses; therefore we considered these thromboses caused rapidly kidney dysfunction. She was treated with two cycles of mPSL pulse, oral PSL and IVCY. [Case 2 and 3] In addition to Case 1, we experienced 2 cases of rapidly progressive ANCA-positive eosinophilic granulomatosis with polyangitis (EGPA) who had similar intrarenal arterial thromboses. [Discussion] It was suggested that kidney dysfunction of ANCA-positive EGPA is caused not only by glomerular injury but also by intrarenal arterial thromboses. EGPA might prone to cause intra renal thromboses due to synergistic effects of ANCA and eosinophil granule protein-induced endothelial dysfunction and platelet activation.

W49-2

Efficacy of rituximab therapy against anti-neutrophil cytoplasmic antibody-related hypertrophic pachymeningitis: A Case Series

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Conflict of interest: None

Objectives. This study aimed to investigate the efficacy of rituximab (RTX) against patients with anti-neutrophil cytoplasmic antibody (ANCA)-related hypertrophic pachymeningitis (HP). Methods. Seven patients were identified by retrospective chart review from local registries at four Hospitals in Japan. All patients met Chapel Hill 2012 Consensus Conference definitions of ANCA-associated vasculitis and were complicated with HP. We assessed the dose of prednisolone (PSL), CRP, and MRI findings of HP before and after RTX administration. Results. Three female and 7 male were evaluated. Median age was 66 years-old. Four cases had HP at the onset of vasculitis. Relapse of HP before RTX administration was found in 2 cases. RTX was used as an initial treatment in one patient. Daily dose of PSL and CRP were decreased from baseline levels 24 weeks after RTX treatment. Evaluation of HP by contrast MRI showed improvement in 6 of 7 cases. No relapse after RTX treatment was observed during the follow-up period. Conclusions. Our case series highlight the efficacy of RTX against patients with difficult-to-treat ANCA-related HP. Future studies in this context in a prospective manner are definitely required to establish the B-cell depletion therapy by RTX as a treatment option for ANCA-related HP.

W49-3

Analysis of 24 patients with childhood-onset of Takayasu arteritis: a retrospective duocenter study

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Conflict of interest: None

[Object] To analysis the characteristics of patients with childhood-onset Takayasu arteritis (TA). [Methods] This study was a duocenter retrospective study. The subjects were 24 patients whose onset were less than 18 years old. [Results] Age at onset was median (range) 13.0 (0.5-18.0) years old. There were 13 female (75%). Classification of TA were I:3, IIa:3, IIb:3, III:1, IV:2, V:12. Thirteen patients (54%) had HLA-B52. Twelve patients (50%) had relapse and number of relapses was 3 (1-6). At last visit, dose of PSL was 0.1 (0-0.3) mg/kg/d, 21 patients (88%) administrated some immunosuppressants and 12 patients (50%) administrated some biologics. Three patients achieved drug free. In HLA-B52 positive patients, duration of initial treatment to relapse was significantly shorter than that in HLA-B52 negative patients (P<0.005). Nine patients (38%) had cardiocascular involvement (AR:4, AAE:1 and AR+AAE:4). Two patients underwent cardiac surgery. Fifteen patients (63%) had a steroid-related complications. [Conclusions] A half of patients with childhood-onset TA had relapse. They had high ratio of using immunosuppressants and biologics. Furthermore, they had high ratio of having cardiovascular involvement and steroid-related complications. This study suggested that their prognosis was not so well.

W49-4

The clinical manifestations and prognosis of patients with large vessel vasculitis in Juntendo Hospital

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Conflict of interest: None

[Object] We investigate the clinical features and prognosis of patients with large vessel vasculitis. [Methods] We enrolled 38 large vessel vasculitis patients, newly diagnosed in our hospital within the period 2008-2017 and examined clinical manifestations, laboratory data, treatment, and prognosis. [Results] 38 patients with large vessel vasculitis were classified into 10 patients with Takayasu arteritis (TAK) and 28 cases with giant cell arteritis (GCA) according to the classification criteria of TAK and GCA of American College of Rheumatology in 1990. The average observational period was 47.2 months, and only 3 patients with GCA died during the observation period. Comparing TAK and GCA, the median age was 25.5 vs 75.5 years old (p <0.001), the median eGFR was 112.1 vs 88.8 (p = 0.009), the cases polymyalgia rheumatica were 0 vs 14 cases (p = 0.006). There was no significant difference between the two groups regarding survival period and relapse free survival period. [Conclusions] There was a difference in age and complication with polymyalgia rheumatica, however there was no significant difference prognosis in this study.

W49-5

The outcome of the therapy for Takayasu arteritis in our hospital and efficacy of Tocilizumab for Takayasu arteritis

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Conflict of interest: None

[Object] The outcome of the therapy for Takayasu arteritis (TA) in our hospital and efficacy of Tocilizumab for TA. [Method] We investigaed the outcome of the treatment in the cases that we administered glucocorticoid (GC) and immunosuppressant for TA from April 1 2005 to October 1 2017. [Results] In this term, we treated 19 cases (12 were primary cases, 7 were relapse) with high dose GC including intense immunosuppressive drugs. Average age at onset was 34.1 and type V was the most (8 cases). In all cases, patients had clinical manifestations and CRP was elevated. In primary 12 cases, between a relapsed group and a responder group CRP level was not significant different. Clinical features, affected vessels, type of disease and the treatment are also not different. In 9 cases (6 were primary, 3 were relapses), TA flared up and we administered biological products. We used infliximab on 3 cases, etenercept on 1 and TCZ on 8. In 8 cases of TCZ, clinical manifestations and inflammation had been improved and we didn't find serious adverse events. And we found improved results on carotid artery ultrasound in most. [Conclusion] In this investigation, we cannot suggest that we predict the relapse of TA. We think TCZ is effective drug for the direct action on inflammation of artery.

W49-6

A case of Takayasu arteritis with progression of vascular lesion during administration of tocilizumab

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Conflict of interest: None

[Case] A 44-years-old female. She was firstly admitted to our hospital presenting with fever, elevated CRP. Enhanced CT showed stenotic changes in aortic arch and pulmonary artery (PA). She was diagnosed with Takayasu arteritis (TAK) when she was 33 years old. Treatment with prednisolone (PSL) 30mg/day and Methotrexate (MTX) was started. However in 40 years old, she developed dyspnea and the stenosis of the pulmonary and coronary artery were getting worse, which leaded to a diagnosis of relapsed TAK. Coronary artery bypass grafting and PA plasty were performed and Tocilizumab (TCZ) was started. 3 years later, although she had no symptom and CRP was normal, CT disclosed the stenosis of the right pulmonary artery. PET also showed FDG uptake were higher in PA. Then, a diagnosis of TAK relapsed was made. Tocilizumab was discontinued and induction therapy with high-dose corticosteroid and MTX were started. Now we are going to introduce infliximab. [Discussion] Recent studies have reported that the efficacy of tocilizumab for TAK. But there is a pitfall. Under treatment with TCZ, CRP shows negative regardless of the disease activity. We should always keep in mind

that the activity of TAK can be masked even when CRP is within the normal range.

W50-1

Change of drug treatment after total joint arthroplasty for rheumatoid arthritis patients

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Conflict of interest: None

[Object] Previous reports showed that surgical intervention including total joint arthroplasty were effective for systemic reduction of RA disease activity. The present study was undertaken to investigate the change of drug treatment after total joint arthroplasty for RA patients. [Methods] This study included 55 RA patients who underwent 67 primary total joint arthroplasty (knee, hip, and elbow) with more than one year of follow-up in Nagoya University Hospital. Drug treatment was compared between at preoperative baseline and postoperative 1 year. Also we performed univariate analysis for patient's baseline characteristics between intensive group (with the additional or altered medication: n = 29) and non-intensive group (with the same or reduced medication: n = 38). [Results] Drug treatment showed no significant difference between at preoperative baseline and postoperative 1 year. TJC (4.2 vs 2.3, $p < 0.05$), SJC (4.0 vs 1.7, $p < 0.01$), VAS (57.1 vs 40.1 mm, $p < 0.05$), CRP (1.45 vs 0.41 mg/dL, $p < 0.01$), and DAS28-CRP (3.8 vs 2.9, $p < 0.01$) were significantly higher in intensive group than non-intensive group. [Conclusions] In RA patients with relatively high disease activity, further medication is required even after total joint arthroplasty.

W50-2

Evaluation relationship between postoperative disease activity of rheumatoid arthritis and drug therapy in each surgical site

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Conflict of interest: None

[Objectives] We evaluated relationship between postoperative disease activity of rheumatoid arthritis (RA) and drug therapy in each surgical site. [Method] Total 208 RA patients who underwent joint surgery including synovectomy, arthroplasty, arthrodesis and joint replacement were retrospectively reviewed. The patients were classified into 42 cases of hand, 20 of elbow, 23 of hip, 84 of knee, and 39 of foot. Pre- and postoperative DAS28-CRP, change of DAS 28 (ΔDAS28), biologics, and change of drug therapy were compared among surgical sites. [Results] Postoperative DAS28 was significantly decreased in elbow, hip, and knee surgery groups ($P<0.05$). Patients with biologics revealed significant improvement of DAS28 after knee surgery ($P<0.05$), and patients without biologics indicated significant improvement of DAS28 after knee, hip, or elbow surgery ($P<0.05$). DAS28 in patients with change of drug therapy was significantly improved after knee or hip surgery, and DAS28 in patients without change of drug therapy was significantly improved after knee or hand surgery ($P<0.05$). [Conclusion] This study suggested that effects of surgery on RA disease activity depended on drug therapy and surgical site.

W50-3

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] To compare the tolerability and discontinuation reasons between 7 biologics in RA. [Methods] 4466 biologics treatment from 2009 to 2017 (female 82.7%, age 57.6y, RF positivity 76.3%, Bio naïve 63.6%, number of each agent; TCZ 895, ETN 891, IFX 748, ABT 681, ADA 558, GLM 464, and CZP 229) were included in this multi-center, retrospective study. Drug tolerability and discontinuation reasons were adjusted by potent confounding factors with a Cox proportional hazards model and evaluated at 36 months. [Results] Adjusted cumulative incidence rates of each discontinuous reason were as follows. Drug inefficacy (TCZ 15.4%, ABT 18.0%, GLM 25.2%, ADA 33.6%, IFX 35.1%, ETN 35.2%, and CZP 37.9%), remission (IFX 15.2%, ADA 11.1%, GLM 8.1%, TCZ 7.2%, ABT 5.7%, CZP 4.9%, and ETN 4.0%), other toxic events (CZP 2.9%, ABT 3.7%, IFX 6.2%, ETN 6.4%, ADA 6.7%, TCZ 7.1%, and GLM 9.1%), and infection (GLM 1.3%, CZP 2.2%, ETN 2.3%, TCZ 2.7%, ABT 2.7%, IFX 2.9%, and ADA 2.9%). Overall adjusted retention rates except remission were TCZ 69.3%, ETN 62.6%, ABT 59.5%, CZP 49.4%, GLM 43.9%, IFX 35.1%, and ADA 33.2%. [Conclusion] TCZ showed lowest inefficacy and highest retention, IFX showed highest remission induction, CZP showed lowest toxic events, and GLM showed lowest infection rate in adjusted model.

W50-4

Perioperative management in RA treated with Tofacitinib ~the second report~

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Conflict of interest: None

[Object] Tofacitinib (TOF) inhibits the multiple cytokines involved in the inflammatory cascade, hence there is concern over the side effect of infection. The perioperative management of RA treated with TOF is a major concern among orthopaedic surgeons. 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 the disease in patients with RA to make an useful perioperative guideline. [Methods] Between January 2015 and September 2017, we experienced 15 operations in RA patients treated with TOF. The average pre-operative TOF discontinuation period was 2.8 days. Oral administration of TOF was restarted after removal of stitches and the total perioperative discontinuation of TOF was 16.6 days on an average. [Results] In this study, 1 of 15 cases had surgical site infection. Flare up of RA occurred in 6 of 15 cases, and on average 15.3 days after discontinuation 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.

W50-5

Perioperative complication after spine surgery in patients with rheumatoid arthritis during biologic agent therapy

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Conflict of interest: None

[Object] The aim of this study was to evaluate the risk factors of biologic agents for rheumatoid arthritis (RA) during perioperative complications after spine surgery. **[Methods]** We analyzed the perioperative complications after spine surgery in 120 patients with RA from January 2006 through December 2016 at our hospital. They were dived into 2 groups. One group was 29 patients treated with biologic agents (bio group). The other one was 111 patients treated with non-biologic agents (non-bio group). **[Results]** In bio group, complications was observed in tow patients. One case had postoperative hematoma and one case had superficial infection. The other hand, in non-bio group, only one case had postoperative hematoma. **[Conclusions]** In this study, there was no serious deep infection in both groups. However, we have to pay attention to deep infection because superficial infection was observed in one of five patients treated with adalimumab.

W50-6

Significance of Remicheck in the treatment of infliximab in patients with rheumatoid arthritis

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Conflict of interest: Yes

[Objective] To clarify the significance of Remicheck Q in the treatment of infliximab (IFX) in patients with rheumatoid arthritis (RA). [**Methods**] Twenty-two patients (2 males and 20 female) treated with IFX were examined. We compared the DAS28ESR and the dose and duration of IFX between the group of Remicheck Q decision positive (group P) and that of negative (group N). [**Results**] Nineteen (86%) of 22 patients belong to group P. In group P, there are no cases tapered IFX (High dose/ shortened period for administration: 10 cases, regular dose[3mg/kg/8weeks]: 3 cases) and 13 (68%) of 19 achieved clinical remission. In group N, 2 (66%) of 3 patients achieved clinical remission. Among them, 2 cases were tapered dose of IFX (3mg/kg/9 weeks) and 1 case was treated at 10mg/kg/8 weeks. Later case changed regimen (6mg/kg/4 weeks). After that Remecheck Q decision changed positive and DAS28ESR decreased from 4.82 to 4.37). [**Conclusion**] If tapered IFX, there is fear that IFX level is under effective trough levels.

W51-1

Low rate of radiographic progression of structural joint damage over 2 years of baricitinib (Bari) treatment in patients (pts) with active rheumatoid arthritis (RA) - overall and Japanese results

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Conflict of interest: Yes

[Object] Radiographic progression of structural joint damage was evaluated over 2 years of Bari treatment in RA pts who were DMARD naive or csDMARD-IR/MTX-IR. **[Methods]** Upon completion of Bari phase 3 blinded-phase for 24 or 52 weeks, pts could enter a long-term extension study, in which they continued to receive the same Bari dose as in the original ph3 study. Pts receiving other than Bari (placebo, MTX, ADA) at the conclusion of the originating study were switched to Bari 4mg. Radiographs were scored using the van der Heijde mTSS. **[Results]** DMARD naive pts starting with Bari 4mg+MTX in the originating study showed significantly less progression than those starting with MTX; Bari-treated MTX-IR pts in a study showed significantly less progression than those starting with placebo (mTSS change 1.13 vs. 2.20 for Bari and placebo at 2 years, respectively, $p<0.001$), and comparable to those starting with ADA, with Japanese subpopulation showing similar trend. In another csDMARD-IR study, Bari 4mg provided a more robust benefit than Bari 2mg. Treatment with once-daily oral Bari resulted in low rates of radiographic progression for up to 2 years. **[Conclusions]** Pts initially randomized to Bari had less progression for 2 years than pts starting with placebo or MTX.

W51-2

Interim Safety Report from Post-Marketing Surveillance of Tofacitinib in Japanese Patients with Rheumatoid Arthritis: An Update

Masayoshi Harigai[1], Tsuneyo Mimori[2], Masataka Kuwana[3], Tatsuya Atsumi[4], Syuji Takei[5], Naoto Tamura[6], Takao Fujii[7], Hiroaki Matsuno[8], Shigeki Momohara[9], Kazuhiko Yamamoto[10], Kazuto Nomura[11], Yutaka Endo[11], Naonobu Sugiyama[11], Tomohiro Hirose[11], Yosuke Morishima[11], Noritoshi Yoshii[11], Michiaki Takagi[12]
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Conflict of interest: Yes

[Object] Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). We evaluated 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 (August 5, 2017 datacut). Adverse events (AEs) were coded using MedDRA/J. Summary statistics are provided. **[Results]** 3508 tofacitinib-treated pts were enrolled (1521.7 pt-years of exposure at 6 months); of these, 802 pts (22.9%) discontinued treatment, mainly due to AEs (n=316; 9.0%) or lack of efficacy (n=296; 8.4%). 2706 (77.1%) completed the 6-month observation period. At least one AE was observed in 1178 pts (33.6%), the most common of which was herpes zoster (HZ) (n=132; 3.8%). Serious AEs occurred in 269 pts (7.7%); the most common were pneumonia (n=23; 0.7%), HZ (n=22; 0.6%) and interstitial pneumonia (n=17; 0.5%). Malignancy was reported in 26 pts (0.7%) and included diffuse large B-cell lymphoma (n=3; 0.1%) and breast cancer (n=3; 0.1%). **[Conclusions]** 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.

W51-3

Serious Infection Events (SIEs) and Associated Risk Factors (RFs) in Patients (pts) including Japanese (JP) with Moderate to Severe Rheumatoid Arthritis (RA) Treated with Baricitinib (Bari)

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Conflict of interest: Yes

[Object] To evaluate SIE and associated RFs of Bari in pts with moderate-to-severe active RA including JP. **[Methods]** Incidence rates (IRs, per 100 patient-year: PY) were calculated using data in ALL BARI RA analysis set which included pts exposed to any Bari dose, and pooled from completed phase 1-3 studies and an ongoing long-term extension study of Bari in RA pts. Potential RFs for SIE were investigated with Cox models. **[Results]** 3492 pts (514JP) were exposed to Bari for 5133 total PY as of Jan 2016. SIE were reported in 150 pts (IR=2.9). Frequent SIE (IRs≧0.2) was pneumonia (0.5), herpes zoster (HZ) (0.4), urinary tract infection (0.3), and cellulitis (0.2); 2 pts with infections leading to death. In JP, SIE were reported in 23 pts (3.4). Frequent SIE (IRs≧0.4) was HZ (1.6), pneumonia (0.6) and pneumocystis jirovecii pneumonia (PCP) (0.4); no pts with infections leading to death. As with another JAK inhibitor, non-serious HZ as well as serious HZ was more frequently seen in JP. All PCP cases were reported in JP. Prior biologic use, advancing age, region of Asia (excluding JP), non-normal BMI, and corticosteroid use were identified as independent RFs for SIE overall. **[Conclusions]** IRs of SIEs were similar between overall and JP pts. Potential RFs for SIE were identified.

W51-4

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

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Conflict of interest: Yes

[Object] Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). We evaluated serious infection events (SIEs) and herpes zoster (HZ) among Japanese patients (pts) with RA treated with tofacitinib using interim post-marketing surveillance (PMS) data (August 5, 2017 data-cut). **[Methods]** Frequency and types of SIEs and HZ are reported for the PMS first 6-month observation period. Incidence rates (IRs; pts with event/100 pt-years) are for the full 3-year PMS period. **[Results]** 3508 tofacitinib-treated pts were enrolled (3403.7 pt-years of exposure at 3 years). At 6 months: 123 pts (3.5%) had SIEs; most common by preferred term were pneumonia (n=23; 0.7%), HZ (n=22; 0.6%), *Pneumocystis jiroveci* pneumonia (n=14; 0.4%) and bacterial pneumonia (n=10; 0.3%). 1 of 3 reported tuberculosis cases was serious. In total, 132 (3.8%) HZ cases (nonserious and serious) occurred. At 3 years, 203 pts (5.8%) had SIEs; 238 pts (6.8%) had serious or nonserious HZ; IRs (95% CI) were 5.7 (4.9, 6.5) for SIEs and 7.1 (6.2, 8.1) for HZ overall. **[Conclusions]** The HZ IR was similar to that reported for Phase 2, Phase 3 and long-term extension clinical trials in Japanese pts with RA, and the SIE IR was within the range of IRs in prior PMS studies of RA biologic treatment.

W51-5

Dose Reduction of Baricitinib (Bari) in Patients with RA Achieving Sustained Disease Control: Results of a Prospective Study

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Conflict of interest: Yes

[Object] To investigate the effects of Bari dose step-down in RA patients (pts). [Methods] Pts completed a ph3 study could enter a long-term extension (LTE) study. Pts received Bari 4mg for ≧15 months and achieved sustained low disease activity ([LDA] - CDAI≦10 for pts from RA-BUILD/BEAM/BEACON [group 1: gp 1]) or remission (CDAI≦2.8 for pts from RA-BEGIN [group 2: gp 2]) at 2 consecutive visits ≧3 months apart were re-randomised in a blinded manner to continue 4mg or step down to 2mg. Pts could rescue (to 4 mg) if CDAI>10 or >2.8. Efficacy and safety were assessed through 48 weeks following re-randomization (Data cut: April 1, 2017). [Results] Dose reduction resulted in significant increases in disease activity, but in both groups most pts maintained the LDA/remission at Week 48 (LDA gp 1: 2mg 67.6% vs. 4mg 80.2%; remission gp 2: 2mg 70.2% vs. 4mg 65.5%). Across both groups rescue rates were 16.6% (2mg) and 8.3% (4mg). Most rescued pts could regain LDA/remission. Across both groups rates of step-down emergent adverse events (AEs) including non-serious infections were lower with 2mg than 4mg, and rates of serious AEs were similar between doses. [Conclusions] Dose taper may be reasonable to attempt in pts achieving sustained disease control with Bari 4mg.

W51-6

A Phase 2b/3 Randomized, Placebo-controlled, Double-Blind Study of Upadacitinib (ABT-494), a Selective JAK-1 Inhibitor, in Japanese Patients with Active Rheumatoid Arthritis and Inadequate Response to Conventional Synthetic DMARDs

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Conflict of interest: Yes

[Object] To study efficacy and safety of upadacitinib (UPA) an oral, selective JAK-1 inhibitor in Japanese pts with active RA and csDMARDs-IR. [Methods] Pts on stable csDMARDs were randomized to receive UPA 7.5,15 or 30 mg once daily or PBO (1:1:1:1) for 12 wks (Period1). Primary endpoint was proportion of pts achieving ACR20 at Wk12 (NRI). [Results] Of 197 pts treated, 187 completed Period1. At Wk12, more pts on UPA 7.5, 15 and 30 mg vs PBO met ACR20 (75.5%, 83.7%,80% vs 42.9%, p<.001), and ACR50/70, DAS28-CRP≦3.2 (53.1%, 69.4% and 72.0% vs 18.4%) and DAS28-CRP<2.6 (36.7%, 57.1%, 50% vs 6.1%). Improvement on UPA was significant by Wk1 and at Wk12, pts had greater improvements (p<.001) in DAS28-CRP (-2.08, -2.39, -2.41 vs -0.79) and HAQ-DI (-0.41, -0.45, -0.49 vs -0.10). AEs, SAEs, infections (serious infections, opportunistic infections, herpes zoster) and lab abnormalities [CPK elevations and lymphopenia] were numerically higher in UPA 30. PE/DVT were not observed and mean hemoglobin levels remained within normal ranges. [Conclusions] The efficacy of UPA was demonstrated, with better responses for stringent endpoints on UPA 15 and 30 vs 7.5 mg. Safety and tolerability were consistent with Ph2 and 3 studies.

W52-1

Efficacy and safety of abatacept (ABT) in combination therapy with MTX in patients with active rheumatoid arthritis (RA) who had an inadequate response to MTX: A phase IV, multi-center, randomized, double-blind, placebo-controlled study

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Conflict of interest: Yes

[Object] To evaluate efficacy and safety of ABT+MTX in Japanese active RA patients (pts) with inadequate response to MTX. [Methods] Pts were included as following; Less than 5 years from RA diagnosis, MTX treatment for ≧3mo, bone erosion+, Bio-naive, Anti-CCP+. All pts were randomly assigned to each group, ABT+MTX or MTX alone. The pts were offered ABT rescue therapy, if insufficient efficacy was observed at week16 and thereafter. Primary objectives: ACR20 response rate at week16 and Joint damage progression (change from baseline [CBL]) in total sharp score using the modified van der Heijde Sharp [mTSS] method) at week24. [Results] ACR20 response rate was 75.4% (153/203) in ABT+MTX and 27.7% (56/202) in MTX alone ($p<0.001$). The mean CBL in mTSS was 0.84 in ABT+MTX and 1.26 in MTX alone ($p=0.017$). The non-progressors rate (subject proportion with CBL in mTSS ≦ smallest detectable change) was 88.1% (ABT+MTX) and 75.4% (MTX alone), indicating ABT+MTX efficacy to inhibit the progression of structural damage. Adverse events (AE) and serious AE (16wks): 54.7% and 2.0% in ABT+MTX, 54.5% and 2.5% in MTX alone. [Conclusions] ABT+MTX was effective in improving clinical symptoms and in preventing joint distraction in Japanese active RA pts with an inadequate response to MTX.

W52-2

Efficacy and safety of sarilumab, a human anti-IL-6 receptor monoclonal antibody, plus methotrexate: outcomes at 52 weeks in a randomized, placebo-controlled, double-blind Phase 3 trial in Japanese patients with active rheumatoid arthritis (KAKEHASI study)

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Conflict of interest: Yes

[Object] To assess efficacy and safety of sarilumab plus methotrexate (MTX) in Japanese patients with active rheumatoid arthritis (RA) and inadequate response to MTX (MTX-IR). [Methods] In this study, patients received subcutaneous sarilumab 150 mg q2w + MTX (S150), 200 mg q2w + MTX (S200), or placebo + MTX (P) for 24 weeks, then patients in P switched to S150 or S200. [Results] ACR20 at Week 24 (primary endpoint) and Week 52 were 67.9% and 71.6% for S150 and 57.5% and 60.0% for S200. ACR20 at Week 52 for P to S150 or S200 were comparable with those in the S150 or S200. Serious treatment-emergent AEs (TEAEs) were reported by 9.9% S150, 6.3% S200, 0 P to S150, and 13.3% P to S200. No deaths occurred. Incidence of AE did not increase from Week 24 to 52. The most common TEAE was nasopharyngitis. Incidence of infections was: 67.9% S150, 52.5% S200, 64.3% P to S150, 53.3% P to S200, with 5 serious infections for S150 group and 1 for P to 200. Incidence of ANC <1.0 Giga/L was comparable for S150 and S200 and not associated with infection. [Conclusions] In Japanese MTX-IR RA patients, sarilumab plus MTX showed sustained clinical efficacy. At Week 52, the safety profiles of S200 and S150 were generally similar, as previously observed, and as expected based on IL-6 class.

W52-3

Sarilumab (a human monoclonal antibody against IL-6 receptor) for Japanese rheumatoid arthritis patients: a Phase 3 study (KAKEHASI) comparing 200-mg and 150-mg every other week

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Conflict of interest: Yes

[Object] We previously reported 24-week efficacy results of KAKEHASI study comparing subcutaneous sarilumab 150 mg q2w + methotrexate (MTX) (S150), 200 mg q2w + MTX (S200), and placebo + MTX (P) in Japanese patients with moderate to severe rheumatoid arthritis (RA) and inadequate response to MTX. Efficacy results at Week 12 of S200 and S150 were analyzed. [Methods] ACR20/50/70 improvements and DAS28-CRP/CDAI/SDAI remission rates at Week 12 were analyzed. Both groups were analyzed for the rate of patients with complete inhibition of CRP (< the lower limit of 0.02 mg/dL). [Results] At Week 12, S200 (n=80) ACR50/70 were numerically higher (31.3% and 18.8%) than the S150 (n=81; 27.2% and 6.2%). ACR20 at Week 12 were similar. Remission rates for DAS28-CRP/CDAI/SDAI were also numerically higher in S200 than in S150 (33.8%/6.3%/8.8% versus 25.9%/1.2%/2.5%). A numerically greater proportion of patients who were treated with S200 achieved complete CRP inhibition compared to patients treated with S150 at Week 2, a difference that was observed at Week 12 (68.0% vs 55.7%, respectively). The safety profiles of S200 and S150 were similar. [Conclusions] The results support sarilumab 200 mg as the recommended dose for RA patients in Japan.

W52-4

Safety and efficacy of long-term treatment with sarilumab, a human anti-IL-6 receptor monoclonal antibody, in combination with non-methotrexate, disease-modifying, antirheumatic drugs or as monotherapy in a randomized, double-blind, Phase 3 trial in Japanese patients with active rheumatoid arthritis (HARUKA study)

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Conflict of interest: Yes

[Object] To assess long-term safety and efficacy of sarilumab added to non-methotrexate conventional synthetic DMARDs (Combo) or as monotherapy (Mono) in Japanese patients with active rheumatoid arthritis (RA). [Methods] In this study, patients received subcutaneous sarilumab 150 mg q2w (S150) or 200 mg q2w (S200) Combo or as Mono for 52 weeks. Primary endpoint was safety. [Results] 30 patients received Combo (S150, n=15; S200, n=15) and 61 Mono (S150, n=30; S200, n=31); 86.8% completed. Rates of treatment-emergent adverse events (TEAEs), serious AEs (SAEs), and TEAEs leading to discontinuation were similar with Combo or Mono. No deaths occurred. Nasopharyngitis and neutropenia were the most frequently reported TEAE. One serious infection was reported in the S200 Combo before Week 24 and in each of Monos after Week 24. No patients with Grade 3-4 neutropenia experienced associated serious infection in any group. Sarilumab Combo and Mono showed improvements in ACR20/50/70, physical function and DAS28-CRP at Week 24, sustained at Week 52. [Conclusions] Safety profile of sarilumab was consistent with IL-6 signaling blockade, established by Week 24 and stable over 52 weeks. Sarilumab Combo and Mono improved clinical signs and symptoms and physical function in Japanese RA patients.

W52-5

A randomized, double-blind study comparing PF-06438179/GP1111, a potential infliximab biosimilar, and infliximab, in patients with moderate to severe active RA with an inadequate response to methotrexate therapy, including subgroup analysis of ACR20 response

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Conflict of interest: Yes

[Object] This study assessed efficacy, safety, and immunogenicity of PF-06438179/GP1111 (PF), a potential infliximab (IFX) biosimilar, vs originator IFX sourced from Europe (IFX-EU), both with methotrexate (MTX), in patients with moderate to severe active RA. [Methods] Patients stratified by geographic regions, were randomized (1:1) to PF or IFX-EU (3 mg/kg IV) at Wk 0, 2, 6 and then every 8 wk, allowing dose escalation (to 5 mg/kg) from Wk 14 in patients with inadequate response. Primary endpoint was ACR20 rate at Wk 14. [Results] Patients (N=650; females, 80.3%) had a mean RA duration of 6.9 years; mean baseline DAS28-CRP was 6.0 in both arms. Wk 14 ACR20 rates (intent-to-treat population) were 61.1% for PF and 63.5% for IFX-EU, using nonresponder imputation for missing data. Treatment difference was -2.4% with the 95%CI (-9.9%, +5.1%) contained within the pre-specified equivalence margin (±13.5%). In subgroup analyses, overall similar Wk14 ACR20 rates between the 2 arms were observed, including within each regional subgroup. In the overall population, safety profiles and antidrug antibody rates through Wk 30 were also similar. [Conclusions] PF and IFX-EU showed similar efficacy and safety. Overall subgroup analyses suggested regional factors did not influence efficacy.

W52-6

Comparison of the efficacy of biologic monotherapy using propensity score matching in RA

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Conflict of interest: None

[Object] This study aimed to evaluate the effectiveness of biologics monotherapy using propensity score (PS) matching. [Methods] We retrospectively examined about 3000 patients who were treated with biologics (FIRST registry). We compare the effectiveness of biologic monotherapy based on retention and CDAI remission rates at 1 year (LOCF). Propensity score (PS) were generated using multinomial logistic regression and the study groups were matched regarding baseline variables. [Results] Patients were treated with TNF inhibitors (1968), TCZ (510) and ABT (519) during July 2003 to Sept 2017 in our institute. TNF inhibitors (59), TCZ (120) and ABT (54) were induced without MTX for patients with organ impairment such as renal dysfunction, There are no differences among biologics in terms of age, disease duration, concomitant use of MTX, GC, prior use of biologics. Baseline disease activity was higher in TCZ. After PS matching retention rates at 1 year were ABT>TCZ (p=0.01) due to less incidence of infection. CDAI remission rates at 1 year were comparable among biologics except for TCZ>ABT (p=0.04). [Conclusions] After PS matching, the effectiveness of biologic monotherapy was almost comparable except for the retention and CDAI remission rate at 1 year between ABT and TCZ.

W53-1

Adult-Onset Still's Disease with hemophagocytosis in vessel lumen observed on skin biopsy: a case report

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Conflict of interest: None

CASE PRESENTATION: A 73-year-old female presented to our hospital with high fever, headache, sore throat, and rash that recurred intermittently. Her medical history included primary hepatic malignant lymphoma. During her hospitalization, there was no finding of lymphoma after an extensive workup including computed tomography, bone marrow examination, and skin biopsy. The patient's initial diagnosis was Adult-Onset Still's Disease (AOSD). Skin biopsy showed dermal perivascular dermatitis with neutrophil infiltrates and hemophagocytosis in vessel lumen. She was treated with oral prednisolone and symptoms improved. After discharge, her laboratory test results showed elevated ferritin levels. In addition to prednisolone, she is being treated with tacrolimus. DISCUSSION: Usually, histopathologic findings of AOSD consist of superficial perivascular dermatitis with varying numbers of interstitial neutrophils. In this case, skin biopsy also showed hemophagocytosis in vessel lumen. Hemophagocytic lymphohistiocytosis is induced by infections, malignancy, and autoimmune disease. Although hemophagocytic lymphohistiocytosis is usually observed in the spleen, lymph nodes, bone marrow, and central nervous system, skin involvement is rare and makes this case significant.

W53-2

TAFRO syndrome: a report of 5 cases

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Conflict of interest: None

[Object] TAFRO syndrome is a severe systemic inflammatory disease proposed in 2010. It is necessary to improve awareness and establish a treatment strategy. [Methods] We clinically examined patients with TAFRO syndrome treated at our hospital. [Results] Cases were 3 males and 2 females. Age of onset were 39-70 years. All cases had anasarca with weight gain of more than 10 kg, thrombocytopenia, renal dysfunction and fever during the course. 1 case was associated with uveitis. The soluble IL-2 receptor elevated in 4 cases, and the value was 6050 U/ml in 1 of them. 1 case had lymph node swelling, 4 cases hepatosplenomegaly, 1 case bone marrow fibrosis, 1 case lymph node tissue finding of hyaline vascular type Castleman disease. IL-6 and VEGF varied from normal to significantly increased by cases, specimens (blood, effusion). Treatment was GC and eltrombopag in 1 case, GC, CYA and TCZ in 3, GC, eltrombopag and RTX in 1. 3 cases had remisson. 1 case had partial remission and became on maintenance hemodialysis. 1 case had multiple cerebral vessel narrowing and died. [Conclusions] It is necessary to know TAFRO syndrome as a differential diagnosis of anasarca, thrombocytopenia, renal dysfunction and fever. In severe cases, combination therapy should be considered at an early stage.

W53-3

A case of relapsing polychondritis with IgA nephropathy and palmoplantar pustulosis~Clinical analysis of 7 patients with relapsing polychondritis~

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Conflict of interest: None

A 79-year-old woman with a history of palmar pustulosis for 30 years had nasal obstruction and nasal bleeding in the spring of 2016 and

developed saddle nose in the summer of 2016. She was admitted with saddle nose, impaired hearing and pustulosis in June 2017. Laboratory data were as follows: CRP 0.19 mg/dl, IgA 738 mg/dl and PR3-ANCA <0.05 U/ml. A urinary analysis revealed occult blood and casts. PET-CT showed a high FDG uptake in the area of the nasal cavity. A biopsy of the nasal mucosa and cartilage was negative for EBER-ISH and granuloma and revealed inflammation cells in the cartilage. A kidney biopsy revealed IgA nephropathy. Therefore, she was diagnosed with relapsing polychondritis (RP) with IgA nephropathy and palmoplantar pustulosis. PSL and MTX were administered and improved her symtons. We performed a retrospective analysis of 7 patients with RP (median age 59 years [interquartile range 37-79], 28% males) encountered between January 2008 and October 2017. The affected areas were the ear in five cases, airway in two cases and nasal cartilage in three cases. PET-CT was performed in four cases and was useful for diagnosing cases of airway lesion. All patients were treated with PSL and other immunosuppressive agents. Four patients were treated with bio-therapy.

W53-4

Characteristic alteration of gut microbiota and T cell function in patients with relapsing polychondritis

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Conflict of interest: None

[Object] We have reported skewed T cell differentiation and characteristic features of gut microbiota in patients with Behcet's disease (BD). We suggested that gut microbiota alteration impaired systemic immunological functions. We then analyzed fecal metagenomic and T cell gene expression data of patients with relapsing polychondritis (RP), and compared the data with those of BD patients and normal individuals (NI). [Methods] We stimulated peripheral blood mononuclear cells (PBMC) of 9 RP patients, 12 BD patients and 10-14 NI with lectin and measured Th17/Treg cell-related gene expressions. We explored fecal microbiota of 23 RP patients, 12 BD patients, and 27 NI by sequencing of 16S rRNA gene. [Results] We observed that Th17 cell related gene expressions increased significantly with lectin stimulation in RP and BD PBMC. The sequencing data showed that Veillonella species increased and decreased significantly in the intestine of RP and BD patients, respectively. [Conclusions] Veillonella species is one of the major short-chain fatty acid (SCFA)-producing bacteria in the human intestine. SCFA was reported to be able to induce regulatory T cells in the intestine. We suggested that compositional alteration of gut microbiota of RP and BD patients reflected each T cell reactivity.

W53-5

Susceptibility of HLA-DRB1 alleles in adult-onset Still's disease patients and its effect on clinical features

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Conflict of interest: None

[Objects] *HLA-DRB1* alleles are major determinant of predisposition for rheumatic diseases. We assessed whether *DRB1* alleles are associated with susceptibility to specific clinical features of adult onset Still's disease (AOSD) in the Japanese population. **[Methods]** *DRB1* genotyping of 96 patients with AOSD and 1,026 healthy controls was performed by PCR-SSOP. Genomic DNA samples from the AOSD patients were also genotyped for *MEFV* by direct sequencing. **[Results]** In Japanese patients with AOSD, we observed a predisposing association of *DRB1*15:01* ($p = 8.60 \times 10^{-6}$, corrected p (Pc) = 0.0002, odds ratio (OR) = 3.04, 95% confidence interval (95% CI) = 1.91-4.84) and DR5 serological group (p = 0.0006, OR = 2.39, 95% CI = 1.49-3.83) and a protective association of *DRB1*09:01* (p = 0.0004, Pc = 0.0110, OR = 0.34, 95% CI = 0.18-0.66) with AOSD. *MEFV* variants were identified in 49 patients with AOSD (56.3%). The predisposing effect of DR5 was confirmed only in patients with AOSD who had *MEFV* variants. Additionally, DR5 in patients with AOSD are associated with macrophage activation syndrome and steroid pulse therapy. **[Conclusions]** The *DRB1*15:01* and DR5 are both associated with susceptibility, and also DR5 is associated with disease type, in Japanese AOSD patients.

W53-6

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

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Conflict of interest: Yes

[Object] To modify the 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 76 patients with active AOSD (including 16 patients with MAS) were applied to the MAS classification criteria. Additional laboratory items that dissociate MAS patients were selected, and modified criteria were constructed. [Results] The sensitivity was 100% and the specificity was 70% when the patients' data were applied to the original classification criteria. The sensitivity of triglyceride and the specificity of AST was lower. White blood cell count, neutrophil, and LDH were good markers in addition to items in original criteria to distinguish MAS patients. After defining cutoff values by ROC analysis, we considered some modified criteria. In addition to elevated ferritin levels as a prerequisite, 2 positive data from platelet count, AST, and fibrinogen, or 3 positive data from platelet count, neutrophil count, LDH, and fibrinogen showed good results. [Conclusions] For the classification of MAS in AOSD, some modifications of the criteria of MAS in SJIA may have good results.

W54-1

A case of relapsing polychondritis with progressively narrowing of the left main bronchus under treatment for rheumatoid arthritis

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Conflict of interest: None

A 71-year-old woman was admitted to our hospital because of rapid deterioration in dyspnea. The patient was diagnosed with rheumatoid arthritis twelve years ago. On the day of admission, she presented with severe hypoxemia and characteristic saddle nose deformity. Chest computed tomography showed that the proximal portion of left main bronchus was interrupted. Bronchoscopy revealed circumferential stenosis in the left main bronchus. Pathological evaluation of a bronchial biopsy specimen revealed degenerated cartilaginous tissue with few infiltrating inflammatory cells. The patient referred to the thoracic surgery department for evaluation of bronchial stenosis. A metallic stent was placed below the lower trachea and extended down the left main bronchus. This intervention could not prevent recurrence of stenosis. To intensify the medication for relapsing polychondritis, the dose of prednisolone was increased to 50 milligrams per day, methotrexate and adalimumab initiated. Nevertheless, bronchial stenosis is now in progress, which enforces us on changing the medical treatment. It remains unclarified which treatment is effective for relapsing polychondritis with severe bronchial stenosis. We report our experience with some literature review.

W54-2

A case of Eosinophilic Sialodochitis with difficulty in distinguishing from Sjogren's Syndrome (SjS)

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Conflict of interest: None

[Case] A 59-year-old woman visited our hospital, complaining low grade fever and elevation in the floor of the mouth for two weeks. She had awareness of dry mouth and positive Saxon's test (1.8g/2min). MRI revealed swelling of sublingual gland and bilateral submandibular glands. Laboratory studies showed RF 99 IU/ml, IgG 1828 mg/dl, ANA x40, anti TPO Ab 23.9 IU/ml and negative SSA Ab. As SjS was likely, biopsy of sublingual gland and lip was performed, showing marked periductal eosinophilic and lymphocytic infiltration. This was compatible with eosinophilic sialodochitis. Although oral discomfort partially improved spontaneously in 3 weeks, it persisted. 10mg of olopatadine hydrochloride for 10 days and 5mg of prednisolone for 3 days were tried, resulting in gradual amelioration of the symptoms. [Discussion] Eosinophilic sialodochitis is a rare disease presenting recurrent salivary gland swelling which is associated with allergy. Its symptoms often resemble those of SjS.

W54-3

Ibuprofen (ibu) may ameliorate symptoms and signs of polymyalgia rheumatica (PMR)

Hiroki Morishita, Shigeko Inokuma, Yoshimasa Goto, Satoshi Miike, Tomohiro Tamachi
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Conflict of interest: None

[Object] PMR patients are increasing in number. Using steroids instead of NSAIDs is strongly recommended. We treated a PMR patient who got a complete remission by ibu, without a steroid, and how ibu effects for PMR was examined. [Methods] PMR patients who had ibu were retrospectively studied for changes in CRP, ESR, Hb, and Alb, and additional regimen including MTX, PSL, colchicin and others. Diagnosis was based on EULAR/ACR. [Results] 6 patients were prescribed with ibu. All of them had had NSAID other than ibu priorly. A 77-y-old female patient had had celecoxib and loxoprofen with no improvement. Soon after 600mg of ibu and 1mg of colchicines started, she felt clear amelioration; CRP steadily decreased from 8.54 to 0.03 mg/dL, ESR from130< to 19 mm/hr within 3 months. As for other 3 patients, although CRP and ESR decreased (CRP/ESR: 8.62/93 to 0.77/34, 17.58/90 to 8.82/34, 13.7/120 to 7.73/114), but did not get into within normal range, MTX was added in 2 patiients, and PSL was in 1. 2 patients who had ibu after steroid, had additional improvement. [Conclusions] Among NSAIDs, ibu may ameliorate PMR, possibly in some case without steroid. Ibu might be better chosen among NSAIDs.

W54-4

Analysis of 2 cases of TAFRO syndrome

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Conflict of interest: None

[Object] TAFRO syndrome is a recently described syndrome, which is characterized by Thrombocytopenia, Anasarca, myeloFibrosis, Renal failure and Organomegaly. As the elevation of IL-6 in body cavity fluid is one of feature of TAFRO syndrome, it's suggested that Tocilizumab is one of the potential therapeutic strategy. Despite its poor prognosis, the pathology of TAFRO syndrome is largely unknown. To understand the pathology of TAFRO syndrome, we performed immunological analysis of 2 cases of TAFRO syndrome. [Methods] The peripheral blood sample and body cavity fluid sample from TAFRO syndrome patients was examined by flow cytometry, multi-plex assay and ELISA assay. [Results] In body cavity fluid, activated effector T cells was the dominant population in T cells, especially in CD8-positive T cells. CXCL10 was markedly elevated in serum samples, and that IL-6, MCP-1 and CXCL10 were highly increased in body cavity fluid samples. After treatment, the number of T cells in body cavity fluid was decreased, and the level of MCP-1 and CXCL10 were reduced in both the serum sample and the body cavity fluids. [Conclusions] In TAFRO syndrome pathology, it's suggested that activated effector CD8-positive T cells may play a significant role, and that CXCL10 and MCP-1 may be important mediators.

W54-5

Clinical findings of 15 patients with Castleman's disease

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Conflict of interest: None

(Object) Castleman's disease (CD) is a lymphoproliferative disorder. IL-6 is overproduced by enlarged lymph nodes, therefore the humanized anti-IL-6 receptor monoclonal antibody tocilizumab (TCZ) has good efficacy for these patients. We will report on the clinical picture of our patient. **(Methods)** There were 15 patients including 12 men and 3 women. The median age was 52 years. **(Results)** There were one with monocentric and 14 patients with multiple centric CD. The period from the first medical institution visit to the start of treatment was about 5 years. The blood tests before treatment were as follows: CRP 5.27±3.09 mg/dl, IL-6 13.8±12.1 pg/ml, IgG 4018±1685 mg/dl, Hb 10.7±2.2 g/dl, Cr 0.85±0.29 mg/dl (Two were on hemodialysis). Radiological findings were as follows: 14 lymphadenopathies, 6 hepatosplenomegaly, 11 pulmonary involvements, and one retroperitoneal tumor. Histologically, 14 cases were plasma cell type and 1 case was hyaline-vascular type. Treatments were as follows: 9 cases with TCZ (no discontinuation), 3 cases with PSL, 1 case by surgical resection, 3 cases of untreated or treatment interruption. **(Conclusions)** We have to enlighten the awareness of CD and use TCZ properly to CD patients.

W54-6

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

[Object] To assess the clinical significance of dyskeratotic cells (DCs) in skin lesions of adult-onset Still's disease (AOSD). [Methods] We assessed histology of skin lesions including persistent pruritic skin lesions in Japanese patients with AOSD (n=15). Moreover, we compared histology of AOSD with dermatomyositis (DM) (n=6), drug eruptions (DE) (n=7), and graft versus host disease (GVHD) (n=6). [Results] AOSD with persistent pruritic skin lesions (n=10) histologically showed DCs only in upper layer of epidermis and horny layer without inflammatory cells infiltrations, indicating dyskeratosis. AOSD with evanescent rash (n=5) histologically showed no DCs. DCs were positive by ssDNA staining, suggesting apoptotic cells. Serum IL-18 showed significantly higher in AOSD patients with dyskeratosis (n=10) than without dyskeratosis (n=5). In contrast to AOSD with DCs, the histology of DM, DE and GVHD

demonstrated DCs existed in all layers of epidermis with inflammatory cells infiltrations. [Conclusions] Persistent pruritic skin lesions in AOSD are specific by prominent epidermal apoptosis involving the upper layers of epidermis. Moreover, hyper IL-18 might be related with dyskeratosis.

W55-1

Factors affecting early outcomes of total knee arthroplasty in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] We evaluated factors affecting outcomes of total knee arthroplasty (TKA) in patients with rheumatoid arthritis (RA). [Methods] Ninety-two RA patients with severe joint destruction underwent TKA with capsulosynovectomy. The patients included 74 females and 18 males, with a mean age of 68 years at the time of surgery. Preoperative and postoperative RA disease activity was measured using the Disease Activity Score 28 (DAS28). Clinical results were assessed using the JOA score. Relationship between outcomes of TKA at postoperative one year and clinical factors was evaluated. [Results] JOA score was significantly improved from preoperative 49.9+/-11.1 points to postoperative 84.1+/-11.8 ($P<0.05$). DAS28 was significantly decreased from 3.9+/-1.0 preoperatively to 2.9+/-1.1 postoperatively ($P<0.05$). Multiple regression analysis revealed that factors affecting outcomes of TKA at postoperative one year were preoperative JOA score ($\beta=0.203$, $P<0.05$) and postoperative DAS28-CRP ($\beta=-0.451$, $P<0.01$). [Conclusions] This study suggested that factors affecting early outcomes of TKA were preoperative JOA score and postoperative DAS28 in patients with RA.

W55-2

Factors affecting the preoperative patients' expectations score of total knee arthroplasty in rheumatoid arthritis

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Conflict of interest: None

[Object] In total knee arthroplasty (TKA), patient expectation was reported to be the most important predictor of postoperative destination. The purpose of this study was to show the factors affecting preoperative patent expectation of TKA in rheumatoid arthritis (RA) patients. [Methods] 35 knees of 35 patients (7 male and 28 female with a mean age of 68.1 years old) with diagnosis of RA, undergoing primary TKA from 2013 to 2017 were included in this study. All the patients were assessed using the patient expectation part of the 2011 Knee Society Score (2011 KSS). The consideration items were age, gender, functional class score of American College of Rheumatology (ACR), uses of biological products (Bio), and surgery history of hip or knee arthroplasty. [Results] Older than 70 years old patients showed the high expectation score compared to younger patients. Female patients showed the high expectation score compared to male patients. Patients without surgery history showed the high expectation score compared to patients with surgery history. There were no significant differences in class score of ACR, and uses of Bio. [Conclusions] We should do more detailed informed consent to young patients or male patients or patients with surgery history to decrease their anxieties.

W55-3

Long-term clinical results of cementless Crusiate-Retaining type Total Knee Arthroplasty in rheumatoid arthritis -Post-operated over 15 years of Hi-Tech knee II TKA-

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Conflict of interest: None

Objective: We have been operated cementless Crusiate-Retaining (CR) type TKA in almost rheumatoid arthritis (RA) patients. Here, we evaluate the clinical long-term results, over 15 years after operation, of CR type Hi-Tech knee II (HTK II) TKA in RA. **Methods:** Between October 1966 to April 2002, 33 RA patients, 37 knees, were operated with CR type HTK II TKA. Average age at operation is 63.3 yo, average follow up period 17 years 6 months. Range of motion (ROM), JOA score X ray examination, and complication, before and after operation, were evaluated. **Results:** ROM was improved before operation 105.5°to after 116.3°. JOA score also 34.2 points to 83.8 points. No patients had loosening change or revision operation. 12 patients (37%) were suffered with spinel compression fracture. Their daily activities were worsened. **Conclusion:** CR type HTK II TKA is characterized with all cementess fixation even patella component, poliethiren insert was made by direct compression mold method, tibial tray have a harder center screw. Our study suggests that the use of cementress CR type HTK II TKA in RA patients shows comparable results. The implant should be considered a sound choice for TKA in patients with RA.

W55-4

Evaluation of kinematics of newly developed PS system Future Knee

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Conflict of interest: Yes

[Object] Cadaver study was performed to assess the kinematics of the implanted knee with newly developed PS system. This system has design to obtain deep flexion maintaining stability form full extension to deep flexion. [Methods] Five fresh frozen cadaver knee specimen were used. In each knee, after the navigation system was set, rotation angle and varus/valgus angle of the femur relative to the tibia was measured during knee flexion. Then rotational, varus/valgus and antero-posterior flexibility of the knee were measured at each flexion angle. [Results] The femur gradually rotated externally during flexion relative to the tibia and the tibia moved in one swing plane during knee flexion. The stability was maintained during knee flexion and rotational flexibility was almost the same with the normal state at 120 degrees flexion. The system has PS mechanism for the simple operation and has the design to sit on the floor for Asian patients. Therefore, flexibility in flexion was important. The result of the cadaver study supported the concept of the design of the new system. [Conclusions] The cadaver specimen study showed the newly developed PS system for Asian patients have good knee kinematics to obtain deep flexion maintaining varus/valgus stability during knee flexion.

W55-5

Effectiveness of joint surgery in patients with rheumatoid arthritis: Significance of Timed Up and Go test and patient-reported outcome

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Conflict of interest: None

[Object] The purpose of this study is to investigate the effectiveness of surgery in a multifaceted manner, based on objective physical function and patient subjective evaluation. [Methods] This is a multicenter study conducted as a research by the Ministry of Health, Labor and Welfare. We evaluated the effectiveness of joint surgery in lower limbs based on physical function (HAQ-DI), activity speed index Timed Up & Go test (TUG), QOL (EQ - 5 D), depressed (BDI - II), global - VAS before and after surgery. [Results] 139 patients with lower extremity surgery were included. Average age 65.4 years, disease duration 17.5 years, female 92.1%, DAS 28 2.95, the main operation was THA 10.1%, TKA 33.8%, forefoot arthroplasty 46%. Patients with preoperative HAQ remission had 32.3%. TUG (12.7 s to 10.7 s), EQ - 5 D (0.63 to 0.68), global VAS (39 mm to 29 mm), BDI - II (12 to 10) were significantly improved. However, significant improvement of HAQ - DI (1.02 to 0.99) was not detected. [Conclusions] HAQ-DI is poor in sensitivity as an evaluation of surgery of RA. On the other hand, TUG quantified the effect of surgery with high sensitivity. In addition, surgery for patients with advanced physical disability greatly improved the degree of depression and was considered extremely useful.

W55-6

Femoral Component Alignment in Total Knee Arthroplasty with Distal Femur Resection Technique Using the Preoperatively Planned Intramedullary Rod Insertion Depth in Rheumatoid Arthritis Patients

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Conflict of interest: None

[Object] An intramedullary guide is the most commonly used method to make a distal femoral cut in total knee arthroplasty (TKA). Because of the femoral anterior bowing, the tip of the guide rod will impinge on the anterior cortex. We hypothesized that the preoperative planned insertion depth of the rod could increase the accuracy of the femoral component positioning (modified conventional technique). The purpose of this study was to determine the accuracy of the modified conventional technique for distal femoral resection in RA patients. [Methods] We investigated 10 RA knees and 91 OA knees underwent TKA using the modified conventional technique for performing the distal femoral resection. The femoral component alignment was evaluated with a CT based three-dimensional software. [Results] In the coronal plane, one RA patient had more than 2º of deviation from the targeted alignment and all of RA patients were within 3º. In sagittal plane, there was one RA patient who had more than 3º and other 9 RA patients were within 2º. In OA patients, 93.4% and 80.2% in the coronal and 93.4% and 86.8% in the sagittal plane were within 3º and 2º, respectively. [Conclusions] The modified conventional technique provides highly accurate postoperative femoral component positioning in RA patients.

W56-1

Symmetrical joint inflammation is developed by sensory neural interaction in a rheumatoid arthritis model

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Conflict of interest: None

[Object] We have demonstrated that regional neural activation induces local inflammatory status, a phenomenon known as “gateway reflex”. We identified four types of the gateway reflex induced by gravity, electric stimulation, pain and stress. Contribution of a neural pathway is also suggested for symmetrical inflammation in several diseases including rheumatoid arthritis. However, the causal neural pathway and molecules that contribute to the symmetrical symptoms during disease development is still unknown. [Methods] We used F759 mice as a cytokine-induced rheumatoid arthritis model. [Results] We here show that symmetrical inflammation in the joints is developed by regional sensory neural pathway via interneurons in the lower thoracic cords. Symmetrical inflammation in ankle joints is suppressed by surgical ablation or pharmacological inhibition of this pathway. It is reported that ATP serves as both a neurotransmitter and proinflammatory factor, and we identified ATP as a key molecule to link the local inflammation and neural pathway to induce the symmetrical inflammation. [Conclusions] Thus, blockades of this regional sensory neural interaction by suppressing ATP may lead to a novel therapeutic strategy for inflammatory diseases, particularly those with symmetric symptoms.

W56-2

A low molecular weight compound that inhibits BAFF binding to its receptor, BR3, suppressed the activation of B cells in vitro and in vivo models of autoimmune diseases

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Conflict of interest: None

[Object] We discovered a low molecular weight compound, BIK13, which inhibits binding of BAFF to BR3 by our original high-throughput screening system. In this study, we investigated inhibitory effects of BIK-13 on B cell functions. [Methods] PBMCs were cultured with B cell stimulants in the presence of BIK-13. B cell differentiation into plasmablasts / plasma cells, AID (activation-induced cytidine deaminase) expression and IgG production by the cells were analyzed by FACS, qPCR and ELISA, respectively. MRL/lpr mice were treated with BIK-13 for 32 weeks and an anti-dsDNA antibody, IL-6 and IL-10 in the serum were measured by ELISA. Infiltration of lymphocytes into organs was analyzed by immunohistochemistry. [Results] Plasmablasts / plasma cells differentiation *in vitro* was inhibited by BIK-13. AID expression and IgG production were also suppressed by BIK-13. Serum levels of an anti-dsDNA antibody, IL-6 and IL-10 in MRL/lpr mice received BIK-13 declined as compared to the control. The proportion of B cells in splenocytes and infiltration of B cells in lacrimal glands were remarkably suppressed in BIK-13-treated mice. [Conclusions] These data collectively suggest that BIK-13 suppresses the B cell functions and may provide a novel therapeutic possibility to treat autoimmune diseases.

W56-3

The effect of IL-6 receptor antibody for the treatment of McH-lpr/lpr-RA1 mice that spontaneously developed ankylosing arthritis

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Conflict of interest: None

[Background] McH-lpr/lpr-RA1 (RA1) mice are new strain mice which spontaneously developed arthritis and finally leads to ankylosis. [Objectives] To examine the effect of mouse IL-6 receptor antibody MR16-1 for the treatment of RA1 mice. [Material and Methods] Male RA1 mice were randomly divided into treated and control groups. MR 16-1 was applied from 10 weeks of age for the treatment group. Saline was applied for the control group. The drug was administered every week with the initial dose of 2 mg, then 0.5 mg. The effects were evaluated by

histological synovitis score, in vivo imaging using ICG-encapsulated liposomes and the expression of serum SAA. [Results] The tissue evaluation was performed at 14 17 and 20 weeks of age. The histological score of treated groups were significantly improved at every age. The interclass correlation coefficient was 0.771. In vivo imaging showed that significant signal decrease in treated groups at 14 weeks, but no significant difference was observed after 16 weeks. Blood SAA was significantly improved at 17 weeks of age. [Conclusion] IL-6 receptor antibody is effective for the treatment of ankylosing arthritis of RA1 mice. IL-6 might be a new potential target of treatment for ankylosing arthritis.

W56-4

IL-6 and TNF-alpha cooperate to regulates the proliferation of RA fibroblast-like synovial cells via the cell cycle regulators

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Conflict of interest: None

[Object] IL-6 and TNF-a play an important role in the pathogenesis of RA, however effects on the proliferation of RA-FLS remains unclear. To reveal roles of those on the proliferation of RA-FLS, we examined the expressions of cell cycle regulators and the cellular viability under stimulations of IL-6 and TNF-a. [Methods] RA-FLS were cultured with or without IL-6/soluble IL-6 receptor (sIL-6R) or TNF-a for 0~32h, 48h, 72h. The expressions of CDKIs ($p16^{INK4a}$, $p21^{Cip1}$, $p27^{Kip1}$) and *Cyclin E1/2* mRNA were measured by Real-time PCR, CYCLIN D and CYCLIN E protein were measured by Western blot, the expression of CYCLIN D and the phosphorylation of RB were observed by immunofluorescence, and the cellular viabilities were measured by WST-8, respectively. [Results] IL-6/sIL-6R decreased the expression of $p16^{INK4a}$, whereas increased CYCLIN D and the phosphorylation of RB. TNF-a increased the expressions of $p27^{Kip1}$, *Cyclin E1/2* mRNA, CYCLIN D, and the phosphorylation of RB. The expression of CYCLIN D and the phosphorylation of RB were synergistically increased by IL-6 and TNF-a. The proliferation of RA-FLS were increased by stimulation of both IL-6 and TNF-a. [Conclusions] Results indicate that IL-6 and TNF-a corporately affect the proliferation of RA-FLS *via* the cell cycle regulators.

W56-5

Analysis of the role of RORgammat+Foxp3+ regulatory T cells in the regulation of autoimmune arthritis

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Conflict of interest: None

[Object] To clarify the role of RORγt$^+$Foxp3$^+$ Treg cells in the development autoimmune arthritis. [Methods] 1) Lymphocytes in draining lymph node were harvested from C57BL/6 mice on 10 days after first CII immunization. RORγt expression in Foxp3$^+$ Treg cells and Foxp3$^-$CD4$^+$ T cells was analyzed by FCM, and compared them with lymphocytes of non-immunized mice. 2) On 10 days after first CII immunization, chemokine receptor 6 (CCR6) and CD25 expression on RORγt$^-$Foxp3$^+$Treg cells, RORγt$^+$Foxp3$^+$Treg cells, and Th17 in lymph node were analyzed by FCM. 3) Lymphocytes in ankle joints and draining lymph node were harvested from C57BL/6 mice after the induction of collagen induced arthritis (CIA), and CCR6 and CD25 expression in CD4$^+$ T cells were examined by FCM. [Results] 1) RORγt expression in Foxp3$^+$ Treg cells and Foxp3$^-$CD4$^+$ T cells was significantly increased in CII-immunized mice compared with non-immunized mice. 2) CCR6 and CD25 expression were increased on RORγt$^+$Foxp3$^+$Treg cells compared with RORγt$^-$Foxp3$^+$Treg cells and Th17 cells. 3) CD25$^+$CCR6$^+$ T cells were increased in inflamed ankle joints compared with lymph node. [Conclusions] RORγt$^+$Foxp3$^+$CCR6$^+$ Treg cells preferentially infiltrated into inflamed joints, and might have an effect on the pathogenesis of CIA.

W56-6

Inhibitory mechanisms of CTLA4-Ig for murine osteoclast formation

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Conflict of interest: None

[Background] Abatacept (CTLA4-Ig) is a fusion protein combining the extra-articular domain of CTLA4 with Fc domain of IgG1. It binds to CD80/86 complex in surface of antigen presenting cells, and blocks T cell activation. Axmann reported CTLA4-Ig directly inhibited the Osteoclast differentiation, and IDO/Tryptophan pathway were proposed as a part of the mechanism. Nevertheless, the whole mechanism remains to be solved. [Purpose] To examine the negative effect of CTLA4-Ig for Osteoclast differentiation, and clarify the mechanism. [Method] *In vitro* study, bone marrow macrophages (BMMs) derived from murine bone marrow were cultured with M-CSF and RANKL four days with or without recombinant CTLA4/Fc Chimera Mouse (CTLA4-Ig). Osteoclasts were counted as TRAP positive cells, and the expression of *NFATc1* were examined with real time PCR. Finally, intracellular calcium oscillation of BMMs with these cytokines were detected with Fura-2. [Results] CTLA4-Ig inhibited Osteoclast differentiation *in vitro*. RT-PCR data resulted in the less expression of *NFATc1* with the higher concentration of CTLA4-Ig. The Fura-2 fluorescence ratiometry data showed that CTLA4-Ig suppressed the calcium oscillation. [Conclusion] CTLA4-Ig inhibited intracellular calcium oscillation and down-regulated *NFATc1* expression.

W57-1

Post-loading therapeutic slump of certolizumab-pegol in rheumatoid arthritis patients: Results from Japanese multicenter registry system TBCR

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Conflict of interest: Yes

[Object] Certolizumab-pegol (CZP) can be used with the loading dose in the initial 4 weeks. Some patients demonstrate the deterioration of disease activity after the loading period (post-loading therapeutic slump). We studied the characteristics of the slump patients. [Methods] Participants were consecutive 87 RA patients treated with CZP in the TBC Registry system. The slump was defined as follows: patients that achieved moderate response at 4 weeks and >0.6 deterioration of DAS28-ESR between 4-8 or 8-12 weeks. We compared the disease activity and characteristics between the slump and non-slump group. [Results] Moderate response was achieved in 56 patients at 4 weeks including 11 slump patients. The slump group demonstrated significantly lower body weight (45.1 vs 54.3kg), lower DAS28 score at 4weeks (2.47 vs 3.24) compared to the non-slump group. DAS28 score at 12 weeks was significantly increased to 3.50 in the slump group. Five patients in the slump group decreased the dosage of prednisolone and/or methotrexate within 12 weeks. [Conclusions] Probably the dose reduction of concomitant medications resulted in the deterioration of disease activity after the loading period. Concomitant medication should not be decreased too early despite the good clinical response of CZP.

W57-2

A dose adjustment of infliximab can be effective the clinical and radiographic outcomes: a retrospective study

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Conflict of interest: None

[Object] To compare the efficacy of A dose adjustment of infliximab can be effective the clinical and radiographic outcomes. [Methods] In this retrospective study, we compared the clinical and radiographic outcomes of 2 groups: the combination therapy with MTX plus 3mg/kg infliximab continuously group 1; N=43) as control and the combination therapy with MTX plus 3mg/kg, 6mg/kg, or 10mg/kg infliximab by the assessment of DAS28 as the strategy of step-up and down (group 2; N=33). The patients sustained high and moderate disease activity for 4 months and increased the dosage of IFX as step-up. On the other hand, the patients sustained remission and low disease activity for 6 months and decreased the dosage of IFX as step-down. [Results] 2-year drug survival for IFX therapy (group 1) was 58% and it was the significant lower compared with that with IFX therapy (group 2) (67%). The remission disease activity as group 1 and 2 were 21% and 41%, and moderate disease activity rate was 58% and 35%. The mean DAS28 and delta Sharp Score was -2.5±2.0 vs. -1.1±0.5 and 1.8±0.8/2year vs. 5.7±1.8/2year as group 1 and 2. [Conclusions] The step-up protocol resulted the continued use of infliximab and suppressed the disease activity and radiographic outcomes.

W57-3

Dose consecutive measurements of serum IL-6 become a predictor of tocilizumab reduction? ~A pilot study~

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Conflict of interest: Yes

[Object] Reports on tocilizumab (TCZ) reduction has been increasing in recent years, but patient background and adjunct markers that can be reduced without relapse were not well understood. The purpose of this study was to examine whether changes in serum IL-6 would be predictor of TCZ reduction. [Methods] Fifteen RA patients treated with intravenous TCZ who achieved DAS28-LDA, spacing the period or TCZ dose reduction were included. Clinical assessment and serum IL-6 measurement were performed at each TCZ infusion. We compared serum IL-6 between the achievement group who complete more than 12 weeks and non-achievement group. [Results] TCZ dose reduction succeeded in 7 cases. Serum IL-6 was significantly reduced in the achievement group (-26.6 pg/ml), but increased in the non-achievement group (+46.3 pg/ml). TCZ spacing was succeeded in 4 out of 11 cases. There was no significant difference in serum IL-6 between the two groups. [Conclusions] Nishimoto reported that lower serum IL-6, the higher the possibility that TCZ could be discontinued. However, there was no report on whether it will be a predictor of TCZ reduction. It was suggested that in cases where serum IL-6 decreases by TCZ reduction, TCZ dose could be reduced.

W57-4

Switching of biologics to treat rheumatoid arthritis (RA) in patients with insufficient response to a first TNF inhibitor (TNFi): from FIRST registry

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Conflict of interest: None

[Object] Purpose of this study is to investigate the effectiveness on choosing the 2nd treatment for patients with insufficient response to a first TNFi. [Methods] Between 2008-2016 a total of 265 RA patients received MTX with persistent disease activity (DAS28-ESR≧3.2) and an insufficient response to first TNFi were included. We compared the effectiveness of TNFi, TCZ, ABT as 2nd-line. [Results] Baseline characteristics were mean age 60.3 years, female 83%, disease duration 8.9 years. Cause for discontinuation of first TNFi was primary nonresponders (26%), secondary nonresponders (53%) and others (20%). The 1 year persistence rate of therapy with TNFi-TNFi, TNFi-TCZ, TNFi-ABT were 65% (n=133), 86% (n=84) and 67% (n=48). Primary nonresponders were more prominent in the groups who switched biologics with TCZ, while secondary nonresponders and others seemed to be effectiveness in the groups with 2nd TNFi. A logistic regression analysis showed that age, ESR and HAQ-DI at baseline significantly predicted a persistent disease activity at 2nd TNFi. CDAI at 1 year was comparable among 2nd TNFi, TCZ, ABT after the adjustment by propensity score. [Conclusions] It is necessary to take into account the characteristics of biologics underlying reasons for an insufficient or factors involved.

W57-5

Evaluation of biological DMARD (Bio) tapering in the patients with rheumatoid arthritis (RA) in daily clinical practice

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Conflict of interest: None

[Object] In EULAR recommendations for management of RA (2016 update), if a patient is in persistent remission after having tapered glucocorticoid (GC), one can consider Bio tapering (BT), especially if this treatment is combined with csDMARD. We evaluate the possibility of BT in patients with RA. [Methods] In this retrospective study, we evaluated 62 RA patients (11.3% of men, 88.7% of woman, average age 59.7 years old, and tapering Bio: ETN (20), ADA (4), GLM (3), CZP (2), TCZ (19), ABT (14)) treated BT. [Results] 13 of 62 cases (21%, ETN (1), CZP (1), TCZ (5), ABT (6)) were flare, but 11 cases were inducted to remission by escalated Bio. The clinical evaluation at the time of BT start did not show significant difference in flare group (F) and continuation group (C) (CDAI: F2.25, C1.49, p=0.215, DAS28: F2.07, C1.75, p=0.157). The flare rate was high in no MTX and csDMARD combination, but there was not the significant difference (MTX: F46.2%, C61.2%, p=0.343, csDMARD: F53.8%, C77.6%, p=0.094). The flare rate was also similar about TCZ with csDMARD combination. The flare rate was significantly high in the GC combination (F61.5%, C24.5%, p=0.011). [Conclusions] BT seems feasible in daily clinical practice, but GC and no csDMARD combination needs attention.

W57-6

The therapeutic effect of Golimumab in patients with rheumatoid arthritis does not depend on the previous biological DMARDs treatment

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Conflict of interest: None

[Object] Golimumab (GLM) is used in 50mg or 100mg with methotolexate in patients with rheumatoid arthritis (RA) who did not respond adequately to other biologic disease modifying antirheumatic drugs (bDMARDs). This study evaluated the influence of pre-bDMARDs for GLM treatment after switched. [Methods] This analysis included 46 patients with RA who switched from other bDMARDs to GLM. Twenty-six patients were switched from anti-TNF bDMARDs (TNF group) and 19 patients were switched from non-TNF bDMARDs (non-TNF group). In

non-TNF groups, 9 patients were switched from Tocilizmab (TCZ group) and 10 patients were switched from Abatacept (ABT group). Clinical Disease Activity Index (CDAI) was evaluated at baseline, 6 months and 12 months after GLM treatment. [Results] CDAI was improved in TNF and non-TNF group at baseline 22.7±14.6 vs 21.7±11.2 to 6 months 11.8±8.0 ($p<0.01$) vs 16.6±14.6 ($p=0.03$) and 12 months 10.3±10.9 ($p<0.01$) vs 8.1±3.3 ($p<0.01$). Improvement rate of CDAI was not significantly differented in two groups (6months: $p=0.53$, 12months: $p=0.62$). In addition, there were no differences in improvement rate of CDAI between TCZ and ABT group (6months: $p=0.27$, 12months: $p=0.21$). [Conclusions] GLM improved disease activity regardless of the type of prebDMARDs therapy in pateitns with RA.

W58-1

Effects of tumor necrosis factor inhibitors and tocilizumab on the glycosylated hemoglobin levels in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To investigate the influence of TNF inhibitors (TNFi) and tocilizumab (TCZ) on the glucose metabolism of rheumatoid arthritis (RA) patients. [Methods] RA patients in whom treatment with TNFi or TCZ was initiated from 2008 to 2015 were studied. We analyzed patients whose glycosylated hemoglobin (HbA1c) levels were ≧6.0% and were measured at 3 months after the initiation. [Results] 147 cases were included (TNFi, n=99; TCZ, n=48). Both the TNFi and TCZ groups had significantly lower HbA1c values at one month and three months after the initiation. Although the pretreatment HbA1c values did not differ (TNFi, 6.6%; TCZ, 6.5%; $p=0.640$), the 3-month treatment HbA1c values were lower (TNFi, 6.4%; TCZ, 6.0%; $p<0.001$) and the changes in HbA1c were greater (TNFi, 0.2%; TCZ, 0.55%; $p<0.001$) in the TCZ group. The reduction of HbA1c was associated with baseline diabetes treatment, hospitalization, medical change, and TCZ. In the multivariate logistic regression analysis, TCZ was associated with the reduction of HbA1c in comparison to TNFi (adjusted OR = 5.86, 95% CI =2.46-13.8; $p<0.001$). [Conclusions] The HbA1c levels in RA patients were significantly lower after the initiation of TNFi or TCZ. Our study suggests that TCZ decreases the HbA1c levels to a greater extent than TNFi.

W58-2

Safety and Efficacy of Alternate-Day Corticosteroids as a Bridging Therapy for Rheumatoid Arthritis

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Conflict of interest: None

[Object] To investigated the safety and efficacy of alternate-day (QOD) corticosteroid (CS) therapy for the treatment of rheumatoid arthritis. [Methods] We retrospectively analyzed all patients (>18-years-old) who started oral CS therapy for rheumatoid arthritis, between 2005 and 2014, at our hospital. Patients were divided into daily (QD) or QOD CS groups to investigate the rates of CS-related major adverse events in each group within the first year. We also investigated the rates of patients free from CS treatment at one year, and the mean decreases in C-reactive protein (CRP) levels at 1 month. [Results] In total, 138 patients were analyzed (QD group, 68; QOD group, 70). The maximum daily CS dose was not significantly different ($P = 0.24$). The infection rate was significantly lower in the QOD group (24.3%) than in the QD group (50.0%; $P < 0.01$), whereas other adverse event rates were similar between the groups. The CS-free rate, at one year, was significantly higher in the QOD (58.6%) than in the QD (26.5%; $P < 0.01$) group. The mean CRP decreases over one month were not significantly different ($P = 0.40$). [Conclusions] QOD CS treatment may lead to lower infection rate, lower corticosteroid dependence than, and possibly show the same short-term efficacy as QD treatment.

W58-3

The effect of the type of 1st TNF inhibitor on treatment response of 2nd biologics-Data from ANSWER cohort-

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Conflict of interest: None

[Object] Monoclonal antibodies (mAb) to TNF have cytotoxic effect for TNF expressing cells. We analyzed the effect of 1st TNFmAb on treatment response of 2nd biologics (bio). [Methods] We recruited the cases who were switched to 2nd bio from TNF-i for 1st bio from Kansai Consortium for well-being for rheumatic disease patients (ANSWER) cohort. We categorized the cases with mAb (IFX, ADA and GOL) for 1st bio into 1st mAb group, and cases with receptor/PEG (ETN and CZP) for 1st bio into 1st R/P. We compared disease activity and retention rate between the two groups. [Results] 132 cases were recruited in 1st mAb group and 66 in 1st R/P. Age, sex and CDAI at baseline and the ratio of 2nd TNF-i usage were similar between the two groups, except the ratio of MTX usage that was higher in 1st mAb group than 1st R/P (86.8% and 62.5%, respectively, $p=2.1\times10^{-4}$). CDAI remission rate of 1st mAb group at 3 and 6 months after switch was higher than that of 1st R/P ($p=0.0064$ and $p=0.021$, respectively). The retention rate of 1st mAb group was higher than 1st R/P ($p=0.022$, Log-rank test). Similar results were obtained with analyses using propensity score matched data. [Conclusion] These results indicate that remission rate and retention rate of 2nd bio are higher when TNFmAb is chosen as 1st bio.

W58-4

Clinical Experience on Certolizumab Pegol ~ Perspective on Disease Activity and MTX combination ~

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Conflict of interest: None

[Object] The position has not been established for Certolizumab

Pegol (CZP) that is the fifth TNF inhibitors in market. To evaluate efficacy of CPZ, it was investigated for association of clinical characteristic prior to CPZ treatment with response to CPZ treatment. [Methods] 42 patients initiated CPZ treatment June 2013 through Aug 2017 at Kurashiki Sweet hospital and Mabi Memorial hospital. Among those, 26 patients who sustained CPZ treatment for at least 24 weeks are target population for this study. Analysis was performed between groups of patients, high disease activity vs low disease activity and concomitant MTX vs no MTX by means of drug persistency rate, DAS28ESR, DAS28CRP, and SDAI. [Results] Overall CPZ persistency rate is 71.2%. Persistency rate for group with high disease activity is high at 90.1% and significantly improved at week 4 however, its rate for group with low disease activity does not have significant improvement. There was a significant improvement in DAS28 and SDAI for groups with MTX use. [Conclusions] Data implies that CPZ is effective option for patients with high disease activity. One of the reason may be that CPZ is capable of doing loading. This analysis suggest that even small dose of MTX may contribute to further efficacy.

W58-5

Use of intravenous fluid and subcutaneous injection preparation, of tocilizumab for rheumatoid arthritis in the AORA registry

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Conflict of interest: None

[Objective] To investigate the use of intravenous fluid and subcutaneous injection preparation, of tocilizumab (TCZ) for rheumatoid arthritis (RA). [Methods] In 77 patients treated with TCZ in the AORA registry, patient background, continuation rate, disease activity score (DAS), and drop out case were compared between the intravenous fluid preparation (IV) and subcutaneous injection preparation (SC) groups. [Results] In the IV (43 patients, 56%) and SC (34 patients, 44%) groups, the mean patient ages were 62 (range, 18-83) and 58 (17-79) years, the mean disease durations were 129 (4-475) and 157 (4-691) months, respectively. A total of 39% and 56% of patients in the IV and SC grouped were switched cases, and 77% and 68% of patients received concomitant MTX administration, respectively. In the IV and SC groups, the 3-year continuation rates were 76% and 84%, respectively. After 52 weeks, low disease activity (LDA) rates were 77% and 76% on DAS 28-ESR, good and moderate response rates were 74% and 75% on EULAR criterion, while 5 and 2 cases were drop out because of adverse event and inadequate effect, respectively. [Conclusion] Patients in both groups had high continuation and LDA rates.

W59-1

Clinical characteristics and prognosis of adult onset IgA vasculitis

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Conflict of interest: None

[Object] The aim of this study is to investigate characteristics and prognosis of IgA vasculitis. [Methods] 46 patients who diagnosed as IgA vasculitis between April 2007 and July 2017 were included. Risk factors associate with all cause death and renal insufficiency were studied by Cox regression analysis. [Results] The average age at onset was 56.7, and 26 (56.5%) cases were female. All had skin involvement, and 19 (41.3%) had gastrointestinal involvement. 23 (50.0%) cases showed proteinuria, and 28 (62.2%) showed hematuria. 36 cases underwent skin biopsy and IgA deposition was recognized in 13 cases. Renal biopsies were performed in 19 cases. 35 patients used steroids and 6 used immunosuppressants. Late onset (Age>60) (RR7.44, p=0.016, 95%CI1.39-137.6) and decreased renal function at diagnosis (RR4.24, p=0.041, 95%CI1.08-28.2) were risk factors of death. Among 38 patients who had not been diagnosed with chronic kidney disease, late onset (RR19.86, p<0.001, 95%CI3.94-361.6), proteinuria (RR3.52, p=0.018, 95%CI1.24-11.54), hematuria (RR3.67, p=0.047, 95%CI1.02-23.49), no joint involvement (RR 4.96, p=0.014, 95%CI1.33-32.46) were risk factors of renal insufficiency. [Conclusions] Late onset IgA vasculitis have poor prognosis. Hematuria and proteinuria relate to poor renal prognosis.

W59-2

Cinical significance of podocyte foot process effacement in adult IgA vasculitis

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Conflict of interest: None

[Object] Adult patients with IgA vasculitis occasionally present with massive proteinuria, rapidly progressing to renal failure. Podocyte injury is well known to cause proteinuria and glomerulosclerosis in various glomerular diseases, however few studies have assessed podocyte injury in IgA vasculitis. This study aims to provide clinical significance of podocyte foot process effacement (FPE) in IgA vasculitis. [Methods] 26 adult patients with IgA vasculitis, who were performed renal biopsy in our hospital between January 2003 and June 2017, were studied. We calculated FPE ratio (FPE length/GBM length) on electron micrograph and analyzed relationships between FPE ratio and, both laboratory and renal pathological findings. [Results] Mean FPE ratio was 0.421±0.18. FPE ratio was closely positively correlated with 24-hour proteinuria (r=0.765, p<0.001). FPE ratio was positively correlated with serum creatinine (r=0.494, p<0.01) and negatively corrected with eGFR (r=-0.58,<p<0.01). In ISKDC classification, FPE ratio of grade V+VI (n=9:0.56±0.18) was significantly higher than grade II (n=6:0.29±0.04) (p<0.01) and grade III+IV (n=11:0.36±0.12) (p<0.01). [Conclusions] Expanded FPE suggesting podocyte injury might leads to increase proteinuria and reduce renal function in adult IgA vasculitis.

W59-3

Clinical features of anti-GBM antibody glomerulonephritis: A series of 12 cases

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Conflict of interest: None

Objective: To clarify the clinical features of anti-GBM antibody glomerulonephritis. **Methods:** We retrospectively assessed the clinical symptoms, laboratory findings, renal biopsy findings and treatment in patients with anti-GBM antibody positive glomerulonephritis in our hospi-

tal from 2001 to 2017. **Results:** 12 patients (mean age at onset 63.8 ± 17.5 years, 5 males and 7 females) were enrolled. Chief complaints were fever (n=7, 58%), chill (n=4, 33%), back pain (n=5, 42%) and gross hematuria (n=4, 33%). 3 cases were initially diagnosed as acute pyelonephritis. One case developed alveolar hemorrhage. The mean serum Creatinine and CRP were 5.81 ± 4.4 mg/dL and 14.7 ± 7.2 mg/dL, respectively. The mean of U-Pro was 1.72 ± 1.3 g/gCre. Although all had microscopic hematuria, 6 patients showed non-glomerular hematuria. MPO-ANCA was positive in 5 cases. The mean percentage of global sclerosis in glomeruli was 18.1 ± 19.2%, crescent formation was 70.0 ± 27.3%. As treatment, mPSL pulse, plasmapheresis and IVCY were performed in 8 (67%), 10 (83%) and 3 (25%), respectively. Maintenance hemodialysis was performed in 10 cases. **Conclusions:** In our study, more than half of the patients had fever, and some cases had pyelonephritis-like symptoms, which could lead to the delay of the diagnosis.

W59-4

HLA-class II associations of Japanese ANCA-associated vasculitis: comparison with populations of European-ancestry

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Conflict of interest: None

[Object] In contrast to European populations, microscopic polyangiitis (MPA) and MPO-ANCA associated vasculitis (MPO-AAV) account for the majority of Japanese AAV and half of granulomatosis with polyangiitis (GPA) patients are positive for MPO-ANCA (MPO-GPA). *HLA-DRB1*09:01* and **13:02* were associated with MPA/MPO-AAV in Japanese, while European genome-wide association study (GWAS) showed association with *HLA-DQ* SNPs. In this study, we examined whether GWAS SNP in *HLA-DQ* (rs5000634) is associated with Japanese AAV independently of *HLA* alleles and whether *HLA* associations are different between MPO- and PR3-GPA. [Methods] Association of rs5000634 and *HLA-DRB1, DPB1* was examined in 467 AAV including 285 MPA and 92 GPA, and 596 healthy controls. [Results] rs5000634A was slightly decreased in MPO-AAV (P=0.044). However, when conditioned on *DRB1*09:01* or **13:02*, the association disappeared, while the association of the *DRB1* alleles remained significant after conditioned on rs5000634. In analysis of MPA- and PR3-GPA, *DRB1*08:02* was increased in MPO-GPA (P=0.0013), but not in PR3-GPA (P=0.72). [Conclusions] In Japanese AAV, the association of GWAS SNP in *HLA-DQ* was attributable to linkage disequilibrium with *HLA-DRB1*. In addition, MPO- and PR3-GPA showed different associations in *HLA-class II*.

W59-5

Association of ANCA-Associated Vasculitis with Proteinase 3 (PRTN3) Polymorphism in a Japanese Population

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Conflict of interest: None

[Object] Incidence of granulomatosis with polyangiitis (GPA) and proteinase 3 (PR3)-ANCA positive vasculitis (PR3-AAV) is low in East Asian populations as compared with European populations. Association of these conditions with a single nucleotide polymorphism (SNP) rs62132295 located upstream of the gene encoding PR3 (*PRTN3*) has been reported in European populations. A trend towards association between this SNP and GPA was also reported in a Chinese population, however, no studies have been reported in Japan. This study analyzed the association between this SNP and AAV patients in a Japanese population. [Methods] 467 Japanese AAV patients and 843 healthy controls were genotyped using TaqMan SNP Genotyping Assay. In addition, allele frequency data of 3,367 healthy controls were obtained from Tohoku Medical Megabank Organization (ToMMo). [Results] The SNP was associated with GPA and PR3-AAV under the allele model (GPA: P=0.0400, odds ratio [OR]=1.50; PR3-AAV: P=0.0457, OR=1.60). The meta-analysis with Chinese population data showed significant association with GPA, but not with microscopic polyangiitis (MPA). [Conclusions] The SNP located upstream of *PRTN3* is associated with GPA susceptibility also in East Asian populations.

W59-6

Clinical study of giant cell arteritis in our department

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Conflict of interest: None

[Object] To investigate clinical and laboratory features of giant cell arteritis (GCA). [Methods] We included 34 patients (9 men, 25 women; mean age 69.8 years) in this study. GCA was diagnosed based on the American College of Rheumatology 1990 classification criteria. [Results] Mean serum C-reactive protein was 8.65 mg/dl. GCA was classified into three types: classic temporal arteritis type (cranial GCA, 13 patients); large-vessel type, affecting the aorta and its major branches without temporal arteries (15 patients); generalized type, affecting both temporal ar-

teries and large vessels (6 patients). Swelling and tenderness of temporal arteries were recognized in temporal arteritis and generalized arteritis. Sixteen of these patients also had histopathologic findings of arteritis, including giant cells in biopsy specimens. Examination of HLA-class 1 expression showed that 10% of patients with cranial GCA and 38.5% of patients with large-vessel GCA were positive for HLA-B39. One third of patients in whole GCA were positive for HLA-DR4. [Conclusions] Our study demonstrated that HLA-class 1 expression in GCA resembles that in Takayasu arteritis, suggesting that these two arteritis types share the same genetic background.

W60-1

Evaluation of clinical phenotype and severity of anti-neutrophil cytoplasmic antibody-associated vasculitis: a cluster analysis

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Conflict of interest: None

[Object] Several characteristics of Japanese patients with ANCA-associated vasculitis (AAV) were reported recently, but a mutual relationship among those characteristics has not yet been elucidated. In addition, appropriate biomarker for treatment effectiveness has also not been established. [Methods] Using dataset of two nationwide cohort studies, we performed cluster analysis. Model 1 included ANCA type, items of BVAS, and ILD and Model 2 included Cr and CRP additionally. Clustering was performed for finding relatively homogeneous clusters. Clinical characteristics and outcomes were compared among clusters. [Results] Except for EGPA or missing of PR3-ANCA test, 427 patients were enrolled. In seven clusters of Model 1, ANCA negative and PR3-ANCA positive group were emerged as distinct two clusters, Other MPO-ANCA positive five clusters were characterized by ear, nose and throat, cutaneous, and renal symptoms, and ILD. Seven clusters of Model 2 were characterized by combination of CRP and Cr level. Overall survival and renal survival differed across the clusters significantly. [Conclusions] Cluster analysis indicated the distinct characteristics of Japanese AAV. CRP and Cr might be useful to evaluate treatment effectiveness.

W60-2

Otitis Media should be Considered as a Marker of Vasculitis in Classification of ANCA Associated Vasculitis

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Conflict of interest: None

[Object] We clarify our accuracy of ANCA associated vasculitis (AAV). [Methods] One hundred and ninety-three patients (91 males and 102 females) with AAV (101 microscopic polyangiitis (MPA), 65 granulomatosis with polyangiitis (GPA) and 27 eosinophilic granulomatosis with polyangiitis were admitted to Niigata University Hospital from 1989 through 2017. The discharge diagnosis and the diagnosis classified by the algorithm of Watts are compared. [Results] Four cases were diagnosed as having MPA with otitis media, lung lesions, crescentic glomerulonephritis. One case was diagnosed as having AAV with otitis media, pulmonary hemorrhage, rapidly progressive glomerulonephritis, purpura. One case was diagnosed as having AAV with maxillary sinusitis, interstitial pneumonia, glomerulonephritis, mononeuritis multiplex. One case was diagnosed as having otitis media with AAV with otitis media, lung nodules. These seven cases were all MPO-ANCA positive and diagnosed as having GPA by the algorithm of Watts. Our accuracy was 96 %. [Conclusion] MPO-ANCA positive AAV with otitis media, lung lesions and kidney lesions are sometimes diagnosed as MPA.

W60-3

The comparison between lung abnormalities on chest computed tomography (CT) in patients with microscopic polyangiitis (MPA) and these in health control subjects who underwent lung cancer screening test

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Conflict of interest: None

Objectives: We compared the lung abnormalities on chest computed tomography (CT) between patients with microscopic polyangiitis (MPA) and health control subjects who underwent lung cancer screening test. Methods: We retrospectively identified 150 MPA patients whose chest CT images before treatment were available. We also evaluated the CT images of 150 sex-, age-, and smoking history-matched control subjects. Pulmonologists and a radiologists determined the presence of a total of 22 CT imaging components for interstitial lung lesions, airway lesions, emphysematous lesions, pleural lesions. Results: The mean age was 70 years old (range 42-89), and female was 59 %. 51 patients had a history of smoking (34 %). Grand glass opacity improved in 41 % of MPA patients, 2 % of controls. Reticular pattern improved in 41 %/ 6 %, interlobular septal thickening 41 %/ 3 %, consolidation 23 %/ 2 %, and honeycombing 23 %/ 1 %. Bronchiolitis improved in 55 %/ 8%, bronchial wall thickening 44 %/ 9%, and bronchiectasis 32 %/ 11%. Emphysematous lesions improved in 37 %/ 10 %, and pleural lesions 53 %/ 7%. Conclusions: A wide variety of lung abnormalities can be identified in patients with MPA. These abnormalities are different from those related to aging and smoking.

W60-4

Long-term observation of clinicopathological characteristics and outcome of Japanese patients with ANCA associated glomerulonephritis

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Conflict of interest: None

[Object] Clinicopathological characteristics and outcome of Japanese patients with ANCA associated glomerulonephritis are presumed to vary among periods. We examined characteristics and outcome of patients with ANCA associated glomerulonephritis according to the periods. [Methods] From 1991 to 2017, a total of 115 patients who were diagnosed as ANCA associated glomerulonephritis in Kanazawa University Hospital and Kanazawa collaborative group was examined in this study. All cases were divided into group I (1991-2000, 34 cases), group II (2001-2010, 44cases) and group III (2011-2017, 37 cases). [Results] Neither age, CRP level, renal function, titer of ANCA nor the rate of crescentic formation at the time of diagnosis had statistical difference among each group. On the other hand, the degree of hemoglobin was increased over the periods (9.0±1.8g/dL (mean±SD) in group I, 9.6±1.8g/dL in group II, 10.9±3.4g/dL in group III. P=0.01). Furthermore, 1-year patient survival rate was

improved in recent year (82% in group I, 91% in group II, 91% in group III). On the other hand, there were no differences in renal survival rate among the treated-periods. [Conclusions] Patient survival rate was improved in patients with ANCA associated glomerulonephritis after 2001.

W60-5

Analysis on current state of treatment of Japanese ANCA associated vasculitis patients using a large insurance database

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Conflict of interest: Yes

[Objective] The aim of this study is to investigate the current status of treatment patterns and mortality rate in remission induction therapy in Japanese ANCA associated vasculitis (AAV) patients. [Method] Among 24,673 cases of hospitalized AAV (microscopic polyangiitis (MPA) or granulomatosis with polyangiitis (GPA) or eosinophilic granulomatosis with polyangiitis (EGPA)) based on a large Japanese insurance database from April 2008 to April 2017, 7,285 cases whose main disease name at discharge of these cases was MPA or GPA or EGPA were extracted. Of these patients, 2,410 cases were study cohort in this study who were treated with prednisolone [PSL] over 30 mg or steroid pulse therapy and their hospitalization days were over 7 days were defined as remission induction therapy group. [Results] The number of the patients of MPA, GPA, and EGPA were 1,511, 385, and 514, respectively. Treated with steroid pulse, rituximab, intravenous cyclophosphamide in MPA, GPA, and EGPA were 60.8%, 63.1% and 57.4%, respectively, and 4.2%, 9.1% and 1.0%, respectively, 14.8%,15.3% and 9.7%, respectively. [Conclusion] Steroid pulse therapy is common and concomitant use of immunosuppressive agent is relatively small treatment pattern as remission induction therapy in Japanese AAV patients.

W60-6

Halth-related Quality of Life Assessed by the SF-36 and the EQ-5D-5L in Patients with ANCA-associated Vasculitis: A Cross-sectional Study in 2 University Hospitals

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Conflict of interest: None

[Object] In a 2-centers cross-sectional study, we aimed to validate the reliability of the SF-36 and the EQ-5D as generic measures of health-related quality of life (HRQoL) and investigate their association with clinical background and indices among Japanese patients with antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). **[Methods]** AAV patients seen in the 2 university hospitals from August 2016 through February 2017 were eligible. They were asked to complete the SF-36, the EQ-5D, and other demographic questionnaires. Physicians completed the BVAS and the VDI simultaneously and recorded other medical information. **[Results]** A total of 62 Japanese patients with AAV participated. The mean physical and role/social component summary scores of the SF-36 were significantly lower than those of the the age- and sex-matched national norms, whereas the mean mental component summary score was not. The mean EQ-5D index value was significantly lower than that of the age- and sex-matched national norm. The physical component summary scores and the EQ-5D values were inversely correlated with the VDI, but not with the BVAS. **[Conclusions]** The SF-36 and EQ-5D demonstrated acceptable reliability among Japanese patients with AAV. HRQoL was reduced in Japanese patients with AAV.

W61-1

Can HCQ prevent progression of nephropathy in patients with systemic lupus erythematosus?

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Conflict of interest: None

[Object] Hydroxychloroquine (HCQ) is recommended in the patients with lupus nephritis. HCQ has been shown to be effective in reduction of proteinuria in mouse models, but not known in SLE patients. [Methods] This is a single-center, retrospective study. We compared the amount of proteinuria in SLE patients with proteinuria of 0.2 g/gCr or more who started HCQ before 5/2017 (HCQ group) and that in SLE patients with proteinuria of 0.2 g/gCr or more between 7/2016-9/2016 (non-HCQ group). We excluded the following patients from the analysis: those who increased or started immunosuppressive agents or ACE/ARB from 1 month prior to the observation period to its end. We defined "improvement" as reduction of proteinuria 0.1 g/gCr or more. [Results] HCQ group included 15 patients and non-HCQ group included 12 patients. There were no group-differences in age, sex, PSL dosage, use of immunosuppressives or ACE/ARB. In HCQ group, proteinuria decreased from 0.51±0.27 g/gCr to 0.35±0.26 g/gCr (P=0.09). In non-HCQ group, proteinuria increased from 0.66±0.46 g/gCr to 0.72±0.68 g/gCr (P=0.62). The proportion of patient who met "improvement" in the HCQ group and non-HCQ group were 10 (67%) and 3 (25%), respectively (p=0.031). [Conclusions] HCQ may prevent progression of nephropathy.

W61-2

Early exposure to hydroxychloroquine predicts good renal response in Japanese patients with lupus nephritis class III or IV

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Conflict of interest: None

[Object] To investigate the efficacy of hydroxychloroquine (HCQ) in addition to mycophenolate mofetil (MMF) in the induction therapy in patients with lupus nephritis (LN) class III or IV. [Methods] Patients who pathologically diagnosed as LN class III or IV and treated with MMF as induction therapy from 2007 to 2017 were evaluated. We divided them into two groups according to whether HCQ was received. In this study, we selected patients who were treated with HCQ from early phase of induction therapy, within 4-weeks from high-dose glucocorticoid initiation for HCQ users. Cumulative complete renal response (CR) for 24 weeks was compared. [Results] We identified 10 patients with HCQ and 11 without. An older age (42.3 vs 32.6 years, P = 0.04) and a smaller number of class III+V (0 vs 4 cases, P = 0.03) were detected in HCQ users compared with the non-HCQ users. A significantly higher cumulative CR rate was seen in HCQ users comparing with non-HCQ users for 24 weeks (p = 0.03). Multivariate analysis indicated that HCQ use was the independent factor correlated with CR achievement (OR 50.33, 95%CI 2.29-40682.4, p < 0.01). [Conclusions] HCQ use from early phase of induction therapy may have additional therapeutic effect on renal response in Japanese LN patients with MMF treatment.

W61-3

Investigation of 112 patients received hydroxychloroquine for systemic lupus erythematosus

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Conflict of interest: Yes

[Object] To examine the details of cases in which hydroxychloroquine

(HCQ) was administered to patients with systemic lupus erythematosus (SLE). [Methods] Among the patients diagnosed as SLE in 1997 ACR classification criteria, 100 subjects who passed 24 weeks or more among 112 patients who received HCQ were analyzed. Twenty-two patients were used in combination with other immunosuppressants at the time of remission induction, and 78 were added during maintenance therapy. [Results] The average of prednisolone in the maintenance therapy group was significantly reduced (8.0 ± 4.6 mg at 0 week, 6.4 ± 3.5 mg at 24 week, 5.0 ± 3.2 mg at last observation; mean 390 days, respectively, paired t-test, p <0.001). Nevertheless, mean SLEDAI significantly improved at 2.6 ± 2.5, 0.8 ± 1.2, and 0.7 ± 1.0 at each time point (paired t-test, p <0.001). In addition, 12 cases with side effect discontinuation were all RNP antibody positive cases (Fisher's exact test, p <0.01). [Conclusions] Additional administration of hydroxychloroquine is expected to significantly reduce prednisolone without worsening the disease activity of SLE. In addition, examples of withdrawing side effects are more frequent in RNP antibody positive cases.

W61-4

Present status of hydroxychloroquine use in SLE at our hospital

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Conflict of interest: None

[Object] Hydroxychloroquine (HCQ) is widely used in systemic lupus erythematosus (SLE) unless contraindicated. We will verify the status of use of HCQ in our department and the clinical course of SLE patients administered. [Methods] 52 SLE patients were included. Changes in dose of complement C3 and anti-dsDNA antibody titers, where HCQ was administered as single agent, or adverse event occurrence status. [Results] There were seventeen cases in which HCQ was used at the time of introduction of remission, and 35 cases in which HCQ was added during maintenance therapy. There was no significant change in complement, anti-dsDNA antibody titer, but SLEDAI was significantly improved. However, there was no significant change in PSL dosage. There were 18 cases of combined immunosuppressive drugs, but 13 of them were reduced in weight and stopped, but no onset of retinopathy occurred within the investigation period. [Conclusions] HCQ improves the disease activity of SLE. On the other hand, the serologic index such as complement and anti-dsDNA antibody did not change, which may have affected steroid weight loss.

W61-5

Steroid Sparing Effect and Laboratory Tests Improvement of Hydroxychloroquine Adding on Patients with Systemic Lupus Erythematosus without Severe Organ Involvement

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Conflict of interest: None

[Object] To evaluate the efficacy and safety of hydroxychloroquine (HCQ) add-on with systemic lupus erythematosus (SLE). [Methods] Steroid reduction and laboratory data were evaluated for 76 SLE outpatient cases with HCQ in our hospital. [Results] Among the 76 SLE patients who were treated with HCQ, 59 patients (46 females, average age 43 years, median age of 7 years, lupus nephritis 17, NPLUPUS 8) were included in current analysis. The median of the treatment periods by HCQ was 607 days. The number of discontinuation due to side effects was 6 (4 rashes, 1 nausea) and the average of the HCQ dose with and without side effects were 5.2 and 4.0mg/kg/day. Prednisolone (PSL) dose before administration, 6 months after, 12 months after administration showed a decreasing tendency to 5.0, 3.8, 3.0mg each. Moreover, in the patients with low complement C3 level before HCQ administration, the median of C3 before, 6 months after, 12 months after were 69, 84, 76 mg/dl, and among the patients with urine protein more than 0.3 g/day, urinary protein were 1.07, 0.50, 0.24 g/gCr respectively. [Conclusions] It was suggested that HCQ add-on might have steroid sparing effect and beneficial effects in laboratory data even to the SLE patients without severe organ involvement.

W61-6

The efficacy of hydroxychloroquine (HCQ) reducing dose of steroid in patients with systemic lupus erythematosus (SLE)

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Conflict of interest: None

[Object] The aim of this study is to evaluate the efficacy and the safety of HCQ as co-treatment in the standard therapy of SLE. [Methods] Twenty-seven patients receiving the maintenance therapy of SLE were enrolled in this study. Dose of prednisolone (PSL), titer of anti-DNA antibody, WBC count, serum complement and SLE disease activity index (SLEDAI) were examined retrospectively at 0, 3 and 6 months after administration of HCQ. [Results] The mean dose of PSL was significantly reduced (mean±S.E) (pre-administration of HCQ:10.1±2.0 mg/day, 6 months after administration of HCQ:4.7±0.7 mg/day, *p=0.013*). There were no statifical significancy between before administration of HCQ and after administration in SLEDAI (1.8±0.5 vs 1.3±0.6, *p=0.53*), the titer of anti-DNA antibody (6.2±2.1 IU/ml vs 0.8±0.6 IU/ml, *p=0.08*), WBC count (6586±4.9 /μl vs 5771±5.0 /μl, *p=0.28*) and serum complement (C3 85±4.2 mg/dl vs 91±5.2 mg/dl, *p=0.44*, C4 19±2.1 mg/dl vs 20±2.6 mg/dl, *p=0.65*). Transient skin rash was observed in one patient after administration of HCQ. [Conclusions] In the patients receiving the maintenance therapy of SLE, it is suggested that administration of HCQ on standard therapy might be enable to reduce the dose of PSL.

W62-1

Efficacy and safaty of hydroxychloroquine against systemic lupus erythematosus - Assessment at 6 months after initiation -

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Conflict of interest: None

[Object] To assess the efficacy and safety of hydroxychloroquine (HCQ) for systemic lupus erythematosus (SLE) in our department. [Methods] Clinical and laboratory data (medication, signs and symptoms, and SLEDAI) of the SLE patients whom prescribed HCQ from Apr 2016 to Oct 2017 in our department were retrospectively collected and analyzed. [Results] 57 patients were prescribed HCQ. Age 42.7±16.9 years, females 91%, and disease duration 114.8±106.5 months. The most common signs and symptoms of SLE were rash (71%), followed by hypocomplementemia (66%) and cytopenia (62%). At initiation of HCQ, dose of PSL was 13.9±14.2 mg, and SLEDAI was 5.0 ± 5.5. Among 30 patients who followed for more than 6 months, PSL was significantly decreased (14.6±12.3[SH1] mg vs 8.5±5.6mg, p<0.05), and SLEDAI was significantly improved (5.1±5.0vs 2.4±2.7, P<0.01) from baseline. 4 cases withdrew and 2 cases reduced HCQ because of adverse events; diarrhea in 2, conjunctival bleeding in 1, and suspected cytopenia in 1. [Conclusions] HCQ may contributed to reduce the amount of PSL and to improve SLEDAI at 6 months. Although HCQ could be continued in majority of the patients, adverse events, especially diarrhea, should be carefully observed.

W62-2

Study on the safety and efficacy of hydroxychloroquine in patients with Japanese systemic lupus erythematosus

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Conflict of interest: None

[Object] he efficacy and safety of hydroxychloroquine (HCQ) in patients with Japanese systemic lupus erythematosus (SLE) has not been verified well. We assessed the efficacy and safety of HCQ for Japanese SLE patients in clinical practice for 6 months. [Methods] The primary endpoint was the retention rate up to 6 months. Secondary endpoints were SLEDAI, BILAG index, the dose of concomitant glucocorticoid. [Results] The retention rate was 81.7 % (94/115 cases). Discontinuation cases of 21 cases were all discontinued the HCQ within 2 months. Secondary endpoint: SLEDAI and BILAG significantly decreased 7.56±6.96 at baseline, 4.37±5.35 at month 3 and 3.94±5.29 at month 6. BILAG index significantly decreased 6.77±7.11 at baseline, 3.67±7.11 at month 3 and 33.35±3.35 at month 6. The dose of concomitant GC also significantly decreased 15.0±22.3 mg/day (PSL equivalent) at baseline, 9.29±14.5 at month 3 and 8.24±14.1 at month 6. In addition, SLEDAI and BILAG were significantly improved in cases during induction therapy with high dose GC, maintenance therapy and HCQ monotherapy. [Conclusions] Our study suggested that HCQ can be started as mainstay in induction therapy, maintenance therapy and monotherapy in SLE treatment with attention to the adverse events immediately after introduction.

W62-3

The 1 year continuation rate of hydroxychloroquine in Japanese SLE patients

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Conflict of interest: None

[Object] Hydroxychloroquine (HCQ) can improve prognosis of SLE patients. Although it is important to continue HCQ, there are not a few patients who stop HCQ due to side effects. We invested 1 year continuation rate of HCQ. [Methods] The subjects were Japanese SLE patients who started HCQ at our hospital between April 1st 2009 and October 31st 2016. The data of continuation of HCQ and severity of side effects were collected retrospectively from the medical records. [Results] Of 125 SLE patients studied, HCQ were stopped in 25 patients (20%). Causes of withdrawal were cutaneous hypersensitivity in 13 patients (10.4%), pigmentation in 2 (1.6%), gastrointestinal symptom in 4 (3.2%), dizziness in 1 (0.8%), headache in 1 (0.8%), eye accommodation disturbance in 1 (0.8%). In 12 patients (9.6%), HCQ was stopped by the reasons other than side effects, and 11 patients (8.8%) dropped out. The continuation rate through 1, 3, 6, 9 and 12 months were 93.5% (102/114),87.6% (87/102),86.7% (80/96),85.8% (76/93),85.8% (76/93), respectively. The median time from HCQ induction to onset of side effects were 2 weeks (0.8-4.0). The continuation rate after resumption was 92.3% (12/13). [Conclusions] Although the continuation rate had decreased through first 3 months, it remained kept above 85% later.

W62-4

Risk factors of latent ocular lesions in patients with SLE who are ineligible for hydroxychloroquine (HCQ) use

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Conflict of interest: None

[Objective] Due to recent approval of HCQ in Japan, introduction of HCQ is often considered for SLE patients with longstanding disease, who potentially have a high risk for HCQ-related retinopathy. This study is aimed to identify risk factors for latent ocular lesions in SLE patients. [Methods] This is a single-center, retrospective study involving 48 patients with SLE who were considered for introduction of HCQ between January 2016 and October 2017. All patients underwent full ophthalmologic evaluation. Demographic and clinical information was obtained by review of medical charts. [Results] Fourteen patients (29.2%) were judged to be ineligible for HCQ use, because of retinopathy (n=8), maculopathy (n=3), and uveitis (n=2). Patients with latent ocular lesions were older (59.6±17.6 vs 40.4±13.2, $p<0.001$) and higher prevalence of diabetes (21.4% vs 0%, $p=0.02$) and had lower eGFR (63.8±19.9 vs 18.2ml^2, $p<0.001$), compared with those without. [Conclusions] Latent ocular involvement is fairly common in SLE patients with long disease duration, especially those with older age, diabetes, and chronic kidney disease.

W62-5

Analysis of withdrawal of hydroxychloroquine due to cutaneous hypersensitivity reaction

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Conflict of interest: None

[Object] Cutaneous hypersensitivities of hydroxychloroquine (HCQ) were reported in domestic clinical trials and post marketing surveillance, and should beware of. We explored risk factors of and clinical problems to them. [Methods] The subjects were Japanese SLE patients who started HCQ between Apr 1, 2009 and Apr 30, 2017 and stopped it due to cutaneous hypersensitivity at our hospital. We also collected and analyzed the data related to HCQ withdrawal from the medical records. We use a dose escalation scheme of HCQ for mild hypersensitivity case with informed consent, starting from 40 mg/day with weekly increments by 40 mg, for patients stopped it due to hypersensitivity. We also organized the result of the scheme. [Results] Of 213 SLE patients studied, Hypersensitivity was seen in 8.9%. Median age was 40 y.o., starting dose 300mg/day, dose/IBW 4.87 mg/kg, BMI 20.8. Anti SS-A antibody was positive in 57.8% and TMP/SMX was used in 22.6%. No patient needed hospitalization or glucocorticoid therapy for hypersensitivity. No relative risk for hypersensitivity was found. Nine patients underwent the scheme and none re-experienced hypersensitivity. [Conclusions] No predicting factor was elucidated. In mild hypersensitivity case, we may use the dose escalation scheme.

W62-6

The safety and effectiveness of hydroxychloroquine for cutaneous involvement in patients with SLE and CLE

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Conflict of interest: None

[Object] We evaluated the safety and effectiveness of hydroxychloroquine (HCQ) for cutaneous involvement of SLE and CLE. [Methods] The skin manifestation was classified into five types; butterfly lush, subacute cutaneous lupus erythematosus (SCLE), discoid lupus erythematosus (DLE), chilblain lupus, lupus erythematosus profundus (LEP), and hair loss. [Results] Thirty-four cases (SLE 28, CLE 6, Female 26 (76 %)), who were continuously treated with HCQ more than 2weeks, were involved in this analysis. Complete or partial improvement was observed in butterfly lush; 4/4 cases, SCLE; 3/4 cases, DLE 12/13 cases chilblain lupus 8/9 cases, LEP 2/3 cases, hair loss 8/10 cases. Skin symptoms in the chronic phase tended to take time to be improved than that in acute phase. In 18 cases of SLE patients, skin improvement was observed in 13 (72%) cases. Within the cases, systemic disease activity of SLE improved in 7 cases but worsened in one case. Side effect was occurred in 5 cases (drug eruption; 4 cases and nausea; 1 case). Discontinuation of HCQ was required in all cases of drug eruption, but we were able to restart HCQ in one case. [Conclusions] HCQ was effective not only for acute skin symptoms, but also for chronic skin symptoms. However, it was ineffective for

some cases of chronic hair loss.

W63-1

Three cases of fasciitis with anti-SRP antibodies: a potential disease manifestation of immune-mediated necrotizing myopathy

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Conflict of interest: None

[Object] To investigate whether fasciitis is histologically demonstrated in anti-SRP antibody-positive patients with immune-mediated necrotizing myopathy (IMNM) or suspected IMNM. [Methods] We performed *en bloc* biopsy and immunohistochemical stains for CD3, CD4, CD8, CD20, CD79a, and CD68 in 3 patients with anti-SRP antibodies in whom high signal intensity was detected in the facsia on STIR MRI. [Results]*En bloc* biopsy specimens showed necrosis, degeneration, or regeneration of muscle fibers, and slight or lack of inflammatory mononuclear cell infiltration around muscle fibers in 3 patients, while fasciitis was detected in 3 patients, and inflammatory mononuclear cells surrounded capillaries in the fascia. In the patient with the most intense inflammatory cell infiltration in the fascia, T cells, clustered CD20-positive B cells and clustered CD79a-positive B cells or plasma cells were detected around capillaries in the fascia. [Conclusions] Immune-mediated necrotizing myopathy (IMNM) is characterized by the lack of inflammatory infiltrates despite the existence of necrosis, degeneration, and regeneration of muscle fibers. However, we found 3 cases of anti-SRP antibody-positive patients with fasciitis. This result suggests that fasciitis is involved in the pathogenesis of IMNM.

W63-2

The clinical characteristics of cancer associated myositis in autoimmune myositis

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Conflict of interest: None

[Introduction] The association between PM/DM and malignancy is well known, and it's also important as a poor prognostic factor line up with interstitial pneumonia. We analyzed patients background, antibody, clinical characteristics, and survival of CAM. [Purpose] We analyzed the patient newly diagnosed as PM/DM/CADM/CAM between Jan 2008 to Sep 2017, retrospectively. [Result] In 134 patients diagnosed as autoimmune myositis, 127 patients whose frozen serum at diagnose was saved were included. 11 patients (9.1%) were diagnosed as CAM. As patients' background of CAM, older age (median 71 vs 49 years, p<0.001), higher serum creatinine (median 0.43 vs 0.55mg/dl, p=0.01), lower serum skeletal muscle enzyme (median 389, 261, 8.5 vs 51, 1398, 22 IU/ml p=0.04, 0.04, 0.01 in LDH, CK, ALD respectively), lower rate of interstitial pneumonia (45.5 vs 80.0%, p=0.01) were identified. Survival was significantly lower in CAM by Kaplan-Meier method (p=0.005). Now we are examining the all patients' profile of myositis related antibody using frozen serum at diagnose. [Discussion] CAM has lower survival compared with those without. Aggressive malignancy survey is needed through all course of treatment, especially in the case of low serum skeletal muscle enzyme and elderly.

W63-3

Evaluation of efficacy in combination therapy with corticosteroid, calcineurin inhibitor and intravenous cyclophosphamide in Myositis-ILD

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Conflict of interest: None

[Object] To investigate efficacy of combination therapy with corticosteroid (CS), calcineurin inhibitor (CNI) and intravenous cyclophosphamide (IVCY) in myositis associated with interstitial lung disease (Myositis-ILD). **[Methods]** 497 adult patients with myositis were enrolled in JAMI cohort, a multicenter retrospective cohort of Japanese patients with Myositis-ILD. We compared survival rate in each treatment regimen group, and between subsets with or without the combination therapy with the three agents using the propensity score matching method. **[Results]** The treatment regimen was classified into four subsets as following: CS alone (n=72), CS+CNI (n=206), CS+IVCY (n=17), CS+CNI+IVCY (n=202). The mortality rate was significantly higher (P <0.0001) in the CS+CNI+IVCY subset. We matched clinical backgrounds of two subsets with or without combination therapy of CS+CNI+IVCY by using propensity score adjusted by age, pulmonary disease activity evaluated by physician, SpO_2/FiO_2, CRP, ferritin, KL-6, SP-D, anti-MDA5. There were no significant (P=0.84) differences of mortality rate between the two subset. **[Conclusions]** Efficacy of combination therapy with CS, CNI and IVCY was not significantly superior to that of the others in Myositis-ILD.

W63-4

Clinical significance of subcutaneous fat and fascial involvement in juvenile dermatomyositis

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Conflict of interest: None

[Objectives] Subcutaneous involvement is more common in juvenile dermatomyositis (JDM) than in adult dermatomyositis (DM). We investigated clinical significance of subcutaneous involvement in JDM. [Methods] Thighs and hips of 18 newly diagnosed JDM patients were evaluated with fat-suppression MRI. Bilateral subcutaneous fat, fascia and muscle were scored from 0 to 8 points by range of disease distribution. Clinical symptoms and serum muscular enzymes were also evaluated. [Results] Abnormal MRI findings in subcutaneous fat and fascia were detected in all patients. Subcutaneous fat score was significantly higher in JDM diagnosed less than 2 months from onset than those diagnosed later (p=0.025). Elevated serum aldolase was observed in all, but only 8 showed elevated serum CK. Serum aldolase was significantly correlated to score of subcutaneous fat (p<0.001, r=0.82) and fascia (p=0.014, r=0.57), but not to that of muscle. Additionally, serum aldolase was significantly correlated to serum triglyceride (p<0.008, r=0.63). [Conclusions] Subcutaneous fat involvement is common in early diagnosed-JDM and also has strong correlation to serum aldolase. Serum aldolase has also correlation to serum triglyceride which may lead to further understanding of pathophysiology of JDM.

W63-5

Clinical characteristics of five cases with anti-TIF1-gamma antibody-positive dermatomyositis

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Conflict of interest: None

Objective: To clarify the clinical characteristics of anti-TIF1-γ (transcriptional intermediary factor 1) antibody- positive dermatomyositis (DM). Methods: Five patients with anti-TIF1-γ antibody-positive DM were enrolled in this study. We retrospectively analyzed the symptoms, complications and laboratory data. Results: The average titer of anti-TIF1-γ antibody was 94 ± 28 (Index, mean±SD). Three cases of them were complicated with malignant tumors; one case was thymic carcinoma, another was lung cancer, and the other was malignant lymphoma. Malignant tumors were found at the time of diagnosis of DM in 2 cases, and 3 years after achieving remission in the other case. Their CK values at diagnosis of DM were bipolarized (3064, 3809, 2979 vs 131, 91 U / I). In the high CK value group, dysphagia was observed in all cases during the course of treatment. Dysphagia improved by rehabilitation in 1 case, and in 2 cases by rehabilitation and high dose intravenous immunoglobulin therapy. Dysphagia did not appear in the low CK value group. Conclusions: In anti-TIF1-γ antibody-positive dermatomyositis, it was suggested that dermatitis appeared first at the beginning of the disease, and that high CK value at the time of diagnosis was associated with the involvement of dysphagia.

W63-6

Clinical Significance of Serum Levels of Anti-TIF1-g Antibody in Patients with Dermatomyositis

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Conflict of interest: None

[Object] Anti-transcriptional intermediary factor 1-γ (TIF1-γ) antibody is frequently detected myositis-specific autoantibodies (MSAs) in adult dermatomyositis (DM) with malignancy. In this study, we analyzed circulating anti-TIF1-γ Ab levels in association with patient's characteristics and disease activity using sequential serum samples. [Methods] We studied 30 Japanese adult DM patients positive for anti-TIF1-γ antibody detected by ELISA. Eighteen patients with anti-TIF1-γ antibody (60.0%) had concomitant malignancy. Sequential serum samples were obtained in 17 patients. [Results] There was no significant difference on anti-TIF1-γ index between patients with and without malignancy. In sequential analysis, anti-TIF1-γ level in patients without malignancy was decreased by more than 30% or turned negative after treatment for DM. However, antibody titer tended to be sustained in patients with malignancy at stage IV. Re-increase of antibody titer was observed at a recurrence of malignancy or increase of DM activity. Three patients had completely succeeded treatments for their malignancy, then anti-TIF1-γ level turned negative as loss of DM activity. [Conclusions] Longitudinal change of anti-TIF1-γ index in individual patients may partially reflect activities both of DM and malignancy.

W64-1

A case of Neurosarcoidosis with parotid bubo which we diagnosed Heerfordt syndrome: a case report

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Conflict of interest: None

A 74-year-old male had lower limb paralysis in X-4 and was suspected to had spinal cord infarction. In X-1, another doctor conducted a skin biopsy and established noncaseating epithelioid granuloma with lymph cell infiltration, which did not meet the diagnostic criteria of sarcoidosis. He visited our hospital with fever, aggravation of erythema, and right arm pain in X. Uveitis was observed. T-SPOT, ACE, and lysozyme were negative. A biopsy of the skin provided similar results. Ga-scintigraphy revealed apparent accumulation on the parotid gland and submaxillary glands. We diagnosed him neurosarcoidosis/incomplete Heerfordt syndrome, and administered 40 mg/day PSL. Right arm pain and fever disappeared immediately after PSL administration. We considered spinal cord infarction and right arm pain were due to neurosarcoidosis. After reducing the PSL dosage to 30 mg/day, he was discharged. The PSL dosage reduced to 18 mg/day currently. Heerfordt syndrome is a rare subtype of sarcoidosis with uveitis, parotid bubo, and facial nerve palsy. In our case, he was diagnosed spinal cord infarction first, but progress revealed it was neurosarcoidosis and he developed Heerfordt syndrome. A case of neurosarcoidosis with Heerfordt syndrome is rare and precious, so we here report this case.

W64-2

A very severe and refractory case of TAFRO syndrome treated with Tocilizumab and Tacrolimus adding to glucocorticoids

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Conflict of interest: None

A 53-year-old man developed fever, fatigue, anasarca, bilateral pleural effusion, ascites, severe thrombocytopenia, anemia, and renal failure. Examinations of infections and cancers were negative. Diagnosis of TAFRO syndrome was made according to the 2015 diagnostic criteria despite negativity of bone marrow biopsy. We administered methyl-prednisolone pulse therapy, high-dose glucocorticoids and cyclosporin A (CsA), however they were ineffective. Renal function worsened and hemodialysis has been administered. After administration of tocilizumab (TCZ) weekly, CRP has decreased. Due to a complication of sepsis, TCZ was discontinued. CsA was discontinued due to no effect. Then he had gradual improvement in renal function. Fever and elevation of CRP appeared, therefore we added tacrolimus (TAC) resulting in improvements of them and thrombocytopenia. The 2015 treatment strategy for TAFRO syndrome suggests CsA and TCZ if it is refractory to glucocorticoids. In this case glucocorticoids and CsA were ineffective, but adding TCZ and TAC was effective. To our knowledge, this is the first case report of TAFRO syndrome administered TAC. And the reports of very severe cases treated successfully are very rare. We suggest the possibility of efficacy of TAC for refractory TAFRO syndrome.

W64-3

A novel therapeutic modality targeting IL-26 for autoimmune and chronic inflammatory diseases

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Conflict of interest: None

[Object] Although IL-26, known as the Th17 cytokine, is upregulated in various immune disorders including RA, the pathophysiologic role of IL-26 in the inflammatory diseases still remains to be elucidated. We recently showed that IL-26 mediates multiorgan fibrosis, and the objective in this study was to characterize the precise mechanisms of IL-26 in chronic inflammation. [Method] Human keratinocytes and HUVEC were analyzed with exogenous IL-26. For *in vivo* experiments, we utilized an imiquimod (IMQ)-induced psoriasis model in human *IL26* transgenic (h*IL26*Tg) mice. [Results] *In vitro* IL-26 stimulation induced a high level of FGF2 in human keratinocytes and HUVEC. Moreover, cell proliferation and tube formation of HUVEC were significantly increased with exogenous IL-26. IMQ-induced vascularization was significantly increased in h*IL26*Tg mice. Expression levels of FGF in inflammatory skin lesions were significantly upregulated in IMQ-treated h*IL26*Tg. Skin vascularization and inflammation in IMQ-treated h*IL26*Tg were clearly suppressed with administration of anti-IL-26 mAb. [Conclusion] Our data strongly suggest that anti-IL26 mAb may have potential clinical use as a novel therapeutic agent for autoimmune diseases, manifested with chronic inflammation and multiorgan fibrosis.

W64-4

Clinical study for 20 cases of SAPHO syndrome

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Conflict of interest: None

Background: SAPHO syndrome is a rare disease in Japan, which has spondyloarthritis (SpA)-like symptoms but is not classified as SpA. The treatment for SAPHO syndrome is not standardized, and biomarkers of the disease are limited. **Objectives:** To assess the clinical and laboratory features of SAPHO syndrome. **Methods:** We examined the HLA alleles: measured the levels of serum IL-6, TNFαreceptor, and IL-17: and assessed the clinical features, laboratory findings, and therapeutic agents in 20 patients clinically diagnosed with SAPHO syndrome. **Results:** Mean age of the patients was 59 years (10 males and 10 females). Smoking rate was 80%. The cutaneous manifestations were palmoplantar pustulosis in 7 cases, and articular involvements were anterior chest wall involvement in 16 cases, and peripheral arthritis in 4 cases. HLA-B39 and B61 were the most frequently detected. HLA-B27 was not detected in any of the cases. Serum TNFαreceptor and IL-6 levels were increased in 5 cases, whereas IL-17 level was increased in almost patients in the pretreatment. Serum IL-6, TNFαreceptor, and IL-17 levels were decreased after treatments. **Conclusion:** SAPHO syndrome involves at least two molecular axes: the TNF/IL-6 axis, and the IL-17 axis.

W64-5

Clinical Implications of Ultrasonography (US) in Monitoring Disease Activity of Relapsing Polychondritis (RP) and Comparative Investigation by US between Auricle of RP, Repeated Trauma and Healthy Subject

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Conflict of interest: None

[Object] To assess the clinical implications of ultrasonography (US) in monitoring disease activity and diagnosis of relapsing polychondritis (RP). [Methods] Firstly, auricular chondritis of patients with RP (n=5) were assessed by US before and after treatments. The relationship between US findings and serum markers were evaluated. Moreover, the comparisons of US findings between the auricle of patients with RP (n=5), repeated trauma (n=5) and healthy subjects (n=5) were also assessed. [Results] US finding before treatment showed low-echoic swollen auricular cartilage with increased power Doppler signals (PDS) in all cases of RP. US findings corresponded to biopsy findings. After treatment, the swollen ear completely resolved. Then, US findings also showed dramatic reductions in swollen cartilage with the decrease in PDS. When serum markers completely improved, but US finding remained in 1 of 5 cases, and this case showed flare due to PSL tapering. Finally, RP could be differentiated from the damage of repeated trauma with producing subperichondrial serous effusion. [Conclusions] US of auricular cartilage in RP possibly facilitates evaluation of auricular lesions and monitoring of disease activity, especially when we consider the treatment response and the timing of drug tapering.

W64-6

The usefulness of Adult-Onset Still's Disease severity classification criteria in daily clinical practice

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Conflict of interest: None

[Object] We aimed to clarify the correlation between the severity classification criteria used to apply the intractable disease support system in Japan and disease activity, and treatment in AOSD. [Methods] (1) We selected the cases with AOSD treated at our hospital from 2007 to 2017. We evaluated disease severity score based on the AOSD severity classification criteria and classified them into mild and moderate, or severe groups. (2) We compared the score with disease activity markers of AOSD. (3) We compared therapeutic approach among three groups. [Results] (1) Twenty-six cases with AOSD and were selected and classified into mild (5), moderate (8), and severe group (13), respectively. (2) There were positive correlation between severity score and ferritin, or CRP (p=0.0644, p=0.0988). (3) Steroid pulse therapy tended to be applied to severe group (p=0.1152). More cases were applied combined use of immune suppressants in severe group than the cases in mild or moderate groups. (p=0.0036). [Conclusions] Our results suggested that severity classification criteria was useful to evaluate the severity of the disease and to decide the therapeutic strategy for AOSD in daily clinical practice.

W65-1

Analysis of the efficacy of the multidrug combination therapy for rapid progressive interstitial pneumonia with anti-MDA5 antibody-positive dermatomyositis resistant to prednisolone, calcineurin inhibitor and cyclophosphamide

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Conflict of interest: None

[Object] To evaluate the efficacy of the combination therapy with mycophenolate mofetil (MMF), rituximab (RTX) and therapeutic apheresis therapy added to PSL, CNI and IVCY for rapid progressive interstitial pneumonia with anti-MDA5 antibody-positive dermatomyositis (DM-RPIP) with several prognostic factors. [Methods] We assessed the efficacy of the multidrug combination therapy for DM-RPIP, and compared multidrug group (Group A, n=14) to previous therapy group (Group B, N=9). [Results] The median of age, gender ratio were 59 years old, 58.3% respectively. The median of pretreatment level of serum ferritin and AaDO2 were 1005ng/dl and 42.1torr. There were no significant difference in age, ferritin and AaDo2 between group A and B. In group A, all cases were used PSL, CNI, IVCY, eleven cases were MMF, nine were RTX, six were intravenous immunoglobulin (IVIgG), and nine were therapeutic apheresis therapy. In Group B, PSL and CNI were used in all cases, MMF was in 1 case, RTX 1 case, IVIgG 6 cases, and therapeutic apheresis 1case. Survival time (Median) and survival ratio in group A were 102 days, 64.3%, in Group B were 199 days, 33.3%. [Conclusions] The multidrug combination therapy for DM-RPIP may be effective, but we must observe their clinical course carefully.

W65-2

Effect and safety of combination therapy with tofacitinib on amti-MDA5 positive interstitial lung disease in dermatomyositis

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Conflict of interest: None

[Object] The aim of this study was to evaluate efficacy and safety of tofacitimab (TOF), a multiple cytokine blockade, on refractory anti-MDA5 Ab + ILD in DM. [Methods] Based on data of 15 patients with anti-MDA5 Ab + ILD who were treated with intensive immunosuppressive therapy; the triple therapy combination of glucocorticoid, CsA and IVCY, we identified poor prognostic factors. We added TOF on the patients who were resistant to triple therapy and predicted to have poor prognosis under the approval of the ethic committee. [Results] We identified poor prognostic factos;1) serum ferritin level >1000 g/ml, 2) GGO/consolida-

tion in all 6 lung fields, 3) newly emerging GGO after triple therapy. Under the triple therapy, all patients (6/6) who satisfied all 3 conditions died from respiratory failure. In contast, additional TOF saved 3 of 5 patients with all 3 conditions (p=0.02 log rank). As adverse effects, all patients showed CMV reactivation, 3/3 of the survivor suffered to Herpes zoster, 1 had adenoviral cystitis and EBV related lymphoproliferative disease. Due to AE, 3 survivors were forced to reduce the intensity of the therapy, but remained well. [Conclusions] The combination therapy, including TOF is suggested to be an effective treatment for refractory anti-MDA5 Ab+ ILD.

W65-3

Selective plasma exchange for rapid progressive interstitial pneumonia of clinically amyopathic dermatomyositis with anti MDA-5 antibody

Maki Kagitani[1], Shogo Matsuda[2], Youhei Fujiki[2], Kenichiro Hata[2], Takuya Kotani[2], Tohru Takeuchi[2], Shigeki Makino[2], Shigeki Arawaka[2]
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Conflict of interest: None

[Background] Interstitial pneumonia (IP) of clincally amyopathic dermatomyositis (CADM) with anti MDA-5 antibody typically shows rapid protress and high mortality. Selective plasma exchange (SePE) is a useful modality which can be used without fresh frozen plasma and high concentration of albumin solution. We report our 3 cases of CADM-IP, showing the effectiveness of SePE. [Cases] The average age was 59.6years. The average ferritin titer was 2223U/mL, from which high mortality is concerned. All cases were given several immunosuppressive therapies. In SePE, the serum albumin concentrate diluted by Ringer's lactate (Dilution Factor was 0.75) was used. Each patient was given 20% more diluted solution than the estimated amount of plasma. After SePE, anti MDA-5 titer decreased in all three cases. A-aDO2 and P/F ratio were either unchanged or improved. All cases were recovered from critical situation, and have been alive. In terms of side effects, one patient showed hypocalcemia after the 1st session, which was addressed immediately by giving calcium injection. Another petient indicated the blood access catheter infection, which was cured by antibiotics without developing critical stuation. [Conclusions] SePE is effective in controlling CADM-IP with anti MDA-5 antibody.

W65-4

The countermeasures for opportunistic infections on intensive immunosuppressive therapy for Anti-MDA5 ab-positive dermatomyositis associated ILD

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Conflict of interest: None

[Object] Early induction of intensive immunosuppressive therapy including corticosteroids, calcineurin inhibitor and intravenous cyclophosphamide (IVCY) has been reported to be improved poor prognosis. However, intensive immunosuppressive therapy might frequently cause opportunistic infections including cytomegalovirus (CMV) infection and pneumocystis jirovecii pneumonia (PCP) due to host's diminished immune function. [Methods] We analyzed 10 patients with Anti-MDA5 ab-positive dermatomyositis associated ILD between 2014 and 2017 in our hospital. [Results] All patients were received intensive immunosuppressive therapy. Four of ten patients were died of respiratory failure due to ILD or PCP. IVCY was given within 9 days after initiation of steroid therapy. Improvement of levels of serum ferritin and titers for anti-MDA5 ab was observed in 6 survivors. Respiratory function test was also improved. CMV antigenemia admitted to a high rate, nine of 10 patients after 40.2days immunosuppressive therapy initiation. IVCY was given 2.4 back in average. Nine patients were all treated with anti-virus agents and organ complication was prevented. Two patients died of respiratory failure due to PCP. Prophylactic treatment with SMX-TMP was not used in two cases because of adverse events.

W65-5

Association between myositis-specific autoantibodies and clinical features in dermatomyositis

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Conflict of interest: None

[Object] Measurement of myositis-specific autoantibodies including anti-ARS ab, anti-MDA-5 ab and anti-TIF1 gammaab is useful to predict clinical courses and prognosis and determine therapeutic strategy for dermatomyositis. However, understanding the clinical features is still important to predict which myositis-specific antibodies are present. [Methods] We analyzed myositis-specific autoantibodies -positive 13 patients with dermatomyositis as follows: anti-ARS ab 4, anti MDA-5 ab 7, anti TIF-1gamma ab 2. Clinical features and organ complications were examined. [Results] Whereas mechanic's hands are known to be observed in anti-ARS ab-positive patients, anti-MDA5 ab positive patients frequently developed. Inverse Gottron's signs and mucosal skin ulcer were specific clinical findings to anti MDA5 ab-positive patients. Broad erythema on the body trunk was observed in anti-TIF1 gamma ab-positive patients. Complication of Interstitial lung disease was observed in all anti-ARS ab and anti-MDA-5 ab positive patients, but not in anti-TIF1 gamma positive cases. [Conclusions] Recognizing clinical features including skin manifestations is useful to predict which myositis specific autoantibodies are involved in patients with dermatomyositis.

W65-6

Evaluation of the efficacy of the combination therapy with mycophenolate mofetil and rituximab added to prednisolone, cyclosporine and cyclopjosphamide for rapid progressive interstitial pneumonia with anti-MDA5 antibody-positive dermatomyositis in 8 cases

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Conflict of interest: None

[Object] We evaluated the efficacy of the combination therapy with mycophenolate mofetil (MMF) and rituximab (RTX) added to PSL, CyA and IVCY in rapid progressive interstitial pneumonia with anti-MDA5 antibody-positive dermatomyositis (DM-RPIP) with several prognostic factors [Methods] We assessed the efficacy of the therapy with above-stated five immunosuppressants in 8 cases. [Results] The median of age, gender ratio (female) were 59 years old, 75%. The median of pretreatment level of ferritin and AaDO2 were 1225ng/ml and 41.8 torr. All the cases were treated with PSL, CyA, CY, MMF and RTX. Four cases were used intravenous immunoglobulin and 6 cases were therapeutic apheresis therapy. The median of dose of the five immunosuppressants were PSL 55mg, CyA 225mg, CY 5500mg (total dose), MMF 1500mg, RTX 375mg/m^2×4 times, respectively. The median of survival time was 199 days. Six cases were alive and 2 cases died from interstitial pneumonia (survival time: 6 days, 22days respectively). Liver damage was shown in 2 cases. Six cases were presented cytomegalovirus infection, 2 cases were fungal infection. [Conclusions] The combination therapy of 5 immunosuppressants may improve the prognosis of DM-PRIP, but we must observe their clinical course carefully.

W66-1

Epidemiological features of Japanese patients with juvenile idiopathic arthritis - Findings of treatment disease activity index throughout the disease course from nationwide survey for the core facilities specialized in pediatric rheumatism -

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Conflict of interest: None

[Object] We conducted a large-scale survey of treatment and disease activity index for juvenile idiopathic arthritis (JIA) in Japan. [Methods] This first nation-wide epidemiological research on JIA was organised by the study group of Ministry of Health, Labour and Welfare. We used the case cards on patients who regularly visit the core facilities specialized in pediatric rheumatism at January 2017. The evaluation data included past and current administration of treatment, blood exam results, JADAS-27, JADAS-71, CHAQ-DI and Poznanski score. [Results] The data of 726 JIA patients from 15 core facilities were evaluated. Nonsteroidal anti-inflammatory drugs and methotrexate were used in 80.7% and 78.2% (average 7.3mg/m2) of patients. Glucocorticoid was ever been administered in 61.0% of patients and is still used in 23.6% of them. Tocilizumab, adalimumab, and etanercept were administered to 297, 124, and 81 patients, respectively. Patients whose Poznanski score worsened during the course of treatment were 62.3% of patients in rheumatoid factor positive arthritis and 43.3% of patients in other types. [Conclusions] The course of treatment for JIA in Japan was revealed.

W66-2

Evaluation of efficacy and safety of canakinumab in patients with systemic juvenile idiopathic arthritis in Phase III clinical trial in Japan

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Conflict of interest: None

[Objectives] A Phase III clinical trial in Japan evaluated efficacy and safety of canakinumab (CAN), a human anti-interleukin-1β monoclonal antibody, in Japanese patient (pt) s with systemic juvenile idiopathic arthritis (sJIA). Here, we report the results of a 28-week (Wk) interim analysis. **[Methods]** Patients received open-labelled CAN 4mg/kg (max 300mg) every 4Wks (q4w) subcutaneously (s.c.). The primary objective was to evaluate the proportion of pts who achieved adapted ACR Pediatric 30 (aACR Pedi30) criteria at Wk8 and who succeeded corticosteroid tapering at Wk28. Pts were allowed to reduce their steroid dose from Wk8. **[Results]** Of the 19 pts that received CAN, 3 discontinued the treatment due to lack of efficacy or adverse event (AE) s by Wk28 and 16 completed the assessment of Wk28. All pts (19/19) achieved aACR Pedi30 at Wk8. 73.7% (14/19) pts achieved corticosteroid tapering at Wk28. Each pt experienced at least one AE. The most frequent AE was nasopharyngitis (26.3%, 5/19). Serious AE (SAE) s were seen in 41.1% (8/19) pts, and the most frequent SAE was JIA (Flare or worsening of sJIA, 21.1%, 4/19). No death was reported. **[Conclusion]** CAN 4 mg/kg q4w s.c. in sJIA pts improved disease activity and a reduction of oral steroid dose was possible in 73.7%. No new safety concerns were reported.

W66-3

Evaluation of disease activity and prediction of disease course using fluorodeoxyglucose positron emission tomography in children with systemic juvenile idiopathic arthritis

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Conflict of interest: None

[Object] To evaluate the efficacy of fluorodeoxyglucose positron emission tomography (FDG-PET) in children with systemic idiopathic juvenile arthritis (s-JIA). [Methods] FDG-PET images from children with newly diagnosed s-JIA were retrospectively reviewed. Accumulations of FDG in the organs were correlated with laboratory findings and magnetic resonance imaging (MRI) findings. The prognosis of the disease was correlated with the FDG-PET findings. [Results] Twenty-nine FDG-PET scans from children with s-JIA were reviewed. Accumulation of FDG was high in the large joints, liver, bone marrow, and spleen. The number of PET-positive large joints showed a positive correlation with serum matrix metalloproteinase-3 levels. Comparison of the MRI and FDG-PET findings for the affected large joints showed that positive FDG-PET accumulations were significantly more frequent when thickened synovium was detected by MRI. The number of PET-positive large joints was greater in patients showing recurrence of s-JIA after treatment. At the cut-off threshold of 4 PET-positive joints, FDG-PET uptake was predictive of recurrent arthritis with 90.9% sensitivity and 80.0% specificity. [Conclusions] FDG-PET findings appear to be a suitable biomarker to evaluate disease activity in patients with s-JIA.

W66-4

Evaluation of chest Xray findings in patients with adult articular juvenile idiopathis arthritis

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Conflict of interest: None

Background and Objectives; Lung involvements in Rheumatoid arthritis (RA) accounts for 19 to 33% of all whereas its prevalence in Juvenile idiopathic arthritis (JIA) is quite low as 4 to 8%. Findings of chest X-ray in adult articular JIA patients were evaluated. **Methods:** Adult articular JIA patients who visited our institute from April to September 2017 and the latest chest X-ray taken over the age of 20 were enrolled in this study. Chest X-ray findings read by two physicians independently and clinical information were evaluated. The findings were classified into following: 1. Infiltration, 2. Linear/streak opacity, 3. Nodular shadow, 4. Cavity formation, 5. Reticular pattern, 6. Granular shadow, and 7. Others. **Results:** Of all 49 individuals (Male:Female, 12: 37, age 20-86, median 28.5 years of age, disease duration: 1-15, median 20 years, RF positive: 34 cases (69.3%)). Abnormality was detected in 15 (30%) patients. RF was positive in 13 out of the 15 patients (86.7%). Clinically no patients manifested continuous respiratory symptoms. **Conclusions:** Abnormality of chest X-ray was detected in 30 % of adult articular JIA patients, however, there was no clinically severe case. Lung CT findings will be evaluated as propensity score matched control study with RA in the next step.

W66-5

Timing of intravenous cyclophosphamide and long-term outcome in children with juvenile systemic lupus erythematosus

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Conflict of interest: None

[Object] To investigate whether timing of intravenous cyclophosphamide (IVCY) as induction therapy influences long-term outcome in juvenile systemic lupus erythematosus (jSLE) [Methods] Totally, 34 patients were enrolled. We divided them into IVCY at onset (n=22) and IVCY at flare (n=12). We retrospectively investigated baseline characteristics, dose of prednisolone (PSL), SLEDAI, complement, and anti-dsDNA antibody at the last observation and the flare. The flare was defined as increasing dose of steroids and changing or adding immunosuppressants for clinical and/or serological findings. [Results] There were no significant differences in clinical characteristics and the number of the flare between two groups. Meanwhile, 24 patients with mycophenolate mofetil (MMF) as maintenance therapy after IVCY showed significantly longer flare-free period than 10 patients without MMF (median: 56.0 vs 21.5 months, p=0.0157). In only class III and VI LN, 19 patients with MMF as maintenance therapy after IVCY had relatively longer flare-free period than 5 patients without MMF (median: 56 vs 34 months, p=0.0512). [Conclusions] Timing of IVCY didn't influence disease activity at the last observation. MMF as maintenance therapy after IVCY significantly influenced flare-free period.

W66-6

Effect of intravenous immunoglobulin treatment as remission induction therapy for anti-TIF1-g autoantibody positive juvenile dermatomyositis

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Conflict of interest: None

[Object] To evaluate the effect of intravenous immunoglobulin (IVIG) for remission of anti-TIF1-γ-autoantibody (aTIF1γ-ab) positive juvenile dermatomyositis (JDM). [Methods] JDM patients with aTIF1γ-ab who had received IVIG as remission induction therapy were retrospectively assessed. [Results] Six children were enrolled. The age at onset was 3.0 (1.3-4.8) years (median (quartile)). All patients received IVIG at recurrence. At initial treatment with IVIG, the dosage of prednisolone was 0.2 ± 0.13mg/kg/day (mean ± SD). Immunosuppressant was concomitantly used in all patients; methotrexate was used for five patients and azathioprine for one patient. Regarding the symptoms before IVIG treatment, two patients had muscle symptoms, four had elevation of myogenic enzyme and all six had cutaneous symptoms. After IVIG treatment, the muscle symptoms initially disappeared in two patients but reappeared in one after four months. Elevation of myogenic enzyme improved in four patients but was elevated again in one. Skin symptoms improved in five patients, but not in one. Of these five, cutaneous manifestation worsened in two patients after 3 and 4 months, respectively. [Conclusions] IVIG treatment as remission induction therapy for aTIF1γ-ab positive JDM might be useful before steroid treatment.

W67-1

Pachydermoperiostosis primary hypertrophic osteoarthropathy with sever arthralgia identified by gene mutation of SLCO2A1

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Conflict of interest: None

Male, 41 years old (yo) had been complaining severe arthralgia. Past History indicated obstruction of intestinal tract at 12 yo and gastric ulcer at 13 yo. He had been suffered from general arthralgia especially at PIP and MP joints of both hands from 38 yo. Finally he complained severe arthralgia at PIP and MP joints with clubbed fingers. Biochemical finding indicated negative rheumatoid factor and anti-CCP antibody and normal MMP-3 level, but slightly increased CRP and ESR levels. Radiological finding indicated periostosis of long bone without bone erosion and osteoporosis. His facial appearance was acromegalic with cutaneous manifestation of pachydermia and cutis verticis gyrate without abnormal growth hormone response. Histological findings of skin indicated edema and hyperplasia of collagenous fiber with infiltration of lymphocytes around small blood bessels compatible with pachydermoperiostosis. In this case mutation of SLCO2A1 gene, which coded prostaglandin transport protein, has been identified. The mutation of SLCO2A1 gene (c.940+1G>A) was located in intron 7 which results in the loss of exon 7 and truncation of PG transporter (p.Arg288Glyfs*7). We suggest that sever arthralgia was originated from over production of prostaglandin E2. Further studies will be required.

W67-2

The effect of the intensified RA treatment on sleeping condition

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Conflict of interest: None

[Background] It was reported that sleep latency and nocturnal awakening were longer in RA patients compared to the general population. [Object] The aim of this study was to examine the effect of the intensified RA treatment on sleeping condition in RA patients. [Methods] We examined 19 RA patients (4 men and 15 women), 64 years of age. Sleep condition was assessed by electroencephalograph and inflammation activities of RA were determined by DAS 28 (CRP) before and after intensified RA treatment. [Results] The mean of DAS 28 (CRP) levels was significantly improved from 5.0 ± 1.4 to 3.3 ± 1.4. The mean of CRP levels before treatment showed a significant positive correlation with the time of Non-rapid eye movement sleep stage N1 ($p = 0.01$) and negative correlation with stage N2 ($p = 0.02$). Although the total sleep time, sleep latency and nocturnal awakening had no significant change, the time of N1 was shorter and N2 was longer before and after intensified RA treatment. [Discussion & Conclusions] As the levels of serum inflammatory cytokines rise during nighttime and early morning, the symptoms of RA exacerbates during the same period. This study suggested sleep quality, but not sleep quantity, was improved due to reducing in RA disease activity by the intensified RA treatment.

W67-3

Distal interphalangeal (DIP) joint involvement and its significance in rheumatoid arthritis (RA) - Analysis based on NinJa 2016 database

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Conflict of interest: None

[Object] DIP involvement, which can be seen in RA, is typical of OA and PsA. DIP joint is thus excluded from the evaluable joints in RA criteria. The aim of the present study is to examine DIP involvement in RA using *NinJa* 2016. [Methods] We used the data of adult-onset RA patients registered in *NinJa* 2016 with information regarding the affected joint distribution available (n=12413). [Results] The prevalence of DIP involvement (tenderness or swelling in the 2nd to 4th DIP) was 2.03% in RA patients as a whole, and 1.78% in those younger than 40. The DIP involvement, which was not related to age, age at onset, duration, stage, class, mHAQ, RF, or ACPA, was significantly more frequent in women. Furthermore, pain, TJC, SJC, and DAS28 were significantly higher in RA patients with DIP involvement than those without it. The number of affected IP joints was significantly correlated with TJC, SJC, and DAS28, albeit weakly. [Conclusions] We demonstrated that DIP involvement was significantly related to high disease activity in RA, albeit infrequently. The limitations of the present study included lack of Xp findings regarding bone proliferation and information about the complication of OA and PsA. However, we consider that it is necessary to pay attention to DIP involvement in active RA.

W67-4

Reconsideration of PSL dose which necessitates perioperative glucocorticoid supplementation

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Conflict of interest: None

[Object] Exogenous glucocorticoid (GC) results in the need for perioperative GC supplementation according to the dose and duration of GC. It is believed that morning dose of less than 5 mg of PSL does not necessitate GC supplementation. However, we are not sure whether this theory fits in small Japanese patients. [Methods] We retrospectively analyzed morning serum cortisol data obtained from our patients receiving a fixed dose of PSL for more than three months, during five years between August 2012 and August 2017. Multiple regression analysis was calculated to predict morning cortisol from age, body weight, PSL dose, and PSL duration. We used ROC curve to choose the optimal cut off point of PSL dose. [Results] 50 patients were enrolled, 13 were men and 37 were women. The average age and body weight were 69 ± 15, and 55 ± 11, respectively. The median PSL dose was 7.1 mg/day [0.5 - 25]. In multiple regression analysis, only PSL dose was statistically significant ($p = 0.034$). The optimal cut-off point was PSL 5 mg/day by ROC analysis. However, there were five patients whose morning cortisol were below 5 μg/dL, although they were taking less than 5 mg of PSL. [Conclusions] Some patients receiving less than 5 mg of PSL might need GC supplementation.

W67-5

Low blood hemoglobin concentrations and treatment response in patients with polymyalgia rheumatica

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Conflict of interest: None

[Object] To study low blood hemoglobin concentrations (Hb) and treatment response in patients with polymyalgia rheumatica (PMR). [Methods] Patients were included retrospectively in this study who had attended the clinic since December, 2013 for more than 6 months and fulfilled the two criteria by Birds and by Jones. Blood Hb at baseline and follow-up were determined, and the correlation between baseline blood Hb and serum C-reactive protein (CRP) was evaluated. [Results] Total of 21 patients (male 15, female 6, Age 71, CRP 4.6 mg/dL, ESR 81mm/h) were evaluated. Baseline blood Hb was 13.0 g/dL and 11.5 g/dL in male and female patients, respectively. Improvement of blood Hb was significant between baseline and each follow-up at 1 month, 3 months and 6 months. There was a negative correlation between blood Hb and CRP at baseline significantly. [Conclusions] Blood low Hb was improved by the treatment in patients with PMR, and found to be correlated with CRP. Further investigations shall be needed in patients with no improvement.

W67-6

Research on using impression of wrist mounted disposable heat pack on patients with Raynaud's phenomenon associated with connective tissue diseases

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Conflict of interest: None

[Object] To assess influences of wrist mounted disposable heat pack on Raynaud's phenomenon in patients with connective tissue diseases. [Methods] 19 outpatients with Raynaud's phenomenon associated with connective tissue diseases (SS 9, SSc 7, MCTD 4, SLE 1) were enrolled. Wrist mounted disposable heat pack (Makipoka; Kiribai, Osaka, Japan) was used in the winter of 2015 and/or 2016, and usage conditions and changes of subjective symptoms regarding Raynaud's phenomenon were investigated by a questionnaire. [Results] 17 patients (89.5%) did not know the wrist mounted disposable heat pack. The heat pack was used mainly for five to six hours a day (9 patients; 47.4%), and when going out (13 patients; 68.4%). 17 (89.5%) of the patients answered that feeling in use of the heat pack was good or very good. Questionnaire revealed an improvement of Raynaud's phenomenon in 14 patients (73.7%). No serious adverse event was found. 16 patients (84.2%) wished to continue using the wrist mounted heat pack. [Conclusions] Wrist mounted heat pack is a useful tool in the management of Raynaud's phenomenon in connective tissue diseases.

W68-1

Management of pregnancy in patients with rheumatoid arthritis (RA), systemic lupus erythematousus (SLE) and Sjogren's syndrome (SjS)

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Conflict of interest: None

[Object] Pregnancy management in RA, SLE and SjS patients was studied in order to elucidate the factors associated with pregnancy outcome. [Methods] RA, SLE, SjS were subjected for the study. Pregnancy was planned in 78 cases (31.2±6.3y/o) (RA (27.6±5.6y/o), 43 of SLE (32.2±6.0y/o), 19 of SjS (31.7±6.8y/o)). Patient information was retrospectively collected and analyzed. [Results] 44 cases (57%, RA 12, SLE 23, SjS 9) become pregnant and 25 cases out of 44 (57%, RA 11, SLE 10, SjS 9) gave normal birth. 7 miscarriages, 6 artificial abortions, 2 neonatal death and no malformation were noted. In SLE, SLEDAI of abnormal delivery group (ADG) (2.85±2.93) was higher compared to that of normal delivery group (NDG) (1.75±2.36). In SjS, ESSDAI of ADG (2.50±5.73) was higher compared to that of NDG (1.75±2.36). Prednisolone was used in 60% (8.0±4.5mg), tacrolimus 14%, mycophenolate mofetil 9%, biologics 8%, and methotrexate 5%. Glucocorticoid dosage was increased in those patients who showed disease flare. There were no patients who continued immunosuppressive agents or biologics during the pregnancy. [Conclusions] These findings suggest that disease activity has significant influence on pregnancy outcome in SLE, RA and SjS. Strict control of disease activity is necessary in these patients.

W68-2

Influence on pregnancy and delivery complicated with rheumatoid arthritis treated by biologics

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Conflict of interest: None

[Objective] We examine the influence of biologics (bDMARDs) on pregnancy and delivery complicated with rheumatoid arthritis (RA). [Method] We investigated 18 cases (11cases which had continued bDMARDs until getting pregnant; group A, 7 cases which discontinued both bDMARDs and conventional synthetic DMARDs; group B) retrospectively on periods to get pregnant and disease activities and perinatal complications. [Result] The average period to getting pregnant was 6.09 months in group A, which was shorter than 13.28 months in group B ($P=0.1015$). Disease activities at the time of planning and getting pregnancy was no significant difference between two groups. The average birth weight of the babies in group A was significantly smaller than group B ($P=0.039$). However, there was no significant difference on the rate of preterm birth, LFD (light for date), premature rupture of membrane and apgar score of the babies. In the cases of LFD babies, the average dose of corticosteroid was significantly more. [Conclusion] Previous reports revealed that it was difficult for RA patients to get pregnant. RA patients who hope pregnancy should continue bDMARDs until getting pregnant. Using biologics before pregnancy does not influence perinatal complications and development of babies.

W68-3

Analysis of risk factors for perinatal complications in 46 cases of pregnancy complicated with SLE

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Conflict of interest: None

[Objective] We examine the risk factor of perinatal complication in the cases of SLE patients. [Method] We investigated the risk factors of abortion, preterm birth, LFD (light for dates), premature rupture of membrane and apgar score in 46 pregnant cases. [Result] In the case of preterm birth, the rate of increasing corticosteroid and corticosteroid pulse therapy associated with the exacerbation of underlying disease was high significantly, and the titer of anti double stranded-DNA antibody was also high. In the case of LFD, the complement was low. In the premature rupture of membrane, there were no significant differences in any factors. Anti double stranded-DNA antibody was extracted as the risk factor for apgar score, but complements were not extracted. [Conclusion] In pregnancy complicated with SLE, we extracted the immunologic activity and increasing corticosteroid accompanied with the exacerbation of disease as the risk factors preterm birth and LFD. Apgar score which was associated with growth and development of babies was related with anti double stranded-DNA antibody significantly. Therefore, it may lead to decrease the risk for both mothers and babies to control the disease activity strictly before pregnancy and maintain immunologic stability.

W68-4

Clinical features in secondary thrombotic microangiopathy associated with connective tissue diseases

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Conflict of interest: None

[Object] Secondary thrombotic microangiopathy (TMA) associated with connective tissue disease is a lethal refractory condition, which no definite treatment. We considered the factors affected prognosis. [Methods] Thirteen patients with secondary TMA treated in our department during 2010 to 2017 were examined for data, treatment and outcome. [Results] Median age was 64 years (2 males, 11 females). The underlying disease was 1 SLE, 8 scleroderma, 2 polymyositis and 2 overlap. Average systolic blood pressure was 170.5 mmHg at onset. Eleven patients underwent PE with median 3 times, and all patients Plt counts achieved more than 150 x 10^3/μL at median 6.5 days. In 12 cases of AKI, the median onset serum Cre was 1.29 mg/dl, and 4 patients needed maintenance dialysis, 11 cases (85%) survived and discharged. However, in the 152 days observation period, 7 cases (include all dialysis patients) died. The cause of death was each one case of pneumonia, alveolar bleeding, pancreatitis, acute circulatory failure, fat embolism, aortic dissection. [Conclusions] Renal death was also poor at survival rate (P = 0.03). Although survival discharge could be expected, death cases were mostly within one year. PE may be desirable to introduce at the early stage, but the effectiveness is unclear.

W68-5

A Clinical Study of Hypertrophic Pachymeningitis Experienced In Our Hospital

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Conflict of interest: None

[Object] Although hypertrophic pachymeningitis (HP) is a relatively rare disease, the number of cases regarding autoimmune disease related HP have increased. Therefore, the relationship between HP and autoimmune disease was examined. [Methods] Twelve cases of HP diagnosed and treated in our hospital over the past 15 years were analyzed. The clinical symptoms, underlying diseases, laboratory findings and therapeutic course were reviewed retrospectively. [Results] Considering the underlying diseases, there were four cases of ANCA associated vasculitis, two cases of IgG4-related diseases, two cases of infection and four idiopathic cases. Regarding the treatment of 10 cases excluding two cases of infection, eight cases were treated with corticosteroid, while one case was treated with adding cyclophosphamide on corticosteroid. The clinical symptoms were improved in all nine cases, but the dural thickening remained in two cases. The dural thickening was improved in one case without any treatment. [Conclusions] Although MRI is useful to diagnose HP, the dural thickening sometimes remains even after immunosuppressive therapy. In addition to imaging findings, Clinical symptoms and cerebrospinal fluid examinations are necessary to be considered to evaluate the therapeutic effect.

W68-6

Paraspinal and intraspinal calcinosis in patients with systemic sclerosis

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Conflict of interest: None

[Object] The aim of this study was to clarify the incidence and related factor of paraspinal and intraspinal calcinosis in patients with systemic sclerosis (SSc). [Methods] 159 patients (male; 22, female; 137) with SSc were studied. Mean age was 62 years old and mean disease duration was 8 years. Paraspinal and intraspinal calcinosis was examined using chest plain CT. Disease type of SSc, Raynaud's phenomenon, digital ischemic loss, digital ulcers, modified Rodonan total skin score (MESS) skin score and autoantibody were examined. [Results] There was paraspinal and intraspinal calcinosis in 27 patients (17%). Twenty-one of 27 patients had calcinosis in the cervical spine. Eleven patients had intraspinal calcinosis, and 7 had spinal cord compression. There was a significant association between calcinosis and digital ischemic loss, digital ulcers. There was no significant association between calcinosis and disease type of SSc, Raynaud's phenomenon, MESS skin score, and autoantibody. [Conclusions] In this study, paraspinal and intraspinal calcinosis in SSc patients associated with digital ischemic loss and digital ulcers. These suggest that paraspinal and intraspinal calcinosis might be caused by vascular insufficiency.

W69-1

Dose Reduction and Termination of Methotrexate in Therapeutic Process of Rheumatoid Arthritis utilizing Biological Products

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Conflict of interest: None

[Purpose] We analyzed effect of combined usage of Methotrexate (MTX) in biological products (BPs) therapy (BPT) for RA including inhibitors for TNF (TNFi), IL-6 (IL-6i: TCZ), and CTLA-4 (CTLA-4i: ABT). [Methods] RA patients (n=170) taken BPT with/without (w/wo) MTX were retrospectively analyzed. 1) DAS28-CRP (DAS) on 0, 3, 6, and 12 months (mo.) after BPT w/wo MTX. 2) Change in dose of MTX (including withdrawal) on 0, 3, 6, and 12 mo. after BPT with MTX cases. [Results] 1) In TNFi group, DAS was gradually decreased regardless of usage of MTX. In TCZ group, initial DAS was higher in MTX-combined group, but the value was decreased to the level of TCZ alone group at 12 mo. after BPT. In ABT group, DAS was gradually decreased regardless of usage of MTX. 2) Dose of MTX in TNFi group was not change after 12 mo. of BPT. While, the dose of MTX in TCZ group was dramatically

decreased after 12 mo. of BPT. The dose of MTX in ABT group was gradually decreased after 12 mo. of BPT. 3) Although MTX terminated cases were 2% in TNFi, and 5-8% in ABT, the ones were 10.3% (3 mo.) and 34.5% (12 mo.) in TCZ. [Conclusions] Among BPs, TCZ alone showed the same effect on DAS as TCZ with MTX. In addition, it is possible that MTX usage could be terminated during process of BPT especially in TCZ cases.

W69-2

No factor could predict relapse after infliximab withdrawal in SDAI remission - Birdie trial-

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Conflict of interest: None

[Object] By biological agents (Bio) remission is a realistic goal and it is a time to think about after remission. Clinical trials suggested deep remission might be an indicator for Bio free. Therefore, IFX (infliximab) free was performed after achievement of SDAI remission (≦ 3.3) for more than 24 weeks, and the risk factor of flare was evaluated. [Methods] Of the 145, 44 (30.3%) achieved SDAI remission. IFX withdrawal was given to 42 patients with consent and disease activity, blood tests, 62 joint echo findings, and IFX concentrations were measured. Risk factor analysis was performed with flare from SDAI remission or IFX re-administration as an end point. Clinical research registration name was Birdie (UMIN 000009435). [Results] 32 out of 42 (76.2%) maintained SDAI remission. There was no significant difference in age, height, weight, disease and SDAI remission period, anti-CCP antibody, IFX concentration, and joint echo findings compared to 10 flared patients. There were 8 cases with undetectable IFX concentration, but only 2 cases were relapsed, and 1 case with anti-IFX antibody did not show relapse. [Conclusions] Although SDAI remission could be an indicator for Bio free, no factors could be detected to identify flared cases beforehand.

W69-3

In adalimumab treatment, Remission induction and treatment continuation at 208 weeks in 186 patients

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Conflict of interest: None

[Object] Clinical usefulness and treatment continuation following 208 weeks of adalimumab (ADA) in rheumatoid arthritis (RA) patients were investigated. [Methods] Subjects were 186 analyzable patients introduced to ADA at the author's institution from May 2009 to Oct 2013. Mean age was 54 years, mean duration of illness 6.8years. 151 received MTX ≧10 mg/week (≧10 group) and 29 MTX<10 mg/week (<10 group). The course of DAS28 (ESR), HAQ and remission rate were analyzed. [Results] Overall DAS28 (ESR) remission rate showed clinical remission in 48% of patients from 12 weeks, and achieved 70% from 208 weeks. Changes in DAS 28 (ESR) 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. Overall HAQ remission rate at 208 weeks was 81%; treatment continuation rate was 63.9%., and those of ≧10 group was 72.3%. [Conclusions] ADA plus an adequate dose of MTX with early escalation in early-stage RA and Bio Naïve patients is the best approach to maximally exploit the ADA potential.

W69-4

Attenuation of methotrexate therapy after successful discontinuation of TNF inhibitor in patients who previously had active rheumatoid arthritis despite treatment with methotrexate and required TNF inhibitor

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Conflict of interest: Yes

[Objective] To assess the possibility of successful attenuation of methotrexate (MTX) therapy after discontinuation of a tumor necrosis factor inhibitor (TNFi) in patients with previous active rheumatoid arthritis (RA) despite MTX therapy. [Methods] Out of 139 patients who had started to be treated with TNFi and MTX for at least 6 months by the lead author until October 2015, 100 patients who discontinued TNFi due to sustained remission were enrolled. [Results] Median age and symptom duration were 57.9 years and 1.2 years, respectively. Anti-CCP antibodies and RF were positive in 84 and 87 patients, respectively. The median highest dose of MTX used for 6 months was 14 [range 6-20] mg/week. After discontinuation of TNFi, 7 and 3 discontinued MTX due to adverse events and planning for pregnancy, respectively. In the other 90 patients, the dose of MTX could be successfully reduced by ≧25% in 55 patients and by ≧50% in 31 patients. Other synthetic antirheumatic drugs were concomitantly used in 44% of patients who reduced the dose of MTX by ≧25%. [Conclusion] Remission induction therapy with TNFi enabled subsequent attenuation of MTX therapy while maintaining remission after discontinuation of TNFi even in patients refractory to previous methotrexate therapy and required TNFi therapy.

W69-5

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

[Object] To evaluate the possibility of MTX cessation in RA patients who have remained in remission with combination of MTX plus tocilizumab (TCZ). [Methods] 25 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. All patients were followed up prospectively every 4 week and we compared the efficacy and safety of these 2 treatment groups at week 96. [Results] 12 patients were assigned to the MTX cessation group and the other 13 cases were to the MTX continuation group. There were no significant elevation of both DAS28-ESR and HAQ-DI score after cessation of MTX and the difference of both parameters between the 2 groups was also not significant. The change of van der Heijde modified Sharp score during 96 weeks (DmTSS) were 2.79 and 2.68 respectively and the difference was not significant. Adverse events were seen in 8 patients in the MTX continuation group and only 1 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.

W69-6

A study of dose reduction and withdrawal of methotrexate in patients with rheumatoid arthritis who started to receive bDMARDs during treatment with methotrexate

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Conflict of interest: None

[Objective] This study examined dose reduction and withdrawal of methotrexate (MTX) in rheumatoid arthritis (RA) patients after remission with bDMARDs, such as abatacept (ABT), tocilizumab (TOC), and tofacitinib (TOF), combined with MTX. [Method] These bDMARDs were started in 175 RA patients between July 2008 and March 2017. We reviewed medical records of 123 patients receiving MTX at bDMARD introduction. [Results] MTX was used concomitantly in 75 of 105 patients given ABT, 30 of 43 given TOC, and 18 of 27 given TOF. Eight patients received more than one bDMARD. There were 105 women. The mean age was 60.4 years. At the start of bDMARD treatment, the mean DAS28-ESR was 5.57, the mean MTX dose was 10.4 mg/week, and PSL was administered in 36 patients. The MTX dose was reduced in 89 patients (72.4%). MTX was withdrawn in 71 patients (57.7%), and the mean time from bDMARD introduction to MTX withdrawal was 40.9 months; MTX was withdrawn due to remission in 49 patients (39.8%). Due to relapse after withdrawal, MTX treatment was resumed in one patient. [Conclusion] After remission achievement, MTX could be withdrawn in 39.8% of patients. Attempting to reduce or withdraw MTX is useful in patients who wish to become pregnant or are concerned about adverse reactions.

W70-1

Management of liver impairment and gastrointestinal symptoms in patients on MTX treatment~Usefulness of daily administration of Foliamin 1mg/day~

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Conflict of interest: None

Background From February 2012, use of MTX up to 16 mg/week became possible. However, dose-dependent adverse events such as liver impairment and gastric disorders posed challenges. Interventions such as increased foliamin dose were routinely applied. ***Objective*** Clinical efficacy of changing foliamin dose from 5 mg/week to 1 mg daily for liver impairment and gastric disorders in MTX-treated patients was investigated at the author's institution. ***Methods*** Among rheumatoid arthritis (RA) out-patients on MTX, 120 with liver impairment and 41 with gastric disorders were studied. Mean age was 57 years, mean MTX dose 11.1 mg/week, mean AST (GOT) at the change was 54, and mean ALT (GPT) 81. Changes in symptoms were assessed up to 3 months. ***Results*** 1) Liver impairment symptoms improved significantly at 1 month, and continued uneventfully up to 3 months, except for one patient. MTX dose decrease was needed for 21 patients while an increase was possible for 8. 2) Gastric symptoms disappeared in 27 patients after 1 month, in 10 after 2 months, 1 after 3 months, and 3 after 4 months with no decrease in MTX dose, except for one patient. ***Conclusion*** Changing the foliamin dose to 1 mg daily was shown to be an effective intervention option for such gastric and liver adverse reactions of MTX.

W70-2

Clinical courses of patients of rheumatoid arthritis complicated with MTX-LPD at our hospital

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Conflict of interest: Yes

[Object] Methotrexate (MTX) is recognized by an effective conventional systemic disease modifying drug (csDMARD) in rheumatoid arthritis (RA) because of good tolerance and a low frequency of inefficacy. However, some patients, receiving MTX may pose an increased risk of lymphoproliferative disease, named of MTX-LPD. We show some cases of patients with RA who developed a LPD during low dose MTX therapy. [Methods] We analyzed about background, clinical course and prognosis of twenty eights cases of RA patients complicated MTX-LPD. [Results] Patients profile is below; females are 24, males are4. 8 cases are Stage II, 14 case are Stage III, 4 cases are stage IV. Mean dose of total MTX are 632.7mg, and maximum doses are 2440mg, minimum doses are 160mg. There are no differences between MTX doses and development of LPD. Pathological analysis was showed that 18 cases were B cell lymphoma, 6 cases were Hodgkin lymphoma, 4 cases were MALT lymphoma. Although 14 of 28 cases were improved, naturally, 5 of 14 cases were relapsed, and were need to chemotherapy. 13 cases were peripheral blood EBV RT-PCR (+), 11 case were EBER (+) at pathology. There cases were all improved, naturally. 3 cases were died. [Conclusions] It was suggested that EBV was related to development of MTX-LPD.

W70-3

Analysis of 21 cases of methotrexate related lymphoproliferative disease (MTX-LPD) in our hospital

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Conflict of interest: None

[Object] The characteristics of Methotrexate-associated lymphoproliferative disorder (MTXLPD) are still unknown. [Methods] The 21 MTXLPD patients at our hospital were selected. Patient backgrounds were extracted from the medical record and conducted a retrospective analysis. [Results] The mean MTX dose and used period were 9mg a week and 6.9 years, respectively. 3 patients developed MTXLPD within 1 year after MTX starting. The pathological type was composed of 9 DLBCL, 4 Hodgkin's lymphoma (HL), 2 T cell lymphoma (TL), 1 follicular lymphoma, 1 reactive change, respectively. 14 LPD cases resulted in spontaneous regression (SR) after MTX stopping, and the others resulted in chemotherapy. 6 cases of chemotherapy resulted in remission, but the one case of HL died due to LPD. LPD recurred in 5 cases of SR and 1 case after chemotherapy. The mean time to LPD recurrence was 29 months, the recurrence pathological type was 4 cases of HL, 1 case of B cell lymphoma, 1 case of TL. The mean sIL-2R level at first LPD was 1762, and at the recurrence was 5383 (U/mL). All the recurrent cases did't regress after stopping of RA treatment. [Conclusions] LPD recurrence might be more frequent and often refractory in HL. Periodic measurement of sIL2-R might be useful for recurrence monitoring.

W70-4

Clinical characteristics and risk factors of lymphoproliferative disease in patients with rheumatoid arthritis treated with methotrexate

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Conflict of interest: None

[Object] The purpose of the study is to demonstrate the characteristics and risk factors of LPD among RA patients concurrently treated with MTX. [Methods] We retrospectively evaluated RA patients with LPD from 2007 to 2017 regarding their clinical features. To analyze the risk of LPD among RA patients concurrently treated with MTX, a case-control study design was used to select control patients who had received MTX but did not develop LPD. [Results] There were 33 patients in the LPD group and 273 in the non-LPD group. Multivariate analysis revealed that elevated level of CRP ($p<0.0001$), high Steinbrocker classification ($p=0.0003$) and low absolute lymphocyte number ($p<0.0001$), were risk factors for LPD. Among 33 patients developing LPD, 17 LPDs regressed spontaneously after MTX cessation (regressive group), and 16 did not regress and needed chemotherapy (persistent group). The titer of sIL-2R and Steinbrocker classification in persistent group were significantly higher than regressive group. [Conclusions] Our data indicated that a significant decrease in lymphocyte count and elevated level of CRP at the LPD diagnosis were associated with LPD developing during MTX treatment. Moreover, the the titer of sIL-2R was an important marker of spontaneous regression of LPD after MTX cessation.

W70-5

Clinical analysis of lymphoproliferative disorder (LPD) in patients with rheumatoid arthritis (RA) treated with methotrexate

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Conflict of interest: None

Objective: To clarify the characteristics of LPD in RA patients treated with MTX. Methods: We retrospectively reviewed the medical records of 27 patients (16 females, 11 males) with RA who developed LPD during MTX treatment in our hospital between January 2007 and August 2017. Results: The median age and RA duration at LPD diagnosis were 73.0 and 7.9 years, respectively. The mean MTX dose at LPD diagnosis was 7.9 mg/week. Twenty patients had Ann Arbor stage 3 or 4 LPD. After MTX withdrawal, the median duration of LPD follow-up was 101 weeks. Thirteen patients (Tx group) immediately underwent chemotherapy, whereas 16 (Fu group) were followed over 12 weeks and 13 (81.2%) suffered spontaneous regression of LPD. Stage 4 LPD was more frequent among 6 patients who died from LPD than among the other 21 (83.3% vs 23.8%, p=0.015), and in the Tx group relative to the Fu group (81.2% vs 18.7%, p=0.024). Long-term LPD relapse occurred in two patients who required treatment intensification with tacrolimus and abatacept, respectively, for RA flare. Conclusion: LPD diagnosis and MTX withdrawal should be performed as soon as possible. Long-term observation is necessary for patients receiving immunosuppressive treatment for RA flare in view of the risk of LPD relapse.

W70-6

EB virus positive mucocutaneous ulcer (EBV-MCU) associated MTX in rheumatoid arthritis patients

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Conflict of interest: None

[Object] EB virus positive mucocutaneous ulcer (EBV-MCU) has been newly categorized in B-cell neoplasm as a self-limited growth in the 2016 revision of WHO classification. [Methods] We evaluated the clinicopathological characteristics of EBV-MCU related with RA patients during administered MTX. [Results] Among 38 MTX-associated Lymphoproliferative disorders (LPD), 12 (38%) EBV-MCU RA patient were retrospective analyzed. Extrnodal sites of EBV-MCU confirmed positive EBER-ISH were as follows: 3 oral mucosa, 7 nasopharynx and 2 skin. The histological type were in 10 B-cell LPD and 2 DLBCL. Mean age was 75 years and MTX dosage was 9.7 mg during 8.8 years with mean DAS-CRP of 2.67. Spontaneous regression by withdrawal MTX were seen 6 cases (50%) and other 3 of 6 cases were treated Rituximab monotherapy. All 12 cases were achieved complete remission without relapse, and alive in observation period of 48 months. After CR of LPD,4 patients were treated with continuous RIT and maintained RA low disease activity. After over 9 month withdrawal MTX, 3 were treated with biologics in adding PSL or csDMARDs caused by RA flare. [Conclusions] EBV-MCU associated RA was self-limited and favorable prognosis by immediately withdrawal MTX. Biologics may be careful administration in flare of RA.

W71-1

Abatacept down-regulates CD64 on circulating monocytes through binding to CD86

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Conflict of interest: Yes

[Object] To investigate direct effects of abatacept/CTLA4-Ig on circulating monocytes. [Methods] Peripheral blood monocytes were isolated from patients with rheumatoid arthritis (RA), those with non-inflammatory rheumatic disorders, and healthy individuals, and were cultured in the presence or absence of CTLA4-Ig or CD28-Ig for 24 hours. Cell surface molecules on monocytes (CD14, CD16, CD32, CD40, CD54, CD62L, CD64, CD80, CD86, CD273, CD274, CD275) and cytokines in culture supernatants (IL-1β, IL-6, IL-8, IL-10, IL-12p70, IFN-γ, MCP-1, TNFα) were assessed using flow cytometry and/or immunoblotting. [Results] In a pilot study involving 5 cases each of RA patients and controls, CD64, CD80, CD86, CCR2, CXCR2 were selected as candidate molecules whose expression levels were modulated by CTLA4-Ig. In the validation study including 27 RA and 13 controls, CTLA4-Ig therapy down-regulated expression of CD64 and CXCR2, but CXCR2 expression was suppressed also by CD28-Ig treatment. These changes were not observed with IgG-Fc alone, and were abolished by anti-CD86 antibody. Finally, CTLA4-induced CD64 down-regulation was confirmed by immunoblotting. [Conclusions] Therapeutic effects of abatacept on RA are mediated, in part, by down-regulation of CD64 and CXCR2 on monocytes through binding to CD86.

W71-2

Serum levels of ROM, an oxidative stress marker at 12 weeks during treatment with tocilizumab is a superior predictor for the clinical remission

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Conflict of interest: None

[Background] Tocilizumab (TCZ) strongly suppresses inflammatory reaction; however, clinicians sometimes see discrepancy between the improved laboratory data and actual symptoms of patients. Therefore, it is necessary to develop a novel biomarker to reflect 'true' patient's symptoms and predict the future clinical remission. [Methods] A total of 35 RA patients (mean age: 64.3 y.o., disease duration: 9.4 y) during treatment with TCZ including 22 naïve and 13 switched were enrolled in this study. Associations between serum levels of ROM, CRP, and MMP-3 at 12 weeks and the remission by DAS28-ESR, CDAI, SDAI and Boolean at 52 weeks were investigated. [Results] Remission rates at 52-week for DAS, CDAI, SDAI and Boolean were 80, 49, 51 and 54%, respectively. ROM levels at 12 weeks in the DAS- and SDAI-remission groups were significantly lower than those in their non-remission groups (DAS: $p = 0.013$; SDAI: $p = 0.044$). ROC curves demonstrated the AUC of ROM was 0.893 ($p = 0.001$) and its cut-off value was 305.5 (sensitivity: 85.7%, specificity: 78.6%). Neither CRP nor MMP-3 was able to predict clinical remission at 52 weeks. [Conclusions] ROM at 12 weeks during treatment with TCZ was a superior predictor to CRP and MMP-3 for the DAS-remission at 52 weeks.

W71-3

Pathological changes in rheumatoid arthritis synovial tissues before and after the use of biologic agents

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Conflict of interest: None

[Object] We examined the impact of biologic agents (Bio) have 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 32 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 and disease activity (CDAI). We used ETN17, IFX6, TCZ4, ADA3 and ABT2. [Results] Fibrinoid necrosis was identified in 6 joints (18.8%) after the use of Bio, which showed significant improvement. Synovial villi were identified in 11 joints (34.4%) after the use of Bio, which showed significant improvement. The Rooney score also improved significantly, from 27.6 to 12.0. The perivascular lymphocytic infiltrate, lymphoid follicles and lymphocyte infiltration decreased significantly. [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.

W71-4

Serum IL-6 concentration under the treatment with tocilizumab in patients with rheumatoid arthritis was correlated with MMP-3

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Conflict of interest: None

[Object] Tocilizumab inhibits almost completely the function of IL-6 and suppresses the acute inflammatory reaction such as C-reactive protein (CRP). After the treatment with tocilizumab, it could be difficult to use the acute inflammatory products as the marker of disease activity of RA. We wonder if serum IL-6 could use as marker of the disease activity and the extension of the interval of tocilizumab. [Methods] Serum Il-6 concentration was measured in 23 patients of RA and 3 patients with Castleman's lymphoma. [Results] Serum IL-6 in RA patients were 95.0 ± 126.4 (8.9-522) pg/ml, which was lower than in Castleman's lymphoma patients. All RA patients showed negative for CRP. MMP-3 were 146.0 ± 223.8 (10-1011.7) ng/ml. Serum IL-6 and MMP-3 were strongly correlated ($p<0.0001$, $r2=0.779$; MMP-3=1.48 x IL-6-5.50) [Conclusions] Tocilizumab makes difficult to judge the RA activity with CRP and ESR. As tocilizumab blocks IL-6 to react with IL-6 receptor, IL-6 might remain in serum without consumption and serum concentration of IL-6 could reflect the disease activity. This study showed that serum IL-6 concentration was elevated and correlated with MMP-3. We supposed that serum IL-6 concentration under the treatment with tocilizumab could be good marker of disease activity.

W71-5

Prediction of efficacy of Abatacept based on changes in rheumatoid factor

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Conflict of interest: Yes

[Object] Change in rheumatoid factor (RF) is known as one of parameters for immune abnormality, suggesting that the efficacy of Abatacept (ABT) might be predictable. [Methods] 89 RA patients who have started ABT at our site have assessed DAS28 after 6 months of treatment. We divided the patients into three groups based on the RF titer, neg-RF (RF < 15), Low-RF (RF 16 <, <100), and high RF (RF > 100) at therapy initiation. The change rate of RF at therapy initiation from 3 months before was calculated and categorized into 3 groups; more than or equal to 20% decrease in RF change rate (RF↓), less than 20% change rate in RF (RF→) and more than or equal to 20% increase in RF change rate (RF↑). [Results] Ratio achieving remission or low disease activity in each group was (neg-RF: Low-RF: High-RF) 70.6%: 60.0%: 35.7%, (RF↓: RF→: RF↑) 66.7%: 42.1%: 41.1%. Compared to the RF↓ group, decrease in efficacy was shown in patients in the RF↑ group. [Conclusions] In patients with high titer RF, especially increasing RF, T cell- B cell interaction is believed to be strongly involved. But the efficacy of ABT was decreased in RA patients with increasing RF value. When treated with ABT, sufficient dose of MTX or combined DMARDs medication must be used for enhancing effectiveness.

W71-6

Genetic polymorphisms associated with herpes simplex and shingles herpes on RA patients under treatmant with bDMARDs

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Conflict of interest: None

[Object] HSV and HZV infections have been reported as side effects of treatment with bDMARDs in RA patients and it is important to evaluate the risk of onset. We searched for single nucleotide polymorphisms (SNPs), which are closely related to herpes onset in RA patients during treatment with bDMARDs, by genome-wide SNP analysis. [Methods] 412 RA patients treated with bDMARDs (INF, ETN, ADA, GOL, CZP, TCZ, and ABT) were included in this study. Among them, 66 patients developed HSV and HZV infections. Comparative tests on about 300,000 SNPs were carried out by genome-wide SNP analysis using Illumina HumanHap 300K, Human 610-Quad or Human Omni ExpressExome chips. Fisher test was carried out and the gene arrangement and characteristics of the upper 300 SNPs with low p value were examined. [Results] Some of the extracted SNP sites were located on the genes of COL12A1, FUT10, LRP1B, and HLADMB. COL12A1 encodes collagen type XII reported to be associated with HSV infection. FUT genes are involved in adhesion and migration of leukocytes. LRP1B, HLADMB are involved in antigen presentation to T cells. [Conclusions] SNP analysis suggested that COL12A1, FUT10, LRP1B, HLADMB genes might be involved in the development of HSV and HZV infections in RA patients treated with bDMARDs.

W72-1

MultidisciplinaryHospital Effort to Address Rheumatoid Arthritis during Pregnancy and Childrearing

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Conflict of interest: None

[Object] Using a survey, the study assessedproblems during pregnancy or childrearing among patients with rheumatoid arthritis (RA). [Methods] Questionnaires were administered to 13 patients with RA, raising children (< 3 years old). Mama Café, was also held. [Results] Nine and 4patients were expecting/had delivered their first child, and second or later child, respectively. PatientsindicatedRA-related anxiety and factors like drug effects on the fetus during pregnancy (76%) and during childrearing (61%). Patients also indicated problems related to activities likepreparing mealsduring pregnancy (38%), and hugging their children or changing diapers during childrearing (84%). patients to address BIO use, occupational therapy during pregnancy, and methods of raising children with minimal impact on joints. Eight patients in the Mama Café. The patients appreciated"meeting, and befriending other persons grappling with similar childrearing issues. [Conclusions] Anxiety was mostly related to druguse during pregnancy and exacerbation of RA symptoms during childrearing. The Mama Café provided an opportunity to meet otherswith RA. Individual requests differed amongthe patients. Thus, an outpatient consultation service and a system for providing multidisciplinary support must be established.

W72-2

A survey on dementia of rheumatoid arthritis patients

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Conflict of interest: None

[Background] According to the epidemiological survey in 2013, it was reported that 46.6%. However, it is said that RA patients have dementia less frequently in various studies. [Purpose] We investigated dementia of elderly RA patients in our clinic and clarify the actual condition. [Methods] Using the Hasegawa Dementia Scale-Revised, we evaluated RA patients at the age of 75 and older who received biological agents. [Results] The patients comprised 6 men and 50 women with an average age of 80.6 years. IFX was administered in 3 patients, ETN in 6, ADA in 8, ABT in 9, GLM in 8, and TFO in 14. Serum CRP levels were less than 1 mg/dl in 55 patients (98%). Tender joints and swollen joints were less than one in 44 (79%) and 51 (91%), respectively. According to an independence degree of daily life, 15 patients (15.8%) were categorized as independence. 47 patients (85%) were categorized as normal. [Discussion] Considering that 85% of patients were without dementia and 15.8% of them were independent in daily life in this study, it is thought that maintenance of QOL through RA treatment is implicated in the prevention of dementia [Conclusion] At our clinic, 85% of elderly patients with RA had no dementia. It is important to maintain QOL through RA treatment for prevention of dementia.

W72-3

Our challenge to prevent infection by team medical care among patients with rheumatoid arthritis treated with biologic DMARDs

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Conflict of interest: None

[Object] We studied the incidence of serious adverse events associated with biologic DMARDs in patients who were treated under our multidisciplinary medical team for Rheumatology established in July, 2012. [Methods] We investigated 183 RA patients who recieved bDMARDs from 2012 to 2017. [Results] Mean follow-up period was 21 months. Of 183 patients, 133 (73%) were bio-naive. MTX and PSL were used in 53% and 29% of the patients respectively. 64 patients (35%) had 2 or more risk factors associated with infection such as 65 old age, diabetes mellitus, use of PSL, and lung or cerebrovascular diseases. bDMARDs include ABT (n=104), ETN (n=50) and others (n=29). Among 13 sever adverse events, 7 had infection (2.15/100 person-year). The characteristics of the patients included age over 70, (n=4), MTX-user (n=6), PSL-user (n=3), and 2 or more risk factors (n=4). [Conclusion] Despite our challenge, severe infection remained a critical issue, especially those having potential rist factors for infection.

W72-4

Current status of RA treatment in aged society

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Conflict of interest: None

[Object] 65 years and older have been elderly people, but the Japan Society for the Elderly and the Japan Society for Geriatrics Association aged 65-74 years old / elderly / aged 75-89 years old / over 90 years old He suggested that he was a senior citizen. We examined the problem of treatment for elderly RA patients at our hospital. [Methods] We examined complications / remedies for 414 elderly RA patients aged 65 years or older. We also conducted a simple dementia test. [Results] 739 RA patients in our hospital and 414 (56.0%) patients over 65 years old, including 221 elderly people, 184 elderly people and 9 super elderly people. Complications are confirmed in 92.5% (387 people) hypertension / renal disorder. The number of complications continues up to 6 diseases, one disease 45.6% / two 31.8% / three 25.1%. In eGFR, by 40.3% of the elderly, 84.3% in the elderly and 88.9% in the elderly. In addition, mild cognitive impairment (41 -79 points) was recognized in 70% in dementia examination, cognitive impairment (40 or less) was confirmed in 4%. [Conclusions] Although MTX and Biologics should gradually decrease according to their actual condition, it is difficult to comply with compliance and comprehension of explanation, as cognitive impairment is also seen as the aging progresses.

W72-5

Which factors contribute to difficulty in oral administration, suppository insertion, and self-injection in patients with rheumatoid arthritis? - from a large cohort of rheumatoid arthritis, KURAMA study -

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Conflict of interest: None

[Object] The purpose of this study was to clarify which factors contribute to the difficulty in oral administration, suppository insertion, and self-injection in patients with rheumatoid arthritis (RA). [Methods] a total of 563 patients (mean age 63.4ys, mean disease duration 12.7ys), who were registered in KURAMA cohort study, were included. The patients were surveyed on the difficulty of oral administration, suppository insertion, and self-injection if they do it as 4 categories. Also demographic, laboratory, and physical examination data on disease activity were collected. Multivariate analyses were performed for the difficulty as an objective variable in respective action. [Results] HAQ-DI was a significant, universal risk factor in all of the three actions. CRP was also a significant risk factor for difficulty in oral administration. Multivariate analyses excluding HAQ-DI showed that pain VAS and Steinbrocker's stage as well as CRP were independent risk factors for difficulty in oral administration and suppository insertion. [Conclusions] This study revealed that functionally-disabled patients who has low HAQ-DI score feel difficulty in oral administration, suppository insertion, and self-injection. Those patients should be particularly helped in nursing practice.

W72-6

Evaluation of Nursing Intervention through foot care VAS (Visual Analogue Scale)

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Conflict of interest: None

[Object] We have been reported concerning foot care in RA patients and studies association of foot issues with patient characteristics, using foot care VAS as patient reported outcome. Here we report association of nursing intervention with foot careVAS score assessment with patient background and clinical characteristics. [Methods] Ninety six patients treated for foot care through Jan 2016 to Oct 2017 are target for this analysis. We assessed association of Foot care VAS (overall impression, persistence, satisfactory; lower the score is, it is better) with various patient background (Age, disease duration (age, disease duration, class, stage, DAS, PtPVAS, and PtGHVAS) [Results] Foot care VAS, there is no correlation with age, disease duration, class, stage. Analysis on DAS28CRP, DAS28ESR, showed that foot care VAS is significantly worse as disease

activity, furthermore, foot care VAS is significantly worse as PtPVAS and PtGHVAS, as well as among group comparison. [Conclusions] These data suggest that, in any disease activity, persistent nursing intervention through foot care is meaningful for RA patients.

W73-1

Influence of oral prednisolone on effect of denosumab on osteoporosis in patients with Japanese rheumatoid arthritis; three years of follow-up ~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 56 patients received continuous DMB therapy more than 36 months from TBCR-BONE. We reviewed the results for 12, 24 and 36 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=20, group GC+) and not receiving group (n=36, group GC-). The rate of decreased PINP and TRAC-5b from baseline to 12, 24 and 36 months were each -3.5% vs -42.0% (p=0.046), -8.7% vs -32.4% (p=0.113), -16.8% vs -33.7% (p=0.215) and -17.5% vs -36.4% (p=0.111), -19.5% vs -30.3% (p=0.521), -20.2% vs -29.5% (p=0.513) in the group GC+ vs GC-. The rate of increased LS-BMD and TH-BMD from baseline to 12, 24 and 36 months were each 5.5% vs 6.7% (p=0.587), 10.4% vs 7.3% (p=0.043), 12.3% vs 12.6% (p=0.738) and 1.3% vs 4.3% (p=0.751), 6.2% vs 5.0% (p=0.838), 8.4% vs 6.0% (p=0.889) 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 36 months.

W73-2

Comparison of the effect of denosumab and teriparatide in patients with steroid-induced osteoporosis resistant to bisphosphonates

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Conflict of interest: None

[Object] Although bisphosphonates (BP) has been used as a first-line drug for steroid-induced osteoporosis, there are some cases with insufficient response. Denosumab (DMAB) or teriparatide (TRPD) can be alternatives to BP. We prospectively compared the effects of DMAB and TPTD on bone mineral density (BMD) in patients who had been resistant to BP. [Methods] Forty patients with steroid-induced osteoporosis whose YAM in lumbar spine and femoral neck 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 (20 cases) or TRPD (20 cases), and the changes of the BMD before and after 52 weeks were determined. [Results] The mean baseline YAM of DMAB and TPTD groups were not significantly different (lumbar spine, 74.0% vs. 72.1%. femoral neck, 62.7% vs. 63.6%). There was also no difference in age, BMI, or total steroid dose between the two groups. The rate of change of BMD after 52 weeks were significantly higher at TPTD group as compared with DMAB group in lumbar spine (6.3% vs. 2.5%), also tended to increase at TPTD group in femoral neck (3.9% vs 0.2%). [Conclusions] It was suggested that TPTD could be a better alternative in patients with steroid-induced osteoporosis resistant to BP.

W73-3

Comparison of denosumab treatment for osteoporosis in rheumatoid arthritis patients with or without prior treatment of bisphosphonate

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Conflict of interest: None

[Object] We report the comparison of denosumab (DMB) treatment for osteoporosis in rheumatoid arthritis (RAOP) with/without prior treatment of bisphosphonate (pBP). [Methods] 38 women treated with 24-month (m) DMB from Toyohashi RA database (TRAD) were used. All cases were divided into two groups with/without pBP (BP; n=18, N; n=20). We compared baseline data, percent change of (%-) bone mineral density (BMD) in lumbar spine (LS-) and total hip (TH-), %P1NP, %TRACP-5b and absolute values of P1NP and TRACP-5b every 6m. [Results] Baseline P1NP and TRACP-5b were significantly larger in N than BP, while other data such as age, disease duration and DAS28-CRP were not significant. Comparisons between BP and N of %LS-BMD, %TH-BMD, P1NP and TRACP-5b at 24m were not significant; 6.4% vs. 6.1%, 3.9% vs. 4.2%, 28.5μg/L vs. 37.4μg/L, 338.5mU/dL vs. 396.6mU/dL respectively, while %P1NP and %TRACP-5b were significant; 36.4% vs. -46.9% ($p<0.001$) and 13.4% vs. -21.6% ($p<0.05$). [Conclusions] DMB treatment for RAOP increased %BMD both with/without pBP. As baseline P1NP and TRACP-5b were lower with pBP, %P1NP and %TRACP-5b were significant between BP and N, while absolute values were not significant. This suggested that %P1NP and %TRACP-5b might not be associated with %BMD when switching BP to DMB.

W73-4

Effects of denosumab on bone mineral density and bone turnover markers in rheumatoid arthritis patients switching from bisphosphonates

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Conflict of interest: None

[Object] To compare the effects of 12-month denosumab treatment on bone mineral density (BMD) and bone turnover markers (BTMs) between treatment-naïve osteoporosis patients with rheumatoid arthritis (RA) and those with previous bisphosphonate (BP) therapy. [Methods] A total of 36 women RA patients with osteoporosis completed 12-month follow-up. Twenty-five patients were osteoporotic treatment-naïve (naïve group), and 11 patients were previously treated with BPs (switch group) (average 7.9 years). BMD and BTMs were measured before and 6 and 12 months after treatment. [Results] BTM levels were higher in the naïve group at baseline. However, the same level of suppression was reached at 6 months in both groups. Spine BMD increased significantly in both groups. At 12 months, significant increases of femoral neck and total hip BMDs were observed only in the naïve group. There was no significant difference in the mean percent changes of BMD of the spine (naïve group: 6.8±0.8, switch group: 5.1±1.5), femoral neck (2.9±1.4, 2.9±1.3), and total hip (1.7±0.9, 1.4±1.1) between these two groups at 12 months. [Conclusions] The treatment effects of denosumab on BMD and BTMs in RA patients are considered to be almost the same between the switch group and the treatment-naïve group.

W73-5

Comparison of the efficacy of the switching treatment from bisphosphonate to either denosumab or daily teriparatide for osteoporosis in rheumatoid arthritis patients

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Conflict of interest: None

[Object] We report the comparison of the efficacy of switching bisphosphonate (BP) to either denosumab (DMB) or daily teriparatide (dTP) at 24 months (m) for osteoporosis in rheumatoid arthritis (RAOP). [Methods] 54 cases treated with switching BP to DMB (D; n=18) or dTP (T; n=36) were used from Toyohashi RA database (TRAD). We compared baseline data, percent change of (%-) BMD in lumbar spine (LS-) and total hip (TH-), %P1NP, %TRACP-5b and absolute values of P1NP and TRACP-5b every 6m. [Results] Baseline P1NP were significantly larger in T than D, while other data such as age, disease duration and DAS28-CRP were not significant. Comparisons of %LS-BMD, %TH-BMD, P1NP, TRACP-5b, %P1NP and %TRACP-5b at 24m between D and T were 6.4% vs. 11.0% (p=0.069), 3.9% vs. 3.9% (n. s.), 28.5μg/L vs. 76.3μg/L, 338.5mU/dL vs. 563.9mU/dL (p<0.001), 36.4% vs. 144.6% and 13.4% vs. 61.8% (p<0.05), respectively. [Conclusions] Switching BP to either DMB/dTP was effective to increase %BMD in RAOP. %LS-BMD tended to increase greatly with dTP. While %TH-BMD similarly increased both with DMB/dTP, recent studies reported the cortical porosity using dTP. They might suggest that switching BP to either DMB/dTP should be carefully selected evaluating risks of vertebral and proximal femoral fractures in each case.

W73-6

Goal-Directed Treatment of Osteoporosis in Patients with Rheumatoid Arthritis Using Daily Teriparatide for Two Years Followed by Anti-resorptive Agents for Three Years, Five years in Total

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Conflict of interest: Yes

[Object] To evaluate if 2-year daily teriparatide followed by denosumab or minodronate with eldecalcitol for 3 years can achieve treatment goal of osteoporosis (OP) reported recently (Goal-Directed Treatment, JBMR2017) in OP in patients with rheumatoid arthritis (RA). [Methods] 22 female RAOP patients were used from Toyohashi RA database (TRAD). Treatment goal was set as T-score>-2.5 at five years when T-score is below -2.5 at the initiation of OP treatment in this study. Bone mineral density (BMD) was measured by DEXA. [Results] Mean age was 70-years. RA duration was 18 years. Number of patients with T-score<-2.5 in lumbar spine (LS), total hip (TH) and femoral neck (FN) at baseline was 13, 18 and 16, respectively. Proportion of patients with T-score>-2.5 at five years was 53.8% in LS-BMD, 22.2% in TH-BMD and 25.0% in FN-BMD. Cut-off values at baseline for achievement of treatment goal calculated using ROC analysis was -3.4 in LS-BMD, -3.0 in TH-BMD and -2.9 in FN-BMD. [Conclusions] Achievement of treatment goal in OP is possible in LS-BMD but difficult in TH-BMD and FN-BMD when 2-year daily teriparatide followed by anti-resoptive agents for 3 years. ROC analysis revealed that early intervention is necessary when treating RAOP aiming treatment goal.

W74-1

Long-term change in lumber spine bone mineral density in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To investigate the change in bone mineral density (BMD) in patients with rheumatoid arthritis (RA) over a 10 year period. [Methods] In a longitudinal study of 36 patients with RA, we collected clinical data and measured lumber spine and hip BMD by dual-energy X-ray absorptiometry at baseline and after at least 10 years. BMD was measured as the percentage of young adult mean (YAM). We compared clinical fatures between patients with an increase in spine YAM of≧5% and those with YAM of <5% during follow-up period. [Results] The mean age was 59.3 years old and the mean disease duration of RA was 10.9 years, and the mean follow-up period was 10.4 years. The spine BMD increased from 86.6% of YAM at baseline to 93.8% of YAM at follow-up. During follow-up period, the rate of treatment with bDMARDs increased and antiresorptive drug intervention rate also increased. The patients with an increase in the spine YAM of≧5% during follow-up period were higher age and lower BMD at baseline, and showed a high rate of antiresorptive drug intervention at follow-up. [Conclusions] Our findings suggest that osteoporosis treatment for RA is important for an increase in spine BMD over a 10-year period. However, the aging changes and low BMD at baseline may be related to the change of spine BMD.

W74-2

Seven years change of bone mineral density in rheumatoid arthritis from the TOMORROW study

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Conflict of interest: None

[Object] We reported that bone mineral density (BMD) of rheumatoid arthritis (RA) was lower than that of healthy individuals (HI) and 3 years change of BMD. We investigated 7 years change of BMD and predictors in RA. [Methods] We analyzed TOMORROW study, which is a prospective cohort for age and sex matched RA and HI. BMD were measured at 3 points (whole body, lower limb, lumbar spine) by DXA. We compared the percent change of BMD (%ΔBMD) between 2010 and 2017. [Results] Participants comprised 172 HI and 119 RA. The %ΔBMD of RA was -2.6% (whole body), -3.6% (lower limb), and 1.8% (lumbar spine), while that of HI was -2.0%, -2.7%, and 0.6%. No significant differences in the %ΔBMD for whole body or lower limb were seen; however, the %ΔBMD of the lumbar spine was significantly increased in both groups (p<0.0001). No significant differences between groups were identified. In RA, the %ΔBMD of the lumbar spine has significantly correlation with cumulative period of bisphosphonate (BP) (r=0.341, p<0.001). The cumulative period of BP was identified as a predictor for increase BMD of the lumbar spine (Odds ratio: 1.32, p=0.004). [Conclusions] The BMD of whole body and lower limb were decrease for 7 years. The continuation of BP is important for increase of BMD at lumbar spine in RA.

W74-3

A status report on medical treatment for osteoporosis in rheumatic patients treated with biologics

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Conflict of interest: None

[Object] The aim of this study was to investigate the status of medical treatment for osteoporosis in rheumatoid arthritis (RA) patients treated with biologics (bDMARDs). [Methods] Sixty-six RA patients (50 females and 16 males, average 67.4±15.6 years old) who had treated with bDMARDs were enrolled in this study, and the medical records were checked retrospectively. The average duration of RA was 11.9±10.4

years, and administrated bDMARDs were as follows; TNF inhibitor 42 cases, IL-6 inhibitor 24 cases. We compared the status of the treatment for osteoporosis in the following respects; 1) age: under 65 years or not, 2) duration of RA: under 10 years or not, 3) sex, 4) body mass index (BMI): under 18.5 or not, 5) use of corticosteroid (CS), 6) presence of orthopedic surgeon's intervention, 7) presence of past fracture. [Results] Forty-one patients (62%) were treated with antiosteoporotic drugs. Treatment ratio was not different in 1)-6) respects, however, patients with past fracture (20 patients in 25cases) was treated with higher ratio than patients without fracture (21patients in 41cases) (p=0.04). [Conclusions] We should consider osteoporotic treatment more seriously in RA patients with fracture risk factors such as elderly, long disease duration, female, low BMI, and the use of CS.

W74-4

Risk factors for the development of glucocorticoid-induced bone loss in childhood-onset rheumatic diseases; A cross-sectional study

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Conflict of interest: None

[Object] To clarify risk factors for the development of glucocorticoid (GC)-induced bone loss (BL) and osteoporosis in childhood-onset rheumatic diseases (CoRD) [Methods] We recruited 39 patients with CoRD to whom GC therapy started between 1984 and 2014, and who were evaluated to have BL or osteoporosis after 3 months to 1.5 years of the treatment. BL was diagnosed as -2 or less of Z-score of the spine L2-4 (LS BMD). The diagnosis of osteoporosis was based on the presence of both a clinically significant fracture history and BL. [Results] Median age at GC start and at evaluation of osteoporosis was 11.2 and 12.0, respectively. Median cumulative PSL-equivalent dose of GCs was 1.2 mg/kg/day. Alendronate was administered within 3 months after GC start in 31% of the participants. BL and fracture history were found in 56% and 18% of the participants, respectively. In the logistic regression analysis, only "alendronate therapy within 3 months after GC start" had statistically significant effect on the development of BL (OR, 0.08; 95% CI, 0.02-0.43; $p<0.01$). We did not find any factors associating with the development of osteoporosis in the analysis. [Conclusions] Early intervention with alendronate may have a preventive effect on the development of BL in GC-treated patients with CoRD.

W74-5

Clinical features of patients with rheumatoid arthritis who had insufficiency fractures

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Conflict of interest: None

[Object] This study aimed to analyze clinical features of patients with rheumatoid arthritis (RA) who had experienced insufficiency fractures (IFs). [Methods] Medical records of RA patients in 2016 were retrospectively reviewed. [Results] Forty-one RA patients were found to have had fractures in 2016. IFs and fragility fractures (FFs) were found in 17 and 22 patients, respectively. Fractures before 2016 were found in 59% of patients with IFs and in 32% of patients with FFs. Prednisolone was administered to 82% of patients with IFs and to 59% of patients with FFs. The average amount of prednisolone was 5.5 mg for patients with IFs and 2.5 mg for patients with FFs. Patients undergoing osteoporosis treatment were 65% in the IF group and 45% in the FF group. Anteroposterior bone mineral density of the lumbar spine, measured using dual energy X-ray absorptiometry, on average, was 0.791 g/cm^3 in patients with IFs and 0.888 g/cm^3 in patients with FFs. [Conclusions] Clinical factors associated with IFs and FFs could include past history of fractures, amount of prednisolone, and bone mineral density. Considering more than half of the RA patients with IFs had undergone osteoporosis treatment in this study, RA patients might need to achieve higher control of increasing the bone strength.

W74-6

Association between bone mineral density of femoral neck and geriatric nutritional risk index in rheumatoid arthritis patients treated with biological disease-modifying anti-rheumatic drugs

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Conflict of interest: None

[Object] Treatment of RA with bDMARDs induces rapid remission. However, osteoporosis remains a problem. The Geriatric Nutritional Risk Index (GNRI) evaluates the risk of malnutrition-related complications in elderly patients and has been shown to be a predictor of many diseases. We evaluated the correlation between GNRI and RA activity, and risk factors for bone loss. [Methods] RA patients (n=146) treated with bDMARDs whose BMD was measured between December 2011 and 2013 were evaluated. We examined sex, age, disease duration, eGFR, dose of steroid, GNRI, DAS28-CRP, SDAI, MHAQ, CRP, and BMD of the femoral neck. Spearman's correlation and multivariate logistic regression analysis were performed. [Results] Inverse correlation were observed between GNRI and duration, DAS28-CRP, SDAI, MHAQ, and CRP. GNRI showed correlation with BMD and BMD ≦70% of YAM. Multiple regression analysis showed that female sex, increased age, and lower GNRI were risk factors for lower BMD. Logistic regression analysis showed that female sex (odd ratio: 3.67) and lower GNRI (odd ratio: 1.15) were risk factors for BMD ≦70% of YAM. [Conclusions] Our findings suggest that GNRI correlated with RA activity and BMD of the femoral neck. Nutritional therapies might improve RA activity and osteoporosis treated with bDMARDs.

W75-1

Radiological findings of bicipitoradial bursitis misdiagnosed as soft tissue tumor: a report of twelve cases

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Conflict of interest: None

[Objective] The bicipitoradial bursa is located between the distal biceps tendon and the radial tuberosity. Bicipitoradial bursitis (BRB) is frequently misdiagnosed as soft tissue tumor on MRI. The objective of this study is to describe radiological findings of BRB and to make this rare clinical entity better known. [Methods] Twelve patients (M:F=3:9; age range, 58-83) with BRB were included in this study. All patients underwent plain radiographs and MRI. Their radiological findings were evaluated and compared with those of 5 patients with soft tissue tumor. [Results] On plain radiographs, 7 patients with BRB showed roughening of the radial tuberosity. On T2-weighted MR imaging, all BRB had a mass-like lesion with very high intensity. Abnormal intensity between the radius and the ulna was observed in 10 BRB. Only one tumor patient with locally advanced myxofibrosarcoma invaded into the proximal radioulnar junction. [Conclusions] MRI features of soft-tissue lesions that are suggestive of malignancy include ill-defined borders; size greater than 5cm; deep location; heterogeneous signal intensity, and so on. Those are also observed in chronic BRB, however, knowledge of regional anatomy and

understanding of the typical MR appearance of BRB are satisfactory for diagnosis.

W75-2

The change of lower limb alignment in standing position after total knee arthroplasty influences the leg length discrepancy

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Conflict of interest: None

[Object] The aim of this study was to examine the influence of lower limb alignment in standing position after total knee arthroplasty (TKA) on the leg length discrepancy (LLD). [Methods] Twenty patients (average 74 years old) who underwent primary TKA were included in this study. We obtained radiographs of both lower legs in entirety in a standing position before and after TKA. We measured the leg length in whole leg and the deviation of mechanical axis at the knee joint (MAD) on anteroposterior radiographs, and the knee flexion angle (KFA) on lateral radiographs. We calculated the discrepancy of each parameter, and examined the relationship between LLD and MAD discrepancy or KFA discrepancy. [Results] Before TKA, only KFA discrepancy correlated with LLD in univariate analysis ($r=-0.49$, $p=0.04$), and both KFA discrepancy ($p<0.01$) and MAD discrepancy ($p=0.02$) correlated with LLD in multivariate analysis (corrected $R^2=0.47$). After TKA, only MAD discrepancy correlated with LLD in univariate analysis ($r=-0.56$, $p=0.04$) and in multivariate analysis (corrected $R^2=0.40$, $p=0.03$). [Conclusions] KFA influences the LLD more strongly than MAD before TKA, however, only MAD influences the LLD after TKA. It thought to be attributed to the improvement of the flexion contracture.

W75-3

The association between age at surgery and long-term clinical outcome of high tibial osteotomy

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Conflict of interest: None

[Object] The purpose of this study was to assess the association between age at surgery and clinical outcomes following HTO using the 2011 Knee Society Score System (KSS). [Methods] We mailed the 2011 KSS questionnaires to consecutive 80 knees who had undergone closing-wedge HTO, and 59 knees (73.8%) returned the complete questionnaire. The mean follow-up period was 12.2 years. The cohort was divided into two groups depending on the age at the time of surgery, and matched pairs were created according to follow-up period. The KSS scores at the final follow-up were compared between these groups and the survival rate using Kaplan-Meier were calculated. [Results] Symptom, satisfaction and expectation scores were not significantly different between 64 and under years old patients and 65 and over years old patients. The overall survivorship of HTO was 99.7% at five years, 96.5% at ten years and 85.2% at fifteen years. There was no significant difference in the survival rate after HTO between two groups divided by the age. [Conclusions] Pain relief and satisfaction after HTO in older patients were comparable to those in younger patients in the mid- to long-term follow-up, although the functional activity was affected by age.

W75-4

Revision Acetabular Reconstruction Using a Murata Chiba Support Ring and Cementless Cup: A Minimum of 15-Year Follow-Up

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Conflict of interest: None

[Object] The purpose of this study is to examine the clinical and radiographic outcomes of reconstruction of acetabular bone deficiency using iliac autografts supported by Murata-Chiba cup supporter (MC support ring) in a revision setting with minimum 15-year follow-up. [Methods] Fifty-nine consecutive revision total hip arthroplasties (57 patients) using the MC support ring were followed for a minimum of 15 years. Clinical outcomes were evaluated using the Japan Orthopaedic Association (JOA) hip score. Radiographic evaluation included assessment for loosening and bone graft incorporation. Kaplan-Meier survival analysis was performed. [Results] At a minimum 15-year follow-up (mean, 17.6 years), 32 patients (33 hips) were alive, 17 patients (18 hips) were deceased, and 8 patients (8 hips) were lost to follow-up. The mean JOA score improved from 53.8 to 72.8 at final follow-up. Four hips required reoperation. Incorporation of the bone graft occurred in all cases. Survivorship at 15 years with re-revision or radiographic failure as the end point was 90.6%. [Conclusions] The reconstruction of acetabular bone deficiency using autografts supported by an MC support ring provided satisfactory clinical and radiological results at 17.6 years postoperatively.

W75-5

Factual investigation for pinhole perforation of medical gloves occurring in orthopedic surgery

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Conflict of interest: None

[Background] The objective of this investigation is fact-finding the frequency of surgical glove perforations which may have improved as a sequel to functional improvement of gloves themselves. [Methods] Collecting spent gloves wore by surgeons and nurses in prosthetic replacement arthroplasties and spine surgeries, with excluding cases when they are replaced halfway through. [Results] Perforations were detected over half cases of prosthetic replacement arthroplasties, and their incidence rate is ranked in order of surgeons, first assistants, and scrub nurses. Also the fact had shown that orthopedic surgeries have higher incidence rate of perforations compared to other surgeries. [Conclusion] Incidence of glove perforations resulted in high rate of exceeding 50%, caused by contacting sharp-edged and heavy bones and instruments. Therefore, it appears to be mandatory, to double-glove and replace gloves during surgery to prevent postoperative infections.

W75-6

Complications after orthopedic surgery in patients with rheumatoid arthritis treated with biological agents

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Conflict of interest: None

[Object] The purpose of this study was to investigate complications after orthopedic surgery in patients with rheumatoid arthritis (RA) treated with biologics (BIO). [Methods] Forty patients treated with BIO underwent 52 operations and had follow-up more than 6 months were included in this study. Average age, disease duration and treatment duration with bio was 63 years, 14 years and 3 years, respectively. [Results] BIO used just before operation included abatacept (17), etanercept (16), adalimumab (6), golimumab (5), tocilizumab (4), infliximab (4). The mean values of CRP and DAS28-CRP before operation were 1.4 mg/dl and 2.5, respectively. Surgery included total knee arthroplasty (12), total hip arthroplasty (5), prosthetic replacement of finger joints (2), forefoot arthroplasty (10), osteosynthesis (6), spine surgery (4), arthrodesis (3),

synovectomy (3), wrist arthroplasty (3), removal of implants (3) and Dupuytren's contracture displacement (1). Postoperative complications included delayed wound healing (7), infection (2), pneumonia (1), reoperation (1). [Conclusion] The complication rate after orthopedic surgery was relatively high (23%) in patients with RA treated with BIO. Especially, delayed wound healing occurred commonly. Therefore, careful observation is necessary in those patients after surgery.

W76-1

The frequency of HTLV-1infection and adult T-cell leukemia in patients with rheumatoid arthritis at an endemic area in Nagasaki prefecture

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Conflict of interest: None

[Object] Three patients with RA developed adult T-cell leukemia (ATL) for 6 yeares. This study was undertaken to clarify the clinical characteristics of RA patients infected with HTLV-1 and the risk factors for development of ATL. [Methods] Sera from 1275 patients with RA were screened for HTLV-1 antibody using CLIA methods. [Results] 1. 106 patients (8.13%) were positive for anti-HTLV-1 ab. 2. The frequency of HTLV-1 carrier had a tendency to rise with age. The ages in RA onset were older in positive patients than negative patients. 3. The frequencies of anti-HCV ab positive and HBV resolved patients were higher in HTLV-1 carrier than those of HTLV-1 non-carrier. 4. The complications of pulmonary diseases such as pulmonary interstitial pneumonia and bronchiectasis, and uveitis were more frequancy in HTLV-1 carrier than those of non-carrier. 5. There were no differences of the positive percentages of RF, ANCA and ANF between HTLV-1positive and negative patients. 6. There were no differences in administration of DMARDs including PSL, MTX, and bDMARDs between HTLV-1carriers and non-carriers. [Conclusions] These findings suggested that HTLV-1 might be involved in the pathogenesis of a subset of RA patients, and the immunosuppressive treatments might be a risk factor of ATL in RA patients.

W76-2

The Risk Factors of Developing Adult T Cell Leukemia in Human T Cell Leukemia Virus Type 1 Positive Patients With Rheumatoid Arthritis in Endemic Area; A Retrospective Cohort Study

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Conflict of interest: None

[Objectives] The aim of this study is to investigate the time-sequential chnage of the risk factors of developing adult T cell leukemia (ATL) in human T cell leukemia virus type 1 (HTLV-1) positive RA patients in HTLV-1 endemic area Miyazaki, Japan. [Methods] We established HTLV-1 positive RA cohort study in Miyazaki from 2012. Disease modyfying anti-rheumatic durgs (DMARDs) including biologics were administrated in the all participants. We evaluated the levels of HTLV-1 proviral load (PVL) and the levels of soluble IL-2 receptor (sIL-2R) as risk factors of developing ATL. [Results] The prevalence of HTLV-1 infection in RA patients was 6.0 % in this cohort. In the distribution of PVL, 20% of HTLV-1 positive RA patients showed highly PVL (> 4%), which was the known risk factor for ATL. No effect to the levels of PVL and sIL-2R by the treatment with DMARDs was observed. A patient developed chronic type ATL, who were treated with MTX and inflixaimab during 3-years observation periods (121 person-years) in this cohort. [Conclusion] There is no impact of anti-rheumatic therapies against the risk factors of developing ATL. A long-term follow-up of HTLV-1 positive RA patients is required to resolve whether the comorbidity of RA and its treatment increase the risk of developing ATL.

W76-3

Clinical course and outcome of hepatitis B virus reactivation in fifty-seven rheumatoid arthritis patients with resolved infection -multicentre, prospective, observational study in Japanese Red Cross Hospitals-

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Conflict of interest: None

[Object] The guideline for HBV reactivation in Japan is based on the theory in which hepatic injury after reactivation was rapidly progressive and frequently poor prognosis. To investigate the clinical course and outcome of HBV reactivation in rheumatoid arthritis (RA) patients with resolved infection. [Methods] The HBV-DNA (RT-PCR) amount and related data were collected in RA patients with resolved HBV infection, treated with steroids, synthetic or biological immunosuppressive drugs. [Results] Among 1129 patients, 3500 person-years, detection of HBV-DNA were found in 57 patients, 1.63/100 person-years, and none of reactivated patients showed aggravation of hepatic function tests. Positivity more than 2.1 log copy/ml were seen in 15 cases, 0.43/100 person-years, in which seven patients were treated with nucleic acid analogue (NAA) and eight had been observed without medication during 10.5 months. Fifteen of reactivated patients, showed positivity more than 2.1 log copy/ml in 9.0 months after reactivation, and 42 patients, 73.7%, were not progressive during 27.5months observation. [Conclusions] Rapid aggravation or poor outcome is not frequent in HBV reactivation in RA patients. We should consider the reset of cut-off value of HBV-DNA for preventive therapy with NAA in guideline.

W76-4

Current investigation of influenza vaccination and infection in Japanese patients with juvenile idiopathic arthritis -Finding from nationwide survey for the core facilities specialized in pediatric rheumatism-

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Conflict of interest: None

[Object] The aim of this study was to evaluate the situation of influenza (Flu) infection and the effect of its vaccine in the patients with juvenile idiopathic arthritis (JIA) compared with the general population in Japan. [Methods] The questionnaires were sent to 13 pediatric rheumatology institutions. The questionnaire included questions concerning Flu attack, Flu vaccination and its side effects in the patients with JIA from Oct. 2016 to May 2017. [Results] A total 473 JIA patients (159 males; 34% and 314 females; 66%, mean age of patients; 13.3, range 2.4-37.3) were enrolled. Two hundred sixty eight (57%) patients took Flu vaccine and its side effects were observed in 58 patients (22%). Although 74 patients (15.6%) suffered from Flu, only 3 patients hospitalized with Flu. Disease activity of JIA flared in one patient after Flu infection. Influenza morbidity was significantly low in JIA patients compared with general population ($p<0.01$), and vaccination coverage over 13 y.o. was significantly higher than general population at the same age ($p<0.01$). These results may indicate that patients with JIA are highly aware of prevention for infectious diseases. [Conclusions] Flu vaccination can be recommended for patients with JIA as well as for general population.

W76-5

Effect of sulfasalazine use on the presence of Pneumocystis organisms in the lung among patients with rheumatoid arthritis: A test-negative design case-control study with PCR tests

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Conflict of interest: None

[Object] To evaluate the effect of sulfasalazine (SSZ) on the presence of *Pneumocystis jirovecii* in the lung in rheumatoid arthritis (RA) patients. [Methods] A retrospective study was conducted at Tokyo Metropolitan Tama Medical Center between 2003 and 2017. All episodes of suspected *Pneumocystis* pneumonia which were examined with polymerase chain reaction (PCR) of respiratory specimens for *Pneumocystis jirovecii* were enrolled. We employed a test negative case-control design; the cases were all episodes positive for PCR, and the controls negative for PCR. The odds ratio for the positive PCR result associated with SSZ use was estimated by Firth's logistic regression. [Results] We identified 36 cases and 83 controls. While none of cases received SSZ, 18 of controls received the drug. In the analysis involving all episodes, SSZ use was negatively associated with the PCR positivity (adjusted odds ratio 0.086, confidence interval <0.001-0.802). The analysis excluding 16 controls who received PCP prophylaxis showed the same association as the primary analysis (adjusted odds ratio 0.085, 95% CI <0.001-0.791). [Conclusions] Our study demonstrated that SSZ use is associated with the absence of *Pneumocystis* organisms in the lung, suggesting the preventive efficacy of the drug against PCP.

W76-6

MTX and a steroid are an important risk factor of Pneumocystis pneumonia development in rheumatoid arthritis patients

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Conflict of interest: None

[Object] Impossible to culture Pneumocystis, so Pnuemocystis's reality is still unclear, and we may treated suspicious case. We performed risk of Pneumocystis pneumonia (PCP) in rheumatoid arthritis (RA) patient. [Methods] In RA patients with acute or subacute IP who are treated in 2011/10/1-2017/8/15 at our hospital, βD-gulucan accomplice more than 11, PCR in septum or BAL (+) and CT view and the elapse which agree with the acuteness PCP, more than 2 of inside was considered by filled 20 examples. LDH, βD gulucan, age and more were shared with 2 flights and MTX, Bio and steroid (Prednisolone: PSL) use considered in statistical way to calculate risk of PCP death. Next, for examine PCP development risk, many objective considered made 506 examples of RA case in 2013 the contrasting group. [Results] Three died by PCP. Only PSL>10 mg use when developing PCP is significant death risk, and no other factor were significant relations. Next examine, age, pulmonary pathological change, MTX and PSL use were high risk for PCP development, and in particular, MTX was very high risk (odds ratio 14.04, $p<0.001$). SASP is low risk intentionally, and risk rises in PSL, by PSL>5mg (odds ratio 12.10, $p<0.001$). [Conclusions] a risk case such as steroid use or MTX should use trimethoprim-sulfamethoxazole.

W77-1

Quantitative analysis of thocacic CT images for connective tissue disease associated interstitial pneumonia -2nd report-

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Conflict of interest: None

Objective: Previously, we reported that a novel method of quantitative analysis of CT images (AZE Virtual Place) was applied for the quantitative diagnosis of interstitial pneumonia (IP) in PM/DM patients. In this study, we performed the same analysis on a new population of PM/DM and SSc, in order to investigate the reproducibility of the procedure. **Methods:** The subjects were 22 PM/DM and 23 SSc who were examined by AZE Virtual Place between 2010 and 2017. The total volume of the lung field was integrated and the CT value of each 100 Hounsfield units was divided by the total volume, which was defined as the relative volume of each regions. We investigated correlations between the each relative volume and with or without IP. **Results:** In the PM/DM group, relative volumes were significantly higher in the -800 to -201 regions in IP group. In particular, we reconfirmed in which regions from -700 to -301 that have greater relative volumes than the cutoff value is a high IP diagnostic capacity. In the SSc group as well, relative volumes were significantly higher in the -700 to -301 regions with IP group. **Conclusion:** In the each group, it was confirmed that IP could be diagnosed quantitatively using the same procedure as in the previous study.

W77-2

Clinical and therapeutic differences between pathologically proven interstitial pneumonia with autoimmune features-usual interstitial pneumonia (IPAF-UIP) and pathologically proven CTD-UIP

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Conflict of interest: None

[Object] Interstitial pneumonia with autoimmune features (IPAF) is a disease concept for interstitial pneumonia; however, clinical course in patients with IPAF and histological UIP (h-UIP) pattern has not been fully evaluated. We compared the clinical characteristics between IPAF-h-UIP and CTD-h-UIP. [Methods] We retrospectively reviewed consecutive patients with pathologically defined UIP, and those fulfilled the IPAF criteria or CTD criteria were included in the study. Clinical characteristics, treatment option, one-year treatment response, and survival were reviewed. [Results] Sixty-six patients fulfilled the IPAF criteria and 31 patients fulfilled the CTD criteria. There were less women in IPAF but age, %FVC, and %DLco were not significantly different between the two groups. Thirty-three patients treated with immunosuppressants (IPAF in 19 (29%), CTD in 14 (45%)). After 1 year of immunosuppressive therapy, 15/19 (79%) patients with IPAF and 14/14 (100%) patients with CTD

had improved or stable (p=0.07). During the study period 14 patients experienced an acute exacerbation (12 in IPAF, 2 in CTD, p=0.09). After adjustment for age and %FVC, IPAF was a predictor of survival time (HR 3.5, p=0.02). [Conclusions] IPAF-h-UIP showed a poorer prognosis than that of CTD-h-UIP.

W77-3

Usefulness of bronchofiberscopy for chest abnormal shadow in rheumatoid arthritis in our hospital

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Conflict of interest: None

[Object] To examine the background that bronchofiberscopy (BF) contributes to the final diagnosis of chest abnormal shadow in patient with rheumatoid arthritis (RA). [Methods] Background, CT images, final diagnosis, complications in RA patients who underwent BF in our hospital from January 2013 to July 2017 were analyzed retrospectively. [Results] 75 patients underwent BF. Final diagnosis based on findings obtained from BF was infectious disease in 20 cases, interstitial pneumonia in 18 cases, malignant tumor in 10 cases and other diseases in 3 cases. 24 patients (32.0%) were undiagnosed. Background (age, gender, duration of RA, class, class, DAS28-CRP, treatment of RA, prevalence of existing lung diseases) did not show any significant difference between the diagnosable group and the undiagnosed group. CT images showed consolidation (C) in 30 cases, ground glass shadow (GGO) in 23 cases, nodular shadow (N) in 10 cases, granular shadow (GS) in 10 cases and other (O) in 2 cases. Diagnostic rate based on the findings obtained with BF were C;53.3%, GGO;39.1%, NS;90.0%, GS:50.0%, O;50.0%. [Conclusions] BF for chest abnormal shadow in rheumatoid arthritis was useful in about 70% of cases in our hospital. Our result suggests that the CT image pattern contributes to the final diagnosis by BF.

W77-4

The prognosis prediction factor and different mortalities in pulmonary arterial hypertension associated with various connective tissue diseases

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Conflict of interest: None

[Object] CTD-PAH, especially SSc-PAH is one of the life-threatening diseases. We investigated the prognosis prediction factor and the cause of death in CTD. [Methods] The PAH patients were enrolled in 2000-17, with pSS 6, SLE 14, MCTD 7, and SSc 13 overlapping 7 of SS. We evaluated right-heart catheterization and WHO functional classification. Pulmonary vasodilators and PSL+ IVCY were carried out in pSS 6, SLE 12, MCTD 5, SSc+SS 4. The short-term therapeutic effect was described as Responder having more than 1 WHO class improvement or mPAP normalization. [Result] Responders were pSS 67, SLE 79, MCTD43, SSc alone 50, SSC+SS 100%. The morbidity of the long-term period were pSS 0, SLE14, MCTD29, SSc alone 67, and SSc+SS 29%. The causes of death in SLE and MCTD were PAH with WHO IV, portal hypertension, and infection after pulmonary transplant. In SSc, those were progressive PAH, interstitial pneumonia (IP), renal crisis, and infection after traumatic injury. Additionally, those were intestinal obstruction and aspiration pneumonia in SSc+SS. [Conclusions] We could expect long-term prognosis by the Responder in pSS, SLE, but not in SSc. Because SSc have characteristic for progressive change in vessel, left heart failure, IP, and intestinal obstruction, they still have higher morbidity.

W77-5

The Clinical Features of Rheumatoid Arthritis Patients with Diabetes Mellitus

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Conflict of interest: None

(Background) With aging of Rheumatoid Arthritis (RA) patients, it is expected that RA patients with Diabetes mellitus (DM) increase. (objectives) To clarify the clinical features of RA patients with DM. (Method) We compared 41 cases of DM and 166 cases of non-DM out of 207 RA patients (average age 66.4 years old,48 male, DAS28CRP 2.13) in outpatients in our hospital. (Results) The mean age of DM cases was older than non-DM cases. (71.9vs65.0 years old, p<0.01). The proportion of corticosteroids (CS) used in DM cases was more frequent than non-DM cases (65.9vs45.8%, p=0.01). The amount of CS used in DM cases was greater than non-DM cases (6.3vs2.5mg, p<0.01). In DM cases, the proportion **o**f biological DMARD used and statins used were more frequent than non-DM cases (36.6vs18.7%, p=0.02 and 39.0vs18.1%, p=0.01). The proportion of methotrexate (MTX) used in DM cases was smaller than non-DM cases (58.5vs65.7%, NS) and the amount of MTX used in DM cases was lesser than non-DM cases (4.1vs5.2mg, NS). (Conclusion) RA patients with DM were older than without DM. The amount of CS used in in DM cases were greater and statins, CS and biologic DMARD were used more frequently than non-DM cases. The amount of MTX used in DM cases were lesser than non-DM cases.

W77-6

The Relationship between the Serum Oxytocin Levels, Disease Activity, the ADLs and the QOL in Patients with Rheumatoid Arthritis complicated depression

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Conflict of interest: Yes

[Object] To investigate the factors associated with depression, including the serum oxytocin (OXT) levels, disease activity, ADL and QOL, and their effects on RA. [Methods] This study included 42-RA-patients. We measured the following variables before treatment with bDMARDs: the baseline characteristics (including age, sex, disease duration, smoking, and BMI), the doses of prednisolone and methotrexate. The disease activity of RA was assessed using the SDAI, depression was assessed using the Hamilton Depression Rating Scale (HAM-D), the ADLs were assessed using the HAQ-DI and the QOL was assessed using the Short Form (SF)-36. The serum OXT levels were determined using an ELISA. [Results] The HAM-D score was significantly correlated with the SDAI, and the mental component summary score (MCS) of the SF-36. However, the serum OXT levels were not correlated with the HAM-D score. The serum OXT levels did not differ to a statistically significant extent, regardless of the presence of depression. Although physical component summary and MCS were identified by multiple regression analysis with HAM-D as the objective variable, but OXT was not selected. [Conclusions] Although RA complicated by depression may be related to the following a poor QOL, the serum OXT levels may not directly correlated.

W78-1

Investigation of the risk of developing non-tuberculos mycobacterial (NTM) infection in patients with rheumatic diseases

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Conflict of interest: None

Objective: To identify the characteristics of the development of NTM infection in patients with rheumatic diseases. Methods: 20 patients were enrolled in this study by meeting the diagnostic criteria of NTM infection. For control, 40 patients were extracted from age, sex, and rheumatic diseases. The medical records of enrolled patients were retrospectively reviewed. Results: Significant difference was found in predominant pulmonary complication (90% vs. 40%, p = 0.0002), especially bronchiectasis (65% vs. 30%, p = 0.013) between the NTM patients and the control patients. Immunological state including peripheral blood leukocyte (6575±1946 /μl versus 5955±1656 /μl; p = 0.19) and the serum IgG level (1278±327mg / dl versus 1319±536mg / dl; p = 0.87) were comparable, but lymphocyte counts (1089±463 /μlversus 1420±513 /μl; p = 0.024) was decresed. Conclusion: NTM infection in patients with rheumatic diseases is likely to develop on the dysfunction of pulmonary barrier rather than the systemic immune state.

W78-2

Association between nontuberculous mycobacterium infection and biological agents in rheumatoid arthritis: single center, retrospective cohort study

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Conflict of interest: None

[Objective] To investigate prognosis of rheumatoid arthritis (RA) patients with nontuberculous mycobacterium (NTM) infection. [Methods] We conducted a retrospective, single center cohort study. All RA patients who were regularly followed up at our division in December 2012 were included. Medical record review was performed in December 2016. We defined exacerbation of NTM as the condition in which pulmonologist had started or changed treatment for NTM. [Results] Among 1648 RA patients, 26 patients had NTM infection at baseline. During observation period, a total of 43 patients died, 41 without NTM and 2 with NTM. NTM infection at baseline were not associated with worse mortality by multivariate analysis (hazard ratio, 2.3; 95% confidence interval, 0.4-7.6; p=0.30). We identified 9 patients with newly diagnosed NTM. Among all 35 patients with NTM infection, 13 patients were treated with a total of 18 biological disease-modifying antirheumatic drugs (bDMARDs) after NTM diagnosis. Patients treated with bDMARDs did not show worse exacerbation of NTM than those without bDMARDs (31% vs 14%, p=0.38). [Conclusions] Patients with NTM did not show worse mortality and bDMARDs were not associated with NTM exacerbation. Careful use of bDMARDs could be tolerated in RA patients with NTM.

W78-3

The clinical course of patients with biologics-treated rheumatoid arthritis complicated with nontuberculous mycobacterial lung infection

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Conflict of interest: None

[Objective] The use of biologics (bio) in rheumatoid arthritis (RA) with lung nontuberculous mycobacterial infection (LNTMI) is not recommended. On the other hand, some Japanese case series of RA with LNTMI after bio-treatment had shown the acceptable outcomes. We investigated the clinical course of patients with bio-treated RA with LNTMI. [Methods] We retrospectively collected the clinical data between 1 Jan 2011 and 31 Mar 2017. The diagnosis of LNTMI was made in accordance with the criteria of related societies. [Results] During investigation period, 13 LNTMI-RA patients (10 were female) were administered bio. Their mean age was 71 years old. The duration between the RA diagnosis and the occurrence of LNTMI was from 1 to 40 years. The species of NTM were *M. avium* (12 cases) and *M. intracellulare* (1 case). Twelve cases had treated with glucocorticoid. Five of 10 had continued bio after diagnosis of LNTMI. All the 3 of 13 cases who first received bio after diagnosis of LNTMI were treated with abatacept. During 3.6 years of the average observational period after LNTMI, 10 were alive and 3 died, of which causes were not associated with LNTMI. [Conclusions] Even if LNTMI-RA, we might treat them by non TNF-α inhibitor carefully, considering whether NTM pathogen is rapid growing or not.

W78-4

The positive rate of IGRA in the diagnosis of latent TB in rheumatoid arthritis patients depends on CD4, CD8, peripheral lymphocyte count

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Conflict of interest: None

[Object] We report that peripheral lymphocytes regulate the response of QFT-Plus and T-SPOT, as the number of lymphocytes, especially CD4, CD8 positive lymphocytes decreases and the positive rate of IGRA tends to decrease. [Methods] QFT-Plus and T-spot were performed on 154 patients undergoing rheumatoid arthritis treatment. Blood count test, CD4, CD8 positive cell ratio, relationship with medication during administration were examined at the same time. [Results] IGRA positive cases best reflected IGRA positivity when CD4 and CD8 cut off values were 684 / μL and 415 / μL or more, respectively. Peripheral lymphocyte count and CD4, CD8 showed positive correlation. The cut off value of the peripheral lymphocyte number showing the positive of IGRA was 1200-1400 / μL. [Conclusions] There is a possibility of underestimating IGRA when the number of lymphocytes decreases, because the positive rates of QFT-Plus and T-SPOT in the diagnosis of latent TB in rheumatoid arthritis patients are affected by the peripheral lymphocyte count. A correlation was found between QFT-Plus and steroid usage. There was a possibility that the difference in the amount of steroid use between positive patients and negative patients of QFT-Plus could have influenced the peripheral lymphocyte count.

W78-5

Periodontal treatment decreases rheumatoid arthritis activity and serum carbamylated protein level

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Conflict of interest: None

[Object] Periodontal disease has been suggested as an environmental risk factor for rheumatoid arthritis (RA). We had previously reported the beneficial effect of periodontal treatment on RA activity and serum levels of citrullinated protein. Recent studies indicated an association between serum carbamylated protein (CarP) and RA. Thus, we aimed to evaluate the effect of periodontal treatment on serum CarP level in patients with RA. [Methods] We evaluated rheumatologic and periodontal parameters, and serum CarP levels by sandwich ELISA in 39 patients with RA, 30 patients with chronic periodontitis (CP), and 43 healthy controls. Of these, 23 patients with RA who received periodontal treatment were subjected to the same clinical and laboratory evaluations after 8 weeks of treatment. [Results] Demographic parameters did not differ among the RA, CP and control groups. Both the RA and CP groups showed significantly higher serum levels of CarP than the control group. A significant decrease was observed in RA activity, as indicated by DAS28-CRP, and serum CarP level after 8 weeks of treatment. [Conclusions] Periodontal treatment decreases RA activity and serum CarP level in patients with RA, reflecting a role of periodontal disease in the protein carbamylation

in relation to RA.

W78-6

The localization of ACPA derived from RA patient in periodontal tissue of mouse periodontitis model

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Conflict of interest: None

[Object] Periodontal disease (PD) is the chronic inflammatory disease caused by periodontopathogenic bacteria. *Porphyromonas gingivalis* (Pg) infection is known as the major pathogenic factor of systemic diseases. Our group established the RA model mouse (SKG mouse) with Pg infection (Pg-RA mouse). The cause of exacerbation of RA by Pg was the activation of osteoclastogenesis (OCD) in Pg-RA mouse. Along with RANKL and M-CSF, immunecomplec (IC) is also important in the activation of OCD. However, it is unclear that the involvement of IC derived from citrullinated protein (CP) and IC in the progression of OCD. In this study, the involvement of Pg which is the majour source of endogeneous CP in bacterial species in the systhesis of IC in the periodontal tissue. [Methods] In order to determine the localization of ACPA, Pg infected mouse PD model was established. After 2 weeks of the occur of PD, ACPA was adaptive transferred from intravenously. Then, the distribution of ACPA in periodontal tissue, spleen, and serum was measured by ELISA [Results] The distributions of ACPA in periodontal tissue, and spleen were observed in Pg infected periodontitis mouse [Conclusion] The possibility of the involvement of IC from ACPA and CP generated by Pg in periodontal tissue was observed Pg-RA mouse.

W79-1

Investigation of Axial PsA and Peripheral PsA using ASAS classification criteria

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Conflict of interest: None

[Object] Spondyloarthritis (SpA) is classified into two domains, Axial-SpA and Peripheral-SpA, by ASAS (Assessment in Ankylosing Spondylitis) classification. We classified psoriatic arthritis (PsA; psoriatic arthritis) into Axi-PsA and peripheral-PsA using the ASAS classification criteria and examined the difference. [Methods] Targeted PsA patients (2003-2014) in 3 hospitals Collaborative nonintervention in other institutions Cross-sectional study was conducted. PsA patients (satisfying CASPAR criteria) in psoriasis patients were included. Cases matching the ASAS classification criteria were divided into two groups and age of onset of psoriasis and PsA / smoking / obesity, psoriasis family history / Comparison of nail lesions / finger flame / presence of tendon sticking flames, blood biochemical test (rheumatoid factor, ACPA, CRP), comorbidities did. [Results and Conclusions] Of 3021 patients with psoriasis, psoriatic arthritis was 431 people. There were 282 cases in which classification by ASAS was possible, among which 98 for Axial-PsA and 184 for peripheral-PsA. In Axial-PsA, obesity / nail lesion / digituminus / enthesitis / CRP positive was abundant, and smoking and diabetes were many in Peripheral-PsA.

W79-2

Investigation on increasing and switching TNF inhibitor in ankylosing spondylitis

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Conflict of interest: Yes

[Object] In Japan, treatment of TNF inhibitor against ankylosing spondylitis (AS) can be used only infliximab (IFX) and adalimumab (ADA). As AS differs from rheumatoid arthritis, there are only two drugs can be selected, so in cases with ineffectiveness even with treatment with biological agents, we often have difficulties with the next treatment. In this study, we compared the efficacy of TNF inhibitor increasing (ADA 80mg administration) and switching in our hospital. [Methods] There were three cases in which ADA was increased, and five cases biological agents were switched (ADA→IFX 1 cases, IFX→ADA 4 cases). Patient profiles, changes in disease activity (BASDAI, ASDAS) were compared at the biginning of administration, at the time of ADA increase or at the time of biological agent switched, and after 24 weeks thereafter. [Results] In 3 cases of ADA increasing, BASDAI was improved in 2 cases and not improved in 1 cases. In 5 cases of biological agent switching, average BASDAI was 6.06 at switching and 1.72 at 24 weeks. [Conclusions] Although the number of cases was small, there were an effective cases of increasing the dosage when the effect of ADA was insufficient. Increasing ADA was considered to be an option for AS treatment along with switching biological agents.

W79-3

Clinical characteristics of spondyloarthritis (SpA) in Japanese patients

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Conflict of interest: None

[Object] To evaluate clinical characteristics commonly manifested in Japanese SpA patients in COMOSpA database. [Methods] Descriptive statistics of patient demographics, clinical characteristics of SpA, comorbidities, and potential risk factors are provided in the Japanese subgroup comparing with those in rest of Asian countries and other countries. [Results] Among 3984 patients included in the study, 161 were from center in Japan, 933 were other Asian nations (China, Taiwan, South Korea, and Singapore), and 2890 were from United States, Europe, and Africa. Mean ages for each group were 48.8, 36.95, and 45.51, and female percentages were 33.5, 22.2, and 39.3%, respectively ($p<0.001$). Radiographic axial SpA patients were significantly fewer in Japanese patients (50.9, 75.5, and 60.6%, $p<0.001$). In contrast, peripheral SpA was more common in Japanese patients (28.6, 5.7, and 15.5. %, $p<0.001$). Psoriasis was also more common in Japanese patients (38.5, 6.1, and 20.0%, $p<0.001$). Functional status (BASFI) and disease activity (BASDAI) tended to be lower in Asian patients compared to non-Asian patients. [Conclusions] Japanese SpA patients demonstrated unique clinical pictures compared to

other Asian and non-Asian countries.

W79-4

The assessment about sacroiliitis and the other axial involvements in psoriatic arthritis

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Conflict of interest: Yes

[Object] 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 lumbar findings in PsA with sacroiliitis and a significant limitation in range of motion. Now we assessed about cervical involvements and sacroiliitis. [Methods] Enrolled fifty-six patients with PsA were classified into with or without sacroiliitis by X-ray, and also into differences with the lumbar and the cervical findings. We compared with those about ASDAS, BASDAI, BASFI and BASMI, and the imagings. [Results] About 39% were sacroiliitis. There were 57% in the lumbar and 58% in the cervical. There was no relation between sacroiliitis and ASDAS, BASDAI and BASFI. But PsA with sacroiliitis was with higher lumbar mSASSS (P=0.03) and higher cervical mSASSS (P<0.0001), and related with BASMI (p=0.002), and higher CRP (P=0.013). PsA with the cervical and the lumbar findings were the same results except CRP. But both arms were higher at age. There was significant difference about proportion with sacroiliitis in the cervical, but not in the lumbar. [Conclusions] PsA with sacroiliitis were significant changes of imaging in the lumbar and the cervical.

W79-5

A cross-sectional study about progression of axial involvement of psoriatic arthritis

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Conflict of interest: None

[Object] To evaluate progression of axial involvement in PsA patients including comparison with AS patients in a cross-sectional manner. [Methods] Spinal radiographs of 35 patients with PsA with spinal involvement and those of 15 patients with AS were evaluated by mSASSS. The relationship between clinical characteristics and progression of spinal involvement was examined. [Results] The mean age/ disease duration/ %sacroiliitis at evaluation in PsA and AS were 57.7/48.1 years, 13.1/17.7 years, and 42.8/100%, respectively. There was a positive correlation between mSASSS levels and disease duration in patients with PsA (y=0.93x+1.5), indicating that increase in mSASSS per year was 0.93. In patients with AS was 1.1. No significant difference was found between them by covariance analysis (p=0.78) In PsA patients with sacroiliits, ΔmSASSS/year was 0.96 (n=15) that was not significantly different from that in PsA without sacroiliitis (0.68, n=20) (p=0.43). ΔmSASSS/year in male and female patients were 1.46 and 0.11, respectively, and there was a significant difference between them (p=0.007). [Conclusions] This cross-sectional study may indicate that the progression rate of axial involvement in PsA was similar to that of AS, and gender difference may affect the progression.

W79-6

Significantly Higher Frequency of HLA-B61 in Patients with Axial Spondyloarthritis (SpA)

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Conflict of interest: None

[Object] Genotypic characterization of the HLA class I gene was performed in patients diagnosed with axial SpA at our hospital. [Methods] PCR-rSSO was used to characterize the HLA-B typing of 55 patients who were classified as having axial SpA according to the ASAS classification criteria at our hospital between February 2015 and August 2017. [Results] Patients diagnosed with axal SpA included 17 men and 38 women. B27 was positive in two cases. Alleles found to be positive in five or more cases were B61 (23 cases); B54 (13 cases); B7, B46, and B51 (9 cases each); B35 and B62 (8 cases each); and B60 (6 cases). Among the HLA-B alleles, only B61 occurred at a relatively high frequency, accounting for positivity in 42% of the total number of cases. This demonstrates a significant difference from the 24% of B61 positivity in the general Japanese population according to the HLA laboratory data ($P < 0.001$). [Discussion] B60 and B61, the major subtypes of B40, are known to increase the risk of ankylosing spondylitis (AS) among Caucasian patients whose HLA-B60 is B27-positive. A survey in Taiwan reported that in B27-negative patients, B60 and B61 alleles were strongly associated with AS. [Conclusions] Our findings also suggest that HLA-B61 is a potential risk factor for axal SpA onset.

W80-1

Recent characteristics of the patients with extensor tendon rapture caused by rheumatoid arthritis

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Conflict of interest: None

[Object] To investigate the characteristics of patients who underwent surgeries for extensor tendon ruptures caused by rheumatoid arthritis (RA). [Methods] Consecutive 116 cases of wrist surgeries performed from 2004 to 2017 were included. We investigated the existence of tendon ruptures, mean age, disease duration, serum CRP level and medications. Joint destruction was evaluated by Larsen grade and Shulthess classification. We compared them between tendon rupture (+) group and rupture (-) group, as well as the former (2004-2009) and later cases (2010-2017). [Results] Tendon ruptures were observed in 54 cases. The rate of rupture (+) group within all wrist surgeries showed no obvious changes in this period. There were no significant differences in patient characteristics between rupture (+) and rapture (-) groups. However, mean CRP levels were lower after 2010 in both groups. In rupture (+) group, Shulthess Type III deformity were observed in fewer cases in 2010-2017 group. Cases with type I and type II deformities showed significantly lower CRP levels, lower late of glucocorticoid use and higher late of bDMARD use. [Conclusions] In our department, surgeries for extensor tendon rupture of RA have not been decreased. But their joint destruction patterns may have changed by bDMARD use.

W80-2

The effect of extensor pollicis brevis insertion pattern on thumb boutonniere deformity in the rheumatoid arthritis

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Conflict of interest: None

[Object] The aim of the current study was to evaluate extensor pollicis brevis (EPB) insertion pattern macroscopically and histologically using cadaveric thumbs, and to compare its incidence with that of rheumatoid arthritis (RA) patients. [Methods] We investigated 103 fingers (50 right and 53 left) of 58 adult cadavers (25 males and 33 females). Next, we reviewed the surgical records of 24 fingers of 19 RA patients with thumb boutonnière deformity. [Results] Macroscopically, the EPB insertion pattern was classified into two types: the EPB ending at the level of the MCP joint (Type P); and the EPB ending at the level of the IP joint (Type D). In the cadaveric fingers, 71% (n = 73) of the fingers were Type P fingers and 29% (n = 30) were Type D. In the RA patients with thumb boutonnière deformity, 33% (n = 8) of the fingers were Type P, while 67% (n = 16) of the fingers were Type D. The incidence of Type D was significantly higher ($P < 0.05$) in the thumbs of patients with RA and boutonnière deformity than in the cadaveric thumbs. [Conclusions] Our results suggested EPB insertion into the distal phalanx might be a potential risk of thumb boutonnière deformity in RA.

W80-3

Morbidity of shoulder destruction and assessment of shoulder function in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] The purpose of this study is to assess morbidity of shoulder destruction and shoulder functions in patients with RA. [Methods] Among 500 shoulders, we investigated shoulder pain, disorder of range of motion (ROM). If the patients have pain and/or ROM disorder, we took X-ray of the shoulder and assess the joint destruction grade according to Larsen grading scale. In term of upper extremity function, we used mHAQ. [Results] 90 shoulders (18.0%) had pain and/or ROM disorder. Especially, 76 patients (15.2%) had bi-lateral shoulder dysfunction. 79 shoulders (15.8%) had ROM disorder. 39 shoulders (7.8%) had ROM disorder although the patients did not have pain. Rotator cuff tear are seen in 29 shoulders with ultrasonography. X-ray was performed in the cases with pain and/or ROM disorder. According to Larsen grade, grade 1 was one shoulder, grade 2 was 6 shoulders, grade 3 was 31 shoulders, grade 4 was 29 shoulders and grade 5 was 23 shoulders. 12 shoulders were not able to wash their hairs according to mHAQ and most of them were Larsen grade 5. [Conclusions] Morbidity of shoulder destruction in patients with RA was 18.0% and bi-lateral morbidity was 15.2%. Most of them who could not wash their hairs were Larsen grade 5.

W80-4

The results of synovectomy in the rheumatoid elbow

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Conflict of interest: Yes

Object: We report on cases synovectomy for RA elbow joint disorder in our department. **Method:** 37 cases 49 elbow joints (4 males, 33 females), the average age at the time of operation is 60.9 years, and the average period of postoperative period is 9.3 years. The operation entered from the outside, the radial head was excised and the synovectomy was performed. For cases in which postoperative follow-up was possible, we examined the presence of swelling / pain, the change in range of joint movement, and the elbow joint function was evaluated. **Results:** The postoperative swelling and pain decreased, the range of movement of the elbow joint before and after surgery improved from 109.1° before operation to 133.4° postoperatively, extension from -32.3° before operation to -20.9° postoperatively, A functional range of movement was obtained. Evaluation of RA elbow joint function also showed significant improvement after surgery. **Discussion:** Since the elbow joint synovectomy is relatively small in surgical invasion, good results can be obtained by performing rehabilitation from the early postoperative day. Therefore, for the elbow joint disorder resistant to conservative treatment, joint destruction It seems useful regardless of the degree of progress.

W80-5

The effects of surgical intervention on body image in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] We aimed to investigate the change in body image (BI) before and after surgery in patients with rheumatoid arthritis (RA). [Methods] Seventy-seven RA patients who do not require surgery (non-surgery group) and 102 RA patients who underwent orthopaedic surgery (surgery group) were included in the current study. All patient completed the total 22 questionaries for BI using body image assessment tool (BIAT) before and 6 months and one year after the surgery in the surgery group. BI was also investigated in patients in non-surgery group at baseline, 6 months and one year later. [Results] Of the four categories in BIAT, Body-Cathexis (CATH), Body-Control (CONT) and Body-Esteem (ESTM) in the surgery group were lower than those of the non-surgery group. CATH, CONT and ESTM improved at 6months, and Body-Depersonalization (DEPER) improved at 1year after the surgery in the surgery group. [Conclusion] BI gradually improved during one year after surgery, but time required for significant improvement was different in each category. As BI can be constantly changing, it would be important for medical staff to assist the patients to accept their BI positively and spontaneously.

W80-6

Investigation of preoperative intranasal colonization in orthopedic surgery in rheumatoid arthritis

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Conflict of interest: None

[Object] Coagulase-negative staphylococci (CoNS) is listed as the major SSI causative organism in orthopedic surgery, but detailed report on the presence or absence of methicillin-resistant CoNS of intranasal colonization is not found. Last year, we reported on active surveillance of intranasal colonization in patients scheduled for the orthopedic surgery of 270 patients at our hospital (JCR 2017). I will do an additional report of 1000 cases this time. [Methods] From July 2016 to the end of July 2017, 1000 cases of consecutive cases in which nasal cavity culture was performed within one month prior to hospitalization for patients scheduled for our orthopedic surgery. 223 men, 777 women, average age 66.4 years old, 197 cases of RA patients, 803 cases except RA patients [Results & Conclusion] The results of intranasal culture showed that S.aureus, S.epidermidis, CoNS (excluding S.Epidermidis) and culture negative

were 18.2, 27.8, 7.8 and 23.9%, respectively. MRSA, MRSE and MR-CoNS (excluding MRSE) with methicillin resistance were 3.2, 22.1 and 1.7%, respectively, and 27.0% of methicillin resistant bacteria were found to exist Especially in patients with RA, the methicillin-resistant bacterial colonization rate was significantly higher ($p<0.05$) than 38.6% compared with 24.2% other than RA patients.

W81-1

Hypocomplementemia is closely related to IgG subclasses other than IgG4 in IgG4-related disease

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Conflict of interest: None

[Object] This study aimed to clarify the clinical significance and mechanisms of hypocomplementemia in IgG4-related disease (IgG4-RD) using a large-scale cohort of 328 patients (pts). **[Methods]** We retrospectively evaluated clinical features including serum IgG-IgG4 levels at diagnosis in 328 IgG4-RD pts. Multivariate logistic regression analysis was performed to search factors related to hypocomplementemia. **[Results]** The pts comprised 201 men and 127 women (average age 63.9 years). At diagnosis, hypocomplementemia was observed in 138 pts. Multivariate logistic regression analysis in all pts indicated that elevation of IgG-IgG4 levels and the presence of pancreatic lesions were independent factors related to hypocomplementemia. Of note, the same analysis in pts with IgG4-RKD showed only elevation of IgG-IgG4 levels was an independent factor, whereas the pancreatic lesion was an independent factor in pts without IgG4-RKD. In IgG4-RKD, the pts with hypocomplementemia showed exacerbation of hypocomplementemia and re-elevation of IgG-IgG4 levels at relapse of renal lesions, while the pts without it did not. **[Conclusions]** This study shows that hypocomplementemia is related to elevation of IgG subclasses other than IgG4 in IgG4-RD, especially IgG4-RKD.

W81-2

Impact of environmental factors and comorbid conditions on serum IgG4 levels and progression to IgG4 related diseases in Japanese population

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Conflict of interest: None

[Objective] The epidemiology of IgG4 related disease (IgG4-RD) is unknown. Allergies and cancer may be associated factors, however, there is no report regarding these issues in general population [Methods] 569 serum IgG4 was measured by the nephelometric assay in Ishikawa. Inquiries about cancer, allergies, blood tests such as IgE and kidney function were performed, and cases of IgG4 135 mg/dl or more were examined for IgG4-RD. In Nagasaki, 1324 serum IgG4 was analyzed by the array method, and analyzed in the same way. [Results and Conclusions] The average IgG4 value in Ishikawa area was 44.3 mg/dl (3 to 254 mg/dl). Serum IgG4 was significantly higher in males, and correlated with IgE value, inversely correlated with systolic blood pressure and eGFR. 18 cases (3.2%) with IgG4 135 mg/dl or more were noted, and 10 subjects examined. One case showed chronic kidney disease with hydronephrosis, periaortitis, and retroperitoneal fibrosis, and diagnosed with a suspected IgG4-RD. In Nagasaki, cases of equivalent value of IgG4 135 mg/dl or more was 2.6%, and IgG4 value tended to correlate with eGFR decrease. The ratio of high IgG4 cases in Ishikawa and Nagasaki is similar, and it is considered that the regional difference in Japan is small.

W81-3

The clinical features of patients with IgG4-related retroperitoneal fibrosis requiring ureteral stents

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Conflict of interest: None

[Object] To examine the clinical features of patients with IgG4-related retroperitoneal fibrosis (IgG4-RPF) requiring ureteral stents. [Methods] Among 17 patients with IgG4-RPF treated at Nagaoka Red Cross Hospital between 2004 and 2017, we retrospectively examined the clinical features and clinical courses of those who required ureteral stents. [Results] Five of the patients required double J stents (3 males and 2 males in their sixties to seventies). The diagnosis of IgG4-RPF was definite in only one of them, and possible in the others. In 3 patients showing bilateral hydronephrosis, back pain was a common symptom and renal function improved rapidly after placing of the double J stents. In 2 patients with unilateral hydronephrosis, renal dysfunction was not improved by stenting alone, but gradually improved with subsequent steroid therapy. Retroperitoneal mass was rapidly reduced after the start of steroid therapy in all patients, and it was possible to remove the ureteral stents within 1 year in most cases. However, in one case bilateral hydronephrosis relapsed after steroid withdrawal. [Conclusions] Although steroid therapy is quite effective for IgG4-RPF, relapse can occur during steroid tapering, and careful long-term follow-up is necessary.

W81-4

Expression of CCL18-CCR8 signaling in affected tissues of IgG4-related disease

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Conflict of interest: None

[Object] To clarify the protein expression and expressing cells of CCL18 and its receptor CCR8 in affected tissues of IgG4-related disease (IgG4-RD). [Methods] 1) The protein expression and expressing cells of CCL18 in labial salivary glands (LSGs) were compared between IgG4-RD (N=3), Sjögren's syndrome (SS) (N=4), and healthy controls (HC) (N=5) by immunofluorescence (IF) staining. 2) The expression of CCL18 was compared between cellular and fibrotic lesions in lacrimal glands of IgG4-RD by IF. 3) The expression of CCR8 in LSGs was compared between IgG4-RD, SS, and HC by IF. [Results] 1) CCL18 was highly expressed in LSGs of IgG4-RD compared with SS and HC, and $CCL18^+$cells were comparable between macrophages, DCs, B cells, and plasmacytes in IgG4-RD. $CCL18^+$macrophages, DCs, and plasmacytes in LSGs of IgG4-RD significantly increased than in SS and HC, and $CCL18^+$B cells significantly increased than in HC ($P<0.05$). 2) CCL18 was highly expressed in fibrotic lesions than in cellular lesions, and the majority of $CCL18^+$cells were macrophages. 3) CCR8 was similarly expressed in LSGs of IgG4-RD and SS, and $CCR8^+$T, B cells, and plasmacytes were comparable between two groups. [Conclusions] Up-regulation of CCL18-CCR8 signaling in affected tissues might contribute to the pathogenesis of IgG4-RD.

W81-5

Clinical features of patients with serum IgG4 elevation (analysis of 1 center)

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Conflict of interest: None

[Objective] To determine what underlying diseases the patients with serum IgG4 elevation have, and whether IgG4 levels is different between IgG4 related disease (IgG4RD) and non-IgG4RDs, and what pattern of organ involvements IgG4RD shows. [Methods] Subjects were consecutive cases whose IgG4 levels were measured from 2009 to 2017, and those whose IgG4 >135 were selected for analysis of clinical features including underlying diseases. Clinical features of Igg4RD were also reviewed. [Results] Serum IgG4 levels were measured in 2228 patients. Among them, 262 cases showed elevation of IgG4 (>135mg/dl), who were176 male and 86 females with the average age was 64.0 ± 14.96 years. IgG4RD were 97 cases and non-IgG4RD cases include 30 CTD (13 of EGPA, 10 of MPA), 25 vasculitis, 25 malignancy, 23 pulmonary diseases, 10 eosinophilia. Serum IgG4 levels in IgG4RD (average;721mg/DL) were higher than those in non-IgG4RDs. Organ involvement of IgG4RD showed 3 patterns; Mikulicz disease dominant, autoimmune pancreatitis dominant and retroperitoneal fibrosis dominant type. [Conclusion] IgG4RD is the most common disease in patients with IgG4 elevation, but other diseases such as vasculitis particularly EGPA, CTD and malignancy shows high IgG4 levels.

W81-6

Cluster analysis with clinical factors can predict therapeutic response and prognosis in IgG4-related disease

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Conflict of interest: None

[Object] To bring the clinical practice of immunoglobulin (Ig) G4-related disease (IgG4-RD) close to personalized medicine, we aimed to classify the patient groups according to the clinical characteristics and clear the therapeutic responses and prognosis in each group. [Methods] We classified 147 patients enrolled to SMART registry into four groups with cluster analysis. We examined the therapeutic responses and prognosis in each group. [Results] The amounts of glucocorticoid in the maintenance treatment were between 5 to 7 mg/day in all groups, but the amounts of the cluster 1: the patients with hypergammaglobulinemia, elevated levels of serum IgG4, and hypocomplementemia, were significant larger than those in the cluster 4: the elder onset patients, relatively low concentrations of peripheral eosinophils. With regard to use of immunosuppressants and relapse ratio, we found the high frequencies in the cluster 1 and the cluster 3: the younger onset patients presented with mild elevation of serum IgG and IgG4. On the other hand, cluster 4 showed low rate of the relapse and often could discontinue steroid. [Conclusions] This research suggested that personalized medicine could be provided in IgG4-RD by classifying patients with clinical features.

English Poster Session

EP1-01

Current status of Bio remission/Bio free in RA treatment in our hospital

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Conflict of interest: None

[Objective] To investigate the current status of Bio remission/Bio free in RA treatment in our hospital. [Patients and Methods] A total of 702 patients were introduced biologic agents (Bio) in our hospital between May 2001 and August 2016. Regarding the number of cases and average age at the time of introduction of each of the first Bio, also (1) DAS remission cases (including extended administration interval), (2) Biological preparation discontinuation (Bio free) cases, (3) Dropout from Bio free cases, in the number of (each) cases under Bio enforcement from the end of March 2016 to the end of August, were investigated. [Results] The number of cases of the first Bio was Infliximab 65, Etanercept 184, Adalimumab 58, Tocilizumab 147, Abatacept 25, Golimumab 23 and Certolizumab pegol 15 cases respectively, and average age at the time of introduction was 55.0, 55.1, 57.0, 55.3, 65.7, 69.1, 58.2-year-old respectively. Among them, 358 cases (75 males, 283 females: Infliximab 24, Etanercept 83, Adalimumab 36, Tocilizumab 155, Abatacept 29, Golimumab 15 and Certolizumab pegol 16 respectively) were underwent Bio between the end of March 2016 and the end of August. Among 335 cases that were possible to calculate DAS, 203 patients were able to obtain DAS remission. (1) During DAS remission cases, 200 patients were continuing Bio, of which the dose was reduced or administration interval was prolonged in 72 cases. On the other hand, among the 335 cases that was possible DAS calculations, there were 132 cases who did not achieve DAS remission and 42 cases of them underwent dose reduction and/or administration interval prolongation. (2) In 14 cases of Bio free, the average period from remission to drug withdrawal was 1.1 years, and the average drug holiday period up to the present was 2.4 years. (3) In 6 cases that Bio free was dropped out, 5 cases resumed the same preparation, but it was dropped out early. [Conclusion] Strategic Bio free is one of our objectives.

EP1-02

The relationsthip between the elevated serum immunoglobulin G4 level and disease activity in patients with rheumatoid arthritis

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Conflict of interest: Yes

[Object] Previous studies indicate that the elevated serum immunoglobulin G4 (IgG4) in rheumatoid arthritis (RA) is common and disproportional to total IgG. The aim of study is to evaluate the level of serum IgG4 and IgG4/total IgG ratio in patients with RA. [Methods] This study investigated the difference the relationship between levels of serum IgG4 and disease activity. The levels of Serum total IgG and IgG4 from 41 patients with RA were determined by nephelometric assay. The patients were divided into two groups according to disease activity: high/moderate (n = 16) and low/remission (n = 25). The sera from 58 other autoimmune diseases were also measured. [Results] When the patients were divided according to clinical activity, the percentages of the positive serum IgG4 were 25 % in active disease group and 4 % in low activity group. However, the serum IgG4 levels of the RA patients with active disease activity were not significantly higher than those of the RA patients with low disease activity (58.3 ± 44.3mg/mL vs. 39.9 ± 30.1mg/mL). No significant relationship was observed between the ratio of IgG4/total IgG and disease activity. The IgG4 concentrations and total IgG/IgG4 ratios were similar between RA and the other autoimmune diseases ($P > 0.05$). [Conclusions] Our results showed that the presence of the elevated serum

IgG4 was not associated with disease activity of RA. Further investigations are needed to explore the clinical significance in a larger study population.

EP1-03

What are influencing on co-working of DASD28 and PS-VAS in rheumatoid arthritis patient

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Conflict of interest: None

(Object) Pain Score with visual analogue scale (PS-VAS) influences on Health Assessment Questionnaire Disease Index (HAQ-DI) in rheumatoid arthritis (RA) patient, as well as 28-joints disease activity score with C-reactive protein (DAS28-CRP). It is also suggested that these two indices have closely correlated and have overlapping effect on HAQ-DI. Our aim is to clarify what effects most in this overlap, and if dissociation, what would affect. (Methods) 514 RA patients were picked up. Their HAQ-DI, every component of DAS28-CRP, physician's global assessment (EGA), PS-VAS, and HAQ-DI were monitored every 3 months. Patients were classified into four groups in according to two categories, whether DAS28-CRP is in remission, and whether PS-VAS is within 15mm with average value in the last year period through treatment; i.e. they were named REM/REM, REM/nREM, nREM/REM, and nREM/nREM. Average values of each component of DAS28-CRP, HAQ-DI, Sharp/van der Heijde Score (SHS), number of comorbidities (Com), and patient's age (Age) were compared statistically with unpaired T-test in according to the four groups. (Results) Most strongly correlated factor was patient's global assessment (PGA) followed by tenderness joint count (TJC), swollen joint count (SJC), HAQ-DI, and EGA, respectively. SHS and Age demonstrated no significant correlation. In REM/nREM and nREM/REM, all factors excluded with SHS and Age demonstrated no significant correlation. (Conclusions) PGA is most important in both of disease activity and pain control, and when pain and disease activity control do not move parallel, joint destruction and ageing are suggested to intervene.

EP1-04

The utility of RemicheckQ among rheumatoid arthritis patients treated with Infliximab: A preliminary study

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Conflict of interest: None

[Objective] From October 1st 2017, a blood exam for measuring Infliximab serum levels by liquid chromatography (RemicheckQ) has been adapted covered by insurance. When the Infliximab serum levels are below 1 ug/mL, it is recognized as negative using RemicheckQ. We set up a preliminary study to identify influential factors in Infliximab serum levels monitored with RemicheckQ. [Patients & Methods] From October 2nd to November 9th 2017, we examined Infliximab serum levels with RemicheckQ among twenty rheumatoid arthritis (RA) patients treated with Infliximab and logistic regression analysis was conducted. The positive-negative assessment of RemicheckQ was set as a dependent variable in logistic regression analysis. Patient age (59 - 87 years), body weight (36 -79 kg) the Infliximab dose (3.0 - 10.4 mg/kg), the length of an interval (5 - 8 weeks), serum C-reactive protein (CRP) levels (0.05 - 4.83 mg/dl), Serum creatinine (Cre) levels (0.46 - 0.87 mg/dl), Erythrocyte sedimentation rate (ESR: 10 - 93 mm/hr) and RA disease activity Indexes such as CDAI (0.2-23.5), SDAI (0.31 - 28.3), DAS28-ESR (1.65 - 6.51) and DAS28-CRP (1.10 - 5.70) were set as possible explanatory variables. [Results] Logistic regression analysis clarified that only ESR became an influential factor of the positive-negative assessment of RemicheckQ with odds ratio 0.94 (95%CI: 0.89 - 0.99). Any other parameters did not show statistically significant influence on the positive-negative assessment of RemicheckQ among RA patients treated with Infliximab as shown with the following statistical results: age (p=0.06), body weight (p=0.87), the Infliximab dose (p=0.15), the length of an interval (p=0.54), CRP (p=0.16), Cre (p=0.10), CDAI (p=0.35), SDAI (p=0.28), DAS28-ESR (p=0.25), DAS28-CRP (p=0.35). [Conclusions] This preliminary study revealed that any parameters except ESR did not influence the result of Remicheck among RA patients treated with Infliximab, though further investigation should be prepared.

EP1-05

Residual synovitis in ankles and feet detected by ultrasonography in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] Twenty eight joints that are usually evaluated for disease activity score of rheumatoid arthritis (RA) do not include ankles and metatarsophalangeal joints. The aim of this study was to investigate the frequency and impact of residual synovitis in ankles and feet detected by ultrasonography (US) in RA. [Methods] Patients with RA who underwent US on 44 joints including hands, fingers, ankles, and metatarsophalangeal joints between April 2016 and August 2017 in Keio University Hospital were enrolled. [Results] Thirty seven patients were included in the analysis. The mean age was 60.6 years old, the disease duration was 7.7 years, and 84% were female. Among them, 10 patients had joint swelling in feet and ankles and 27 patients were considered to have no swollen joint by physical examination. The patients in the former group had significantly higher disease activity (DAS28 4.1 vs 1.9, $p<0.05$) with none in remission. In the 27 patients with no swollen joints in ankles and feet by physical examination, 13 (48%) had active synovitis detected by US in those joints (US positive group). Although the majority of both groups were in remission according to DAS28, no patients in the US positive group were assessed to achieve remission according to Boolean criteria while 38% in the US negative group. Body mass index (BMI) was much higher in the US positive group than the US negative group (22.3 vs 19.8, $p<0.05$), and the residual disease activity in ankles and feet was reflected in pain visual analog scale most sensitively (29mm vs 9mm, $p<0.05$). [Conclusions] Residual synovitis in ankles and feet detected by only US was less frequent in patients with patients with less BMI. The synovitis was well reflected in pain symptoms.

EP1-06

Mid-term clinical outcome of constrained condylar knee prosthesis for patients with rheumatoid arthritis

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Conflict of interest: None

[Object] Legacy constrained condylar knee (LCCK) prosthesis are used for revision and complex primary total knee arthroplasty. Especially, knees with rheumatoid arthritis (RA) show instability and/or bone loss, and are often undergone LCCK prosthesis. As there are few reports of LCCK in RA, we investigated clinical and radiographic outcome of LCCK in patients with RA. [Patients & Methods] Between January 2000 and December 2015, LCCK prosthesis were performed in 33 knees of 26 patients with RA at Kyushu Medical Center and Kyushu University Hospital. Total 22 knees of 16 patients of the postoperative follow-up more than 2 years were analyzed in this study. The average of follow-up duration was 7.0±2.7 years (2.5-12.7), all were female, and the average of age and RA duration at the surgery was 59±9.5 years (43-74) and 27.8±12.5 years (5-62), respectively. Primary operation of LCCK was performed at 13 knees, and revision was at 9 knees. Clinical results were analyzed by Knee Society Score (KSS) knee and function at preoperative time and final visit. Imaging outcome was investigated by femoral tibial angle (FTA), four component alignment angles, and radiolucent line at pre-/post-operative time. [Results] In clinical results of all patients, KSS knee (14.9±13.6→84.0±28.4) and function (33.5±28.6→58.2±13.9) were sta-

tistically improved after operation. In radiographic outcome, postoperative FTA was improved from 165.6±17.2 (148-213) to 173.0±1.3 (169-174). Radiolucent lines around components were seen in 16 knees (73%). Only one case had progressive radiolucent line around stems of femoral and tibial components, and had been suspected as minor infection due to the blood test data and the local findings. There is no failure or revision of LCCK. [Conclusions] LCCK prosthesis in RA patients were achieved to successful mid-term clinical result. In radiographic finding, only one case showed progressive radiolucent line, but no revision of LCCK has undergone.

EP1-07

Subcutaneous tocilizumab is effective even in elderly patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To examine the clinical outcome of subcutaneous tocilizumab (TCZ-SC) in patients with elderly RA. [Methods] Forty RA patients were divided into 2 groups; less than 60 years old (Young group; 21 cases) and more than 60 years old at the administration of TCZ-SC (Elderly group; 19 cases). The average age of Young group was 49, and that of Elderly group was 75 years old. The disease duration has no significant difference (7.3 years in Young group vs 8.7 years in Elderly group). The ratio of bionaive patients was 76 % in Young group, and 74 % in Elderly group. Not significant difference was detected in doses of methotrexate (3.5 in Young vs 1.5 in Elderly (mg/week)) and of prednisolone (1.4 in Young vs 3.3 in Elderly (mg/day)). In addition, there was no significant difference between the two groups in anti CCP antibody (95 in Young vs 192 in Elderly (IU/l)), DAS28 (4.0 in Young vs 5.0 in Elderly), and MMP-3 (334 vs 568 in Elderly (ng/ml)). The time course of DAS28, serum MMP-3 at the administration of TCZ-SC, 3, 6, and 12 months after its administration was analyzed. Statistical analysis was performed using Graphpad Prism 6J and p-value <0.05 was defined as significant difference. [Results] DAS28 in Elderly group was 5.0 at the administration of TCZ-SC, and significantly downregulated to 2.1, 2.0, and 1.8, at 3, 6, and 12 months after its administration. Young group (DAS28 was 4.4 at the administration of TCZ-SC) showed the same tendency. MMP-3 in Elderly group was 568 ng/ml at the administration of TCZ-SC, and significantly decreased to 341, 270, and 182 ng/ml at 3,6, and 12 months. Young group showed the same tendency. The adverse event was 3 cases in Elderly and 1 case in Young. [Conclusions] TCZ-SC showed good clinical outcome even in elderly patients with RA.

EP1-08

The clinical outcome of abatacept in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To evaluate the efficacy and safety of abatacept (ABA) in patients with rheumatoid arthritis (RA). [Methods] Thirty-two RA patients (26 females and 6 males) who were administered with ABA and could be followed more than 6 months were recruited. The mean age was 53.6 years old (46 to 80) and the average RA disease duration was 12.6 years. The mean dose of methotrexate was 3.4 mg/week (0 to 12) and the mean dose of methylprednisolone was 2.9 mg/day (0 to 10) at ABA administration. The retention rates, the time courses of DAS28 and remission rate, and the adverse event were examined. [Results] The retention rates were 64 % at 1 year and 53 % at 2 years. DAS28 was 3.3 at the administration of ABA, and significantly decreased 2.6, 2.3, and 2.2 at 3, 6, and 12 months after ABA administration. The remission rate was 44 % at the administration, and increased to 74 % at 3 months and preserved up to 12 months (77%). One case was ceased with ABA because of the onset of other collagen disease (systemic lupus erythematosus). [Conclusions] ABA demonstrated good efficacy to DAS28 and remission rate and safety.

EP1-09

A case of tuberculosis and cryptococcus co-infection in a patient with rheumatoid arthritis

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Conflict of interest: None

Cellular-mediated immunity dysfunction is a known risk factor for both tuberculosis and cryptococcosis. However, tuberculosis and cryptococcus co-infection is rare. An 81-year-old woman with 1-year history of rheumatoid arthritis had been treated with methotrexate (10mg/week), hydroxychloroquine (300mg/day), and prednisolone (5 mg/day). She did not have a past history of evident exposure to tuberculosis. The patient presented with headache, decreased consciousness, and fever. Coarse crackles were heard in Right lung field, and an abdominal examination indicated moderate ascites. On chest CT, new cavitary nodules were seen in the right lung and peritonitis was observed in abdominal CT. Acid-fast staining of her sputum showed negative results. However, the culture for *Mycobacterium tuberculosis* was positive in samples of sputum. A lumbar puncture was performed to rule out meningitis, and her celebrospinal fluid (CSF) cryptococcal antigen was positive, and *Cryptococcus neoformans* was cultured from her CSF. Therefore, we diagnosed pulmonary tuberculosis co-infection with cryptococcal meningoencephalitis. Antituberculosis chemotherapy was initiated, and the patient was started on combination therapy with amphotericin B. The symptoms improved during hospitalization. She has been discharged from hospital and is currently undergoing antituberculosis treatment with fluconazole. This is a rare case of concurrent infection with *Mycobacterium tuberculosis* and *Cryptococcus neoformans* in a rheumatoid arthritis patient without biologic agents. It is necessary to check CSF study if the cause of headache and fever is unclear during antituberculosis treatment.

EP1-10

Semiconstrained total elbow arthroplasty performed on RA elbow exhibiting a fork like deformity in which the olecranon fracture occurred and became nonunion after internal fixation: A case report

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Conflict of interest: None

A case of a man who was 66-year-old (X) at the time of performing total elbow arthroplasty (TEA). His RA onset was X-32. In X-11, his left elbow had already exhibited a fork like deformity and he was caught left olecranon fracture. An internal fixation was performed with tension band wiring (TBW) technique. But the fracture part had become nonunion. There was progress of multidirectional instability gradually. X-ray and CT showed that the humeral condylar region had fork like deformity and the trochlea disappeared, and the nonunion olecranon was displaced to the ulnar side of the ulnar. In X, left TEA and re-fixation of the olecranon fracture were performed. The nonunion site was identified and the joint was opened from the site. The medial humeral condyle was osteotomized with leaving surrounding soft tissue for the latter bone grafting. Reaming, rasping and osteotomy were performed both humeral and ulnar side. Two suture anchors were driven into the dorsal aspect of the distal ulna for use in the latter cortical suture techniques. The humeral and ulnar component were inserted with cement. It was no space to set the plate to fix the fracture site internally, so internal fixation was abandoned. Then the tendinous portion of the triceps is raised in a rectangular shape as a distal based flap. The osteotomized medial humeral condyle was inserted between the olecranon and the ulna. Then the site was covered with the re-

flected tendinous flap and the flap was sutured using the suture anchors that described previously. The ulnar nerve was transferred to the frontal side. The arm was immobilized with plaster cell for four weeks. Then the ROM and ADL exercise were started. Although it is short as 9 months after surgery, ROM from -40 to 130 is obtained and there is no skin trouble. No loosening of the component, union of the grafted humeral medial condyle is obtained and no dislocation is seen between the ulnar and the olecranon on X-ray.

EP1-11

Two RA cases of multiple extensor tendon ruptures treated by transfer of flexor digitorum superficialis tendon

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Conflict of interest: None

[Case1] A 47-year-old female with rheumatoid arthritis (RA) had destructive left wrist and multiple extensor tendon ruptures in her index through little fingers. She received total wrist fusion with wrist synovectomy. The third and fourth flexor digitorum superficialis tendons (FDS III and IV) were pulled out up to the level of radiocarpal joint and passed through radial subcutaneous tissue and FDS III were sutured with the second and the third extensor digitorum communis tendons and FDS IV were sutured with the fourth and the fifth extensor digitorum communis tendons (modified Boyes method). Postoperative median nerve palsy was detected then carpal tunnel was released and neurolysis of median nerve was performed 8 days after the primary surgery. Median nerve palsy recovered 8 months after the primary surgery. The switching of transferred tendons from flexion to extension was acquired at 9 weeks. The extension lag was 15-degree in index and 0-degree in the other fingers 1 year after the surgery. [Case2] A 57-year-old female with RA had destructive right wrist and multiple extensor tendon ruptures in her long through little fingers. She received Darrach procedure with wrist synovectomy. Modified Boyes method was performed. Intraoperative carpal tunnel release and neurolysis of median nerve were performed. However, hypesthesia of right thumb through long finger were detected and diagnosed as median nerve palsy. Five months after the surgery, the hypesthesia almost fully recovered. The switching was acquired at 6 weeks. The extension lag was 10-degree in long and 5-degree in the other fingers 10 months after the surgery. [Conclusions] Modified Boyes method was effective method in multiple extensor tendon ruptures. [Clinical significance] The treatment of multiple extensor tendons ruptures due to RA more than 3 fingers is difficult for achieving good outcome. Modified Boyes method is very useful method but postoperative median nerve palsy should be paid attention.

EP2-01

Clinical Evaluation of Skin infections in Systemic Lupus Erythematosus Patients and Idetification Their Risk Factors

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Conflict of interest: None

Objectives: To determine the frequency of skin infections in patients with Systemic Lupus Erythematosus (SLE) and identification of risk factors related to skin infections. Methods: The study was conducted in department of rheumatology, BSMMU, Dhaka from October 2014 to April 2016. A total 136 SLE patients were enrolled and followed for 1 year. Evaluation schedule was baseline, special and final visits. To determine skin infection as well as lupus specific skin lesions clinical definitions and dermatologist opinion were applied. Relevant laboratory tests were done. Multivariate analysis was done for risk factors. Results: Out of 131 cases 5 male and 126 female were completed 1 year follow up. Mean age was 28.8 ±8.2 years. The frequency of skin infections was 26.7% (35/131). The most common skin infections were tineasis 42.9% (15/35). Other infections were herpes infection 34.3% (12/35), paronychia 20% (7/35), and scabies 17% (6/35), multiple skin abscess 8.6% (3/35). Among the tineasis onycomycosis (33%) and tinea versicolor (33%) were most common. Herpes zoster was the most common herpes infection 58% (7/12). Risk factors for developing skin infections were higher disease activity (odds ratio [OR] 21.447, 95% confidence interval [95% CI] 1.01-451.88), low complements level (OR=147.828, 95% CI 4.93-4425.89), dosage (>10 mg/day) of prednisolone (OR=16.694, 95% CI 1.05-265.15), and immunosuppressive drugs usage (OR=22.580, 95% CI 1.12-452.39). Conclusions: In this series, skin infections were common and similar to others observation. Higher disease activity, higher dose of prednisolone, usage of immunosuppressant and low complementlevel were the risk factors for infections. Judicious use of immunosuppressant may reduce risk of infection.

EP2-02

Long-Term Prognostic Factors For Relapse or Exacerbation In Patients With Pulmonary Sarcoidosis

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Conflict of interest: None

[Object] Sarcoidosis is a systemic granulomatous disease that can affect multiple organs, and in particular lung involvements are common and found in more than 90% of the patients. Spontaneous remission is often observed within 2 years and chest radiographic stage, skin involvements, over 40 years old or smoking history are reported as poor prognostic factors in pulmonary sarcoidosis. However, there were no comprehensive reports about factors of relapse or exacerbation and characteristics of favorable patients without treatment in the long-term period more than 2 years. Aim of study is to identify prognostic factors of relapse or exacerbation in patients with pulmonary sarcoidosis in the long-term period. [Methods] Ninety-three patients who had visited at our Hospital between January 2007 and December 2016 and clinically diagnosed as pulmonary sarcoidosis, were enrolled. They were divided into two groups, which presented relapse or exacerbation and spontaneous remission. Clinical, laboratory and imaging data were collected from medical records and statistically analyzed. [Results] In 93 patients, 78% were women and mean age at diagnosis was 50.3 ± 16.4 years old. Mean observation period was 10.0 ± 8.8 years. Overall relapse or exacerbation rate was 20.4% (n=19) and mean period to relapse or exacerbation was 7.3 ± 8.2 years. Then, we purified 64 patients who were observed for more than 5 years, and relapse or exacerbation was found in 7 patients. When compared characteristics at diagnosis between two groups, decrease of peripheral number of lymphocytes, frequency of bilateral hilar lymphadenopathy, less than 3.5 in the ratio of CD4/CD8 in bronchoalveolar lavage fluid (BALF), or oral glucocorticoid use were significantly highlighted in relapse or exacerbation group (P=0.017, 0.046, 0.018, and 0.033, respectively). [Conclusions] Our long-term observational cohort study identified unique prognostic factors of relapse or exacerbation.

EP2-03

Factors predicting recovery of oral intake in patients with dermatomyositis and polymyositis with dysphagia; A retrospective multicenter study

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Conflict of interest: None

[Object] Dermatomyositis (DM) and polymyositis (PM) sometimes developed dysphagia, requiring dysphagia diet or tubefeeding. However, some patients regain complete oral intake. This study aimed to reveal

swallowing ability outcomes and prognostic factors of patients with DM and PM with dysphagia. [Methods] We retrospectively conducted consecutive patients with DM and PM who fulfilled targoff criteria and analyzed them with dysphagia. We defined dysphagia if patients fulfilled having dysphagia symptoms, abnormal findings in swallowing evaluation, and required dysphagia diet or tubefeeding. We divited into two groups based on intake status and also evaluated the factors predicting intake using a logistic regression analysis. [Results] Of the 241 patients with DM and PM, 24 patients developed dysphagia, 10 patients required dysphagia diet and 14 patients required tubefeeding. Twelve patients with dysphagia screened myositis specitic autoantibodies; anti-TIF1-γ (n =5), anti-MDA-5 (n =3) antibodies, and anti-SRP antibody (n =1). After treatment, 18 patients recovered complete oral intake, whereas 6 achieved incomplete intake. The median time between the dysphagia onset and complete oral intake was 18.8 weeks. Clinical characteristics and treatment were similar, however, follow up period was shorter, Intravenous immunoglobulin was higher, tubefeeding and development of aspiration pneumonia were lower in the complete intake group. In the multiple logistic regression analysis, not requiring tubefeeding [hazard ratio (HR) 10.01, p= 0.005] and developing dysphagia after prednisolone treatment[hazard ratio (HR) 5.7, p= 0.02] were significant independent factors predicting complete oral intake. Overall mortaliry rate were 44% and 67% in the complete intake group and incomplete intake group, respectively (P= 0.64). [Conclusions] Our findings indicated that DM and PM patients in whom dysphagia didn't require tube feeding and developed after the prednisolone treatment tended to recover oral intake.

EP2-04

Antineutrophil Cytoplasmic Antibody Vasculitis with Pauci-immune Glomerulonephritis in a 39 year-old male presenting with acute loss of vision: A Case Report

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Conflict of interest: None

Introduction Vasculitis is a process caused by inflammation of blood vessel walls which has been recognized for a long time. Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides are a group of systemic vasculitis characterized by pauci-immune necrotizing inflammation of small-to medium-sized blood vessels. Inflammatory ocular disease in ANCA-associated vasculitis is a frequent manifestation but sudden visual loss comprises only of 6% among patients with ANCA-associated vasculitis. We report an adult male who suffered acute loss of vision associated with ANCA-associated vasculitis and pauci-immune glomerulonephritis. The association is not yet established due to lack of sufficient epidemiological and clinical data. **Case Report** A 39-year old male, non-hypertensive, non-diabetic, with history of increasing creatinine level, was admitted and experienced an episode of bilateral amaurosis fugax. Eye exam showed advanced glaucomatous optic neuropathy on the right, normal left eye findings. Thorough search for infection, Giant Cell Arteritis, and malignancy was negative. Work up showed negative brain magnetic resonance imaging (MRI) and hypercoagulable analysis. Renal biopsy revealed pauci-immune glomerulonephritis with 20% cellular and fibrocellular crescents, 8% global glomerulosclerosis. Serologic test revealed positive p and c-ANCA. He was then managed as a case of pauci-immune glomerulonephritis with positive ANCA vasculitis. Three 500mg intravenous methylprednisolone pulse was instigated followed by 375mg/kg Rituximab therapy weekly for 4 weeks. Improvement of vision was demonstrated with the therapy. **Conclusion** Inflammatory ocular disease is common occurrence among ANCA-associated vasculitis but significant and sudden reduction of visual acuity is infrequent. More importantly, physicians must recognize systemic involvement along with ocular symptoms to promptly instigate investigation and initiate appropriate treatment due to the gravity of this condition.

EP2-05

Mechanic's hands: A helpful hand in diagnosis of anti-synthetase syndrome

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Conflict of interest: None

[Object] Anti-synthetase syndrome (ASS) is a rare disease entity with polyarthritis, inflammatory myopathy, fever, interstitial lung disease (ILD), Raynaud's phenomenon, mechanic's hands (MH) and presence of auto-antibodies against aminoacyl-tRNA synthetases, especially anti-Jo-1. MH is rare symptom, but can be a diagnostic clue to ASS, as showing in our case. [Case report] A 57-year-old man, without other comorbidity, was referred to hepatology with liver function test (LFT) elevation. Before visiting our hospital, he had a 1-month history of fever and was treated with antibiotics for two weeks in primary clinic. He was non-smoker and his job was a high school teacher. On physical examination, he had a mild fever (37.8ºC) and tenderness in both wrist and knee joints, but no muscle weakness was noted. Laboratory test showed AST/ALT 320/192 IU/L, CRP 1.43 mg/dL and hepatitis viral markers were all negative. Chest X-ray revealed left costo-phrenic angle blunting. Despite using hepatotonics for 5 days, there was no change in LFT and he was consulted to rheumatology for polyarthralgia. MH was noticed. Additional laboratory tests showed a positive anti Jo-1 antibody and elevated muscle enzymes. Result of electromyography, thigh MRI and muscle biopsy was accordance with inflammatory myositis. Chest CT revealed organizing pneumonia patterns in both lower lobes, suggesting ILD. He met criteria for ASS. High dose steroid was commenced and not only his symptoms including fever, polyarthritis but also LFT and chest X-ray were improved after 1 month of treatment. [Conclusions] The prognosis of ASS is primarily dependent on the severity of ILD and myositis. Early recognition of MH might help in early detection of ILD and myositis in patient with ASS, leading to be better outcome. This case highlights the important role of MH in the early diagnosis of ASS.

EP2-06

Analysis of Symptoms in Very Early Phase in Patients with Adult-onset Still's Disease

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Conflict of interest: None

[Background] The initial symptoms of Adult-onset Still Disease (AOSD) are non-specific and confusing with those of common cold, which can lead to the diagnostic delay. [Objectives] To clarify characteristic features in AOSD in very early phase and to find the key symptoms and markers to an earlier diagnosis. [Methods] We retrospectively reviewed consecutive AOSD patients in our hospital from April 2012 to July 2017. Symptoms and laboratory data before diagnosis were collected form their charts and analyzed. [Results] A total of 62 patients were enrolled. The mean age at diagnosis was 45.9 and female was 81%. The duration from the first symptoms to the first visit to a medical facility was 18.7 days, from the first visit to the first blood test was 5.8 days, from the first blood test to the fulfillment of Yamaguchi's Criteria was 11.0 days, and from the fulfillment of Yamaguchi's Criteria to the treatment was 22.2 days. During the course Fever was found in all patients, skin lesion in 91.9%, arthralgia in 87.1%, sore throat in 66.1% as the first symptom. Laboratory and imaging tests demonstrated liver enzyme elevation in 82.2%, white blood cell count (WBC) increase in 80.6%, lymphadenopathy/splenomegaly in 72.6%, negative RF and ANA in 56.5%, ferritin elevation in 82.3%. Patients who presented with sore throat as the first symptom fulfilled Yamaguchi's Criteria in 13.6 days after the onset, which was shorter than that of patients with the other symptoms (fever, 24.0 days; arthralgia, 45.7 days; skin lesion, 31.5 days). However, the duration from the Yamaguchi's Criteria fulfilment to treatment initiation in the patients with sore throat was 38.5 days. [Conclusions] Although symptoms of AOSD developed rapidly with sore throat, fever and liver enzyme elevation, delayed diagnosis was not rare and it was attributed in part to non-assumption of the disease. Paying attention to the combination of these symptoms can lead to an earlier diagnosis.

EP2-07

Clinical features of 61 patients with polymyalgia rheumatica

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Conflict of interest: None

[Object] The aim of this study was to investigate the clinical features in Japanese PMR patients at our hospital. [Methods] We Sixty-one patients with PMR diagnosed according to Bird's criteria or 2012 provisional classification riteria for PMR. We examined laboratory findings (CRP, ESR, feritin, IgG, CH50, MMP-3, and autoantibody (ANA, RF, ACPA, anti-double-stranded DNA antibodies, anti-Ro antibodies, anti-Sm antibodies, MPO-ANCA, PR3-ANCA,), primary dosage of predonisolone, the incidence of malignancy and new bone fructure, [Results] Two patients (3.2%) have RF positive, and No patient has ACPA positive. Thirty patients (21.3%) have ANA positive. Five patients complicated with Giant cell arteritis. Six patients complicated with malignancy. In eleven patients (18.0%), PSL therapy could be withdrawn. [Conclusions] It tends to shoten at time before leading to a diagnosis as PMR with a musculoskeletal ultrasound sonography (MKUS) rather than without a MKUS. When we diagnose as PMR, we should use a MKUS positively.

EP2-08

Translation, cross-cultural adaptation and validation of the Pain Catastrophizing Scale (PCS) into Bengali in patients with chronic non-malignant musculoskeletal pain

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Conflict of interest: None

[Object] Translation and cross cultural adaptation of Pain Catastrophizing Scale (PCS) to Bengali and its validation in Bangladesh. [Methods] This was an observational study conducted in the department of Rheumatology of Bangabandhu Shiekh Mujib Medical University, Bangladesh. Forward-backward translation was applied to translate the questionnaire from English to Bengali. Ninety-five patients suffering from chronic non-malignant musculoskeletal pain participated in the study. Reliability and validity were assessed using internal consistency and convergent validity respectively. Factor analysis was performed to examine the scale structure. [Results] The internal consistency for 'helplessness', 'magnification', 'rumination', and 'total' of the Bengali PCS were Cronbach's α =0.87, 0.72, 0.90 and 0.92 respectively; test-retest reliability of the scale were ICC = 0.93, 0.79, 0.87 and 0.78 respectively. Moderate negative correlations were observed between the Bengali PCS and physical and psychological functioning. Factor analysis demonstrated the adequacy of the three-factor structure of the Bengali PCS; 'helplessness', 'magnification', and 'rumination'. [Conclusions] The Bengali version of PCS is a valid and reliable tool to measure and diagnose pain catastrophization. PCS scores in our population were found harmonious with the original scale and other available studies. This scale can now be used in our Rheumatology practices planning for therapeutic interventions who are suffering from pain.

EP2-09

Three cases of IgG4 related disease presenting leg edema solely

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Conflict of interest: None

[Background] IgG4 related disease (IgG4RD) is a systemic disease potentially affecting lots of organs. Here, we present 3 cases of leg edema with retroperitoneal mass. Two of them were diagnosed with IgG4RD later by CT-guided biopsy and successfully treated by glucocorticoid. (CASE 1) A 67-year-old female patient presenting leg edema visited our hospital, where abdominal CT revealed retroperitoneal tumor and elevated serum IgG4 (297 mg/dl) was noted. CT-guided biopsy for the tumor demonstrated numerous IgG4 positive plasma cells. Oral prednisolone (0.7mg/kg) led the tumor to decrease and the symptom to disappear. (CASE 2) A 69-year old woman referred to our hospital for edema of lower limbs. IgG4 was elevated to 216 mg/dl. Biopsy of retroperitoneal tumor unveiled by CT was biopsied. Her clinical course resembles that of case 1. (CASE 3) A woman, who is 82 years old, visited our hospital due to leg edema unknown origin. Although serum IgG4 was not elevated (54 mg/dl), retroperitoneal mass was found by CT, suggesting IgG4RD. However, she refused further examination and discharged to a care home. [discussion] IgG4 related disease might be more popular than expected. It is important to consider IgG4RD in the differential diagnosis of common symptoms such as leg edema.

EP2-10

Musculoskeletal Disorders among Garment industry Workers in Bangladesh

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Conflict of interest: None

[Object] To estimate the prevalence of musculoskeletal (MSK) symptoms and disorders and to look for possible relationships between the major MSK complaints and types of work among garment workers in Bangladesh. [Methods] This cross sectional pilot study was carried out among 350 workers in two garment factories by face-to-face interview. The COPCORD (Community Oriented Program for Control of Rheumatic Disorders) methodology was adopted for the survey. The workers were classified into cutting, sewing, finishing and quality control operators. Trained interviewers identified subjects with musculoskeletal pain and rheumatologists examined the positive respondents. [Results] The point prevalence of musculoskeletal pain was 61.71%. The parts commonly affected during the preceding 7 days of interview in the whole group were shoulder (17.9%), lower back (15.2%), neck (13.8%) and knee (10.8%). The cutting operators suffered more from back (15.4%), neck (15.4%) and lower limb (11.5%); sewing operators from lower limb (12.4%), back (8.5%) and upper limb (7.7%); finishing operators from lower limb (50%) and quality control group from back pain (50%). Multiple regional pains were more frequent (n=155) among all operators. The sewing and cutting operators suffered from multiple regional pains more than other operators. The prevalence of Rheumatoid arthritis (RA) 0.9%, spondyloarthropathy (SpA) 1.42%, undifferentiated arthritis (UA) 1.1%, nonspecific low back pain (NSLBP) 4.6%, soft tissue rheumatism (STR) 3.7%, osteoarthritis (OA) 0.9% and lumbarspondylosis 1.1%. Nonspecific pain was the commonest condition (63.71%). [Conclusions] Musculoskeletal disorders are common causes of morbidity, disability, and work loss among the garment workers of Bangladesh where male and female workers are almost equally affected. Multiple regional involvements are common in this occupational group. Mechanical disorders are the commonest.

EP2-11

Greater trochanteric fracture is a complication in the early phase after total hip arthroplasty for rapidly destructive coxopathy

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Conflict of interest: None

[Object] Greater trochanteric fracture (GTF) is a postoperative complication of total hip arthroplasty (THA), and the incidence has been reported to be approximately 5%. This study was aimed to investigate GTF after THA for rapidly progressive coxopathy (RDC), on which there is no information at the moment. [Methods] RDC was diagnosed as progressive joint space narrowing at the rate of ≥2mm/year radiographically in the

hip without any morphological abnormality. Each hip with RDC was also examined with magnetic resonance imaging (MRI). In our institute, 28 and 122 hips underwent THA through the same transgluteal approach for RDC and OA, respectively, from 2015 to 2016. Each patient was received the same postoperative rehabilitation and followed up for at least 1 year. The occurrence of GTF was compared on the basis of the diseases, MRI findings, ages, prostheses, and genders. [Results] GTF occurred in 4 out of 28 hips with RDC (14%) at 3-8 postoperative days, whereas there was no GTF in the hips with OA (P<0.05). No difference was found in the GTF incidence in the hips with RDC between ages at operation, types of the prosthesis used, or genders. From MRI findings, 14, 11, and 3 hips with RDC were classified into stages 1, 2, and 3, respectively. No GTF occurred in the hips at stage 1 with bone marrow lesion (BML) found in the antero-lateral portion of the femoral head. In contrast, there were 3 and 1 GTF in the hips at stage 2 with extensive BML in the proximal femur and stage 3 with aggressive femoral head destruction, respectively. The incidence of GTF at stages 2 and 3 (29%) was significantly higher than that at stage 1 (0%) (P<0.05). [Conclusions] This study indicates that BML expanding into the proximal femur by RDC may predispose the greater trochanter to develop fracture in the early phase after THA.

EP2-12

Antiphospholipid syndrome (APS) in a young adult patient post myocardial infarction: a case report

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Conflict of interest: None

Introduction Myocardial infarction (MI) in young adults accounts for roughly 3% of all cases of coronary artery disease. Determining the underlying etiology requires a more comprehensive investigation since atherosclerosis is a less common cause in a young adult. This report shows a young adult female who presented post MI and was proven to have antiphospholipid syndrome. Case Presentation A 38 year old female came in for consultation due to easy fatigability. One year prior to her initial consult, she was admitted at another institution due to sudden onset of difficulty of breathing. She was managed then as a case of acute myocardial infarction. Medical management was done and was sent home improved on: Amlodipine, Carvedilol, Digoxin, Clopidogrel, Isosorbide mononitrate, Atorvastatin, Losartan. In the interim, she has episodes of easy fatigability on strenuous tasks and episodes of paroxysmal nocturnal dyspnea (PND). Workup for the cause of myocardial infarction was done. She was noted to have elevated lupus anticoagulant and normal IgG/IgM anti-Cardiolipin antibodies, and normal IgG/IgM Beta-2 glycoprotein antibodies. Repeat lupus anticoagulant was elevated 4 months after initial testing. Treadmill stress Sestamibi myocardial perfusion imaging done showed the following result: large prior transmural myocardial infarction in the basal to apical inferolateral, inferior, and adjacent inferoseptal segments with no evidence of inducible myocardial ischemia. She was started on warfarin on top of adjusting her cardiac medications. She noted decreased episodes of PND and decreased severity of easy fatigability on follow-up. Conclusion In young patients with myocardial infarction workup for non-coronary disease entities is crucial in the subsequent management of patients. In patients with APS with MI, revascularization is done in the acute setting. Secondary prevention includes oral anticoagulation on top of control of risk factors and use of antiplatelet agents.

EP2-13

Cross-cultural adaptation, validation of the Korean version of the functional index for hand osteoarthritis (FIHOA)

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Conflict of interest: None

[Object] To translate and assess the validity and reliability of the Korean version of the functional index for hand osteoarthritis (FIHOA) [Methods] The functional index for hand osteoarthritis (FIHOA) is a 10 item questionnaire using semi-quantitative scoring on a four grade scale. The adaptation of the FIHOA from English into Korean was established according to guideline of cross-cultural adaptation of self-reported measures. After adaptation, FIHOA test and retest was performed at 5-7 days' interval. Test-retest reliability of each item and total scores was calculated by Spearman's correlation coefficient and intraclass correlation coefficient (ICC). Internal consistency reliability was evaluated as the adjusted item-total correlation and Cronbach's alpha. Internal construct validity was appraised through factor analysis. External construct validity was assessed by correlating FIHOA with HAQ and VAS on hand pain. [Results] Total number of 100 patients completed FIHOA test and retest. Spearman's rho for total scores was 0.87, and the value for single item correlation was ranged from 0.62 to 0.86. ICC for the total score was excellent (0.83) and ICC between single items were good or excellent (0.59-0.89). Adjusted item-total correlation for all items presented adequate performance (0.49-0.78). Cronbach's alpha after deleting each item showed high internal consistency (0.86-0.88). Factor analysis revealed that Korean version of FIHOA is not unidimensional. Significant correlations between FIHOA with HAQ (r=0.62, p<0.01), FIHOA with HAQ score of hand function (r=0.71, p<0.01) and VAS on hand pain (r=0.47, p<0.01) were observed. [Conclusions] The Korean version of FIHOA is a reliable and valid instrument for evaluating functional disability in Korean hand OA patients.

EP2-15

Impact of osteoarthritis on household catastrophic health expenditures in Korea

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Conflict of interest: None

Object: Osteoarthritis (OA) is senile disease which prevalence is increasing. This study explores the impact of OA on household catastrophic health expenditures (CHEs) in Korea. **Methods:** We used data of 5,200 households from the Korea Health Panel Survey in 2013 and estimated annual living expenses and out-of-pocket (OOP) health expenditures. Household CHE was defined as a household's total OOP health payments equal or exceeding 10, 20, 30, or 40% of household's capacity to pay. To compare the difference of OOP health expenditure between households with OA individuals and those without OA cases, households were matched 1:1 for the presence of a member with another chronic disease including neoplasm, hypertension, heart disease, cerebrovascular disease, diabetes, or osteoporosis. The impact of OA on CHE was determined by multivariable logistic analysis. **Results:** A total of 1,289 households were included in the groups, and households with and without OA patients paid mean annual OOP health expenses of $2,789 and $2,607, respectively. The prevalence of household CHE at threshold levels of 10%, 20%, 30%, and 40% was higher in the households with OA patients than those without OA patients (P < 0.01). The presence of OA patients in each household contributed to CHE at each threshold of 10% (OR 1.48, CI [95% confidence interval] 1.16-1.87), 20% (OR 1.29, CI 1.01-1.66), and 30% (OR 1.37, CI 1.05-1.78), but not of 40% (OR 1.17, CI 0.87-1.57). **Conclusions:** The presence of OA patients in Korean households was significantly related with CHE. Policy makers should try to reduce OOP expenditures in households with OA patients.

EP2-16

Retrospective evaluation of non responder for denosumab in osteoporosis treatment

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Conflict of interest: None

(Object) We have evaluated non-responder for denosumab (d-mab) in during osteoporosis (OP) treatment retrospectively. (Methods) Patient who were treated with d-mab for osteoporosis from September 2013 to September 2017 continuously for more than 2 years, were enrolled. Their bone mineral density (BMD) was measured with dual energy X-ray absorptiometry method. Patient's BMD in lumbar spine (LS), femoral neck (FN), greater trochanter (GT), and whole femur (WF) were measured at the start of d-mab administration, and at every 6 months when d-mab was administrated. Change of BMD from the baseline of each part was calculated for every measurement. Patients were classified in according to change of BMD in every part. That is if final BMD is less than that of baseline, it was counted as one, and the count was named as the name of each count group, in summarized as number. Parameters such as patient's age, sex, length of administration, drug Naive, complication of rheumatoid arthritis and other comorbidities, glucocorticoid steroid thrown, bone metabolism markers such as tartrate-resistant acid phosphatase 5b (TRACP-5b), and BMD at baseline and its change, were statistically evaluated for each group. Statistically significant level was set within 5%. (Results) 201 cases were picked up. In these, 69 of counted zero (G-0), 78 of counted one (G-1), 30 of counted two (G-2), 14 of counted three (G-3), and 3 of counted four (G-4) were consisted. G-4 had been extruded from analysis because number was too small to make evaluation. In parameters, only BMD change after 6 months from baseline was the only factor that demonstrated statistically significant. G-3 had demonstrated significant decrease of BMD than the other groups. The other factors demonstrated no statistical correlation. (Conclusions) As d-mab is antibody drug, existence of non-responder is predictable. Our results supported the hypothesis.

EP2-17

Combat fatigue in psoriatic arthritis (PsA) patients

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Conflict of interest: Yes

Objective Fatigue is commonly associated with psoriatic arthritis (PsA). However, information about its prevalence and associated factors is sparse, particularly in Asia. The primary objective was to find the prevalence of PsA fatigue. The secondary objective was to explore its associated risk factors, particularly emphasis on Minimal Disease Activity (MDA). **Methods** PsA patients that fulfilled CASPAR criteria were consecutively recruited from local Rheumatology clinics. Fatigue was assessed by a 13-item questionnaire (FACIT-F). Data collected and analyzed included: demographic data, disease-activity data and quality-of-life parameters, which included SF-36, HAQ-DI, pain (VAS) and general health (VAS). **Results** Severe fatigue was found in 29 (25.0%) of 116 eligible PsA patients recruited. This was defined as FACIT-F score <30. The univariate model identified these associated factors of fatigue: pain-perception, MDA, the Mental Component Summary (MCS), and the Physical Component Summary (PCS) of the SF-36. The final regression model identified PCS as the strongest associated factor of severe fatigue, $p<0.001$. In Pearson's test, the FACIT-F score showed a positive relationship with the PCS score, with moderate strength of association ($r=0.63$; $p<0.001$). No associations with fatigue were found between skin severity, arthritis conditions and duration, inflammatory markers, comorbid disease and medication use. 59 (50.9%) of them had achieved MDA but 16.9% (10/59) still felt severe fatigue. FACIT-F score was compared in those with and without MDA achieved, it was statistically higher in those with disease remission (39.1+/-9.3 vs 33.0+/-8.8; $p<0.001$). **Conclusion** Severe fatigue was common in PsA patients, and the PCS was the strongest associated factor indicating its multifactorial nature. Achieving MDA could alleviate the fatigue intensity to certain extent. Treatment for PsA-related fatigue should adopt a multidisciplinary approach in addition to disease-activity control.

EP2-18

Do we come from the same angle? Analyses of real-world therapeutic and diagnostic status of psoriatic arthritis in rheumatologists and dermatologists

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Conflict of interest: Yes

[Object] Psoriatic arthritis (PsA) contributes to enormous burden of disease, and early diagnosis and adequate therapeutic managements should be essential. However, inadequate diagnosis and suboptimal therapies have been reported. We intended to analyze the real-world clinical practice for PsA and compare whether different viewpoints existed between rheumatologists and dermatologists. **[Methods]** We conducted a cross-sectional observational study by face-to-face interviews with rheumatologists and dermatologists who took care of PsA patients with enriched experience. **[Results]** A total of 50 rheumatologists and 30 dermatologists completed the interviews, whose basic characteristics were shown in Table 1. Regarding the top-three diagnostic procedures, more dermatologists focused on the absence of rheumatoid factor or anti-citrullinated protein antibody (Table 2.). More rheumatologists thought isolated arthritis as the challenges of diagnostic confirmation than dermatologists, and more dermatologists thought interpretation of radiograph as the counterpart (Table 3). We also analyzed the ongoing prescription for PsA and sorted by different subspecialties (Table 4). **[Conclusions]** The status quo of diagnostic and therapeutic management was analyzed and there were some differences between subspecialities. Interdisciplinary cross-talking would be important for comprehensive care of PsA.

EP2-19

Efficacy and safety of hydroxychloroquine (HCQ) in Japanese SLE patients in daily clinical practice

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Conflict of interest: None

[Object] To clarify efficacy and safety of HCQ used for SLE patients in clinical practice. [Methods] Cases of SLE treated with HCQ in University of Tsukuba hospital between September 2015 and June 2017 were identified from electrical medical charts. We retrospectively analyzed their 1) baseline characteristics, 2) target lesions, 3) efficacy when HCQ was used more than 6 months, 4) safety profile, and 5) risk factors for drug-induced cutaneous adverse reactions. [Results] 1) Thirty-four cases of SLE were treated with HCQ. Twenty-seven cases (85%) were female with a mean age of 37.6 years. The mean disease duration was 11.2 years. Skin involvement was developed in 26 cases (81%), arthritis in 21 cases (66%), hematological abnormalities in 20 cases (63%), and lupus nephritis in 9 cases (28%) during their whole SLE course. Anti-Ro/SSA antibody was positive in 17 cases. 2) HCQ was used to treat skin involvement in 17 cases (50%), arthritis in 9 cases (26%), hematologic abnormalities in 6 cases (18%), lupus nephritis in 3 cases (9%). 3) Skin involvement and arthritis were improved in six cases (60%) and one case (50%) respectively with HCQ use more than 6 months. There was no significant change in complete blood count or urinary protein. 4) Twelve cases (37.5%) experienced adverse events and of these six cases (50%) were drug-induced cutaneous adverse reactions, three cases (25%) diarrhea, one case headache, one case retinal detachment, and one case branch retinal vein occlusion. The cumulative continuation rate of HCQ was 69% at 6 months and 60% at 12 months. 5) Positive rate of anti-Ro/SSA antibody was significantly higher in cases with drug-induced cutaneous reactions (6/6, 100%) compared with cases without them (12/26,

46%) (p=0.0257). [Conclusions] HCQ was effective for skin involvement and arthritis in SLE. The most common adverse event was cutaneous adverse reaction and it was likely that anti-Ro/SSA antibody was a risk factor of HCQ-induced cutaneous skin reaction.

EP2-20

Lupus presenting as severe Raynaud's disease with digital ischemia, nephritis and APS treated with Rituximab - a Case Report

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Conflict of interest: None

46 year-old female who was referred to Rheumatology service for severe Raynaud's of fingers and toes. History 5 years ago of digital ischemia of bilateral 5th toes resulting to autoamputation, was managed as ANCA-associated vasculitis given Azathioprine. At the time of the Rheumatology referral, she presented with severe Raynaud's of fingers and toes with gangrene of right hand digits. Investigations Chest X-ray showed bibasal pneumonia. 2D echo showed mildly elevated pulmonary artery pressure. Arterial duplex scan of both extremities was normal. Blood tests: anemia, thrombocytopenia, ESR 120, normal CRP, positive direct Coomb's test, low titer ANA 1:40 p-ANCA 1:20. Low C3 and C4. Positive serologies: antidsDNA, anti SSA, B-2 glycoprotein IgG and anticardiolipin IgG. Hematuria and proteinuria on urinalysis, 24-hour urine protein of 2.6g, serum creatinine of 1.96 mg/dL. Treatment Managed as SLE with severe Raynaud's, nephritis and secondary APS. She was given pulse steroids for 3 days after being given antibiotic to treat her Pneumonia. Given Nifedipine, Sildenafil and Bosentan for the severe Raynaud's. Anticoagulation with LMWH was also started. However, her right hand progressed with swelling and digital ischemia of her right 3rd-5th digits. Patient referred to hand orthopedic surgeon and was assessed to have hand compartment syndrome and surgical release was done. Creatinine became increasingly high and patient was placed on hemodialysis. Rituximab was also given. Patient was discharged with improved perfusion of her right hand digits. Discussion Digital gangrene in SLE can have a complex etiology due to several factors such as presence of APS, Raynaud's disease or lupus vasculitis. Treatment is also multifactorial and involves treating vasospasm, instituting anticoagulation and controlling SLE flare with IV methylprednisolone. Rituximab is an option as seen in case reports of digital gangrene in SLE.

EP2-22

Lupus Like Syndrome from Use of Infliximab in a 48 year old Female Diagnosed Case of Refractory Dermatomyositis with Vasculitic Neuropathy and Interstitial Lung Disease

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Conflict of interest: None

Introduction: Dermatomyositis (DM) is an inflammatory myopathy composed of proximal muscle weakness and characteristic rash (heliotrope, gottron's papules) diagnosed through muscle biopsy, muscle enzymes, and nerve conduction. Standard regimen includes glucocorticosteroids and cyclophosphomide. If patient is refractory, the use of Infliximab an anti-TNF has limited data but may be an area of interest as it is anti-inflammatory agent. Case Report: This is a case of a 48 year old female known DM presenting with proximal muscle weakness and characteristic rash. Standard treatment provided partial relief. Patient had chronic non-productive cough, numbness on extremities, allodynia, and absent proprioception diagnosed with ILD and vascular neuropathy. Completed cyclophosphamide therapy for six months but symptoms persisted. Patient initiated on Infliximab therapy. She completed initiation phase with a dose of 3mg/kg at 0, 2, and 6 weeks, then maintenance phase of every 2 months thereafter. Response was being able to walk without assistance, resolution of rash, and significant decrease in neuropathy. One year of Infliximab patient developed bipedal edema, new erythematous macular rash on extremities, butterfly rash, joint pains, malaise, and severe weakness. Work up done was negative for heart failure, malignancy, nor dermatomyositis in flare. Patient was positive ANA speckled, positive direct Coomb's, and decreased complement 3 consistent with lupus. Discussion: Some studies show that TNF and other cytokines are elevated in muscle biopsy of DM patients implicating a role in inflammatory myopathy. Hence the use of Infliximab is an area of interest as this property may be beneficial to refractory DM. Lupus like syndrome (LLS) may be from a drug that triggers an autoimmune response. Infliximab is a drug that is definite in causing LLS. Conclusion: Although Infliximab has potential in DM management, appropriate dose remains to be established to avoid developing LLS.

EP3-01

Tofacitinib inhibits granulocyte-macrophage colony-stimulating factor-induced NLRP3 inflammasome activation in innate immune cells

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Conflict of interest: None

Objective: Granulocyte-macrophage colony-stimulating factor (GM-CSF) has emerged as a crucial cytokine that activates myeloid cells to initiate tissue inflammation. However, the molecular actions of GM-CSF against innate immunity are still poorly characterized. Here, we investigated the *in vitro* effects of GM-CSF on the activation of human myeloid cells, neutrophils, and the underlying intracellular signaling mechanism including inflammasome activation. **Methods:** Human neutrophils were separated from healthy volumteers. Neutrophils were stimulated with cytokines and cellular supernatants were analyzed for interleukin (IL)-1β and caspase-1 by enzyme-linked immunosorbent assay methods. Pro-IL-1β mRNA expressions were analyzed by real-time PCR method. **Results:** Stimulation with GM-CSF alone, but not tumor necrosis factor-α, was shown to increase the release of IL-1β and cleaved caspase-1 (p20) from human neutrophils. GM-CSF stimulation also resulted in the phosphorylation of Janus kinase (JAK) 2/ signal transducer and activation of transcription (STAT) 3 and STAT5 in neutrophils, which was prevented by treatment with tofacitinib. Tofacitinib completely abrogated GM-CSF-induced IL-1β and caspase-1 (p20) secretion from neutrophils. Furthermore, GM-CSF stimulation induced pro-IL-1β mRNA expression in neutrophils and induced NOD-like receptor family pyrin domain containing 3 (NLRP3) protein expression, whereas tofacitinib pretreatment marginally inhibited GM-CSF-induced pro-IL-1β mRNA expression and prevented NLRP-3 protein expression. **Conclusions:** These results indicate that GM-CSF signaling induced NLRP3 inflammasome activation and subsequent IL-1β production by affecting neutrophils, which may cause the activation of innate immunity through affecting inflammasome. Therefore, GM-CSF is a key regulator of NLRP3 inflammasome and IL-1β production by activating innate immune cells, and tofacitinib can impact this process by blocking JAK/STAT signaling pathways.

EP3-02

Changes of Treg and Th17 cells in P2X7R-regulated acute gouty arthritis model of rat

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Conflict of interest: None

[Object] To investigate the effect of P2X7R on Treg and Th17 cells in acute gouty arthritis model of rats and its role in acute gouty arthritis. [Methods] Sixty male SD rats were randomly divided into three groups: After establishment of acute gouty arthritis model, rats were given P2X7R agonist ATP, P2X7R inhibitor BBG and PBS, respectively. The rats were sacrificed at 6h, 12h, 24h and 48h after treatment. The spleen of the rats were grinded and the CD4+T lymphocytes were sorted out by magnetic beads. The expression of Treg and Th17 cells were detected by

flow cytometry. [Results] **1**. The expression levels of Treg and Th17 in the spleen: After treatment at 24h, The expression levels of Treg and Th17 in the ATP group were significantly higher than that in the BBG and control groups (P=0.000, 0.04); The difference of Treg and Th17 expressions between BBG and control group were also statistically significant (P=0.017, 0.032) and the expression levels of Treg and Th17 in control group were higher than that in BBG group; There were no significant differences in the three groups at 6h, 12h and 48h after treatment (P=0.052, 0.271, 0.4; P=0.114, 0.285, 0.165). **2**. The expression trend of Treg and Th17 in different time periods: After treatment, the levels of Treg and Th17 were increased at 6h and 12h, but decreased gradually at 24h. **3**. The ratio of Treg/Th17 was decreased in the four time periods, but compared to BBG and control groups, the ratio of Treg/Th17 in the ATP group were lower and the differences were statistically significant (P<0.05) at 24h. There were no significant differences on the ratio of Treg/Th17 among the three groups at 6h, 12h and 48h after treatment (P=0.225, 0.078, 0.103). [Conclusions] Activation of P2X7R promoted the expression of Treg and Th17 cells in acute gouty arthritis model but decreased the ratio of Treg/Th17 that showed an acute change trend along with the time, suggesting that P2X7R-regulated the ratio of Treg /Th17 cells affected acute gouty arthritis.

EP3-03

Knee osteoarthritis synovial fluid leukocytes and the association of pro-inflammatory monocyte/macrophages with clinical outcomes

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Conflict of interest: None

[Object] - To determine the prevalence, subtypes and activation state of T cells and monocyte/macrophages (MΦs) in knee osteoarthritis (KOA) synovial fluids (SFs)- To identify whether KOA SF pro-inflammatory MΦs predict KOA phenotypes. [Methods] 70 SF and 39 blood samples from patients with radiographic KOA were used to determine the frequency of leukocyte populations in KOA SFs and the characteristics of MΦs and T cells using flow cytometry. KOA patients provided answers to questionnaires to determine symptomatic scores: WOMAC and KOOS. Linear modelling (adjusted for sex, BMI and age) was used on the data to determine correlations. P<0.05 was considered significant. [Results] MΦs (median=36.4%) were found to be the main leukocytes present in KOA SF followed by T cells (32.8%), being CD3+CD4neg (18.45%), mainly cytotoxic T cells, usually more abundant than T helper (TH) cells (12.3%). Further analysis of MΦs showed that KOA SF MΦs are enriched for the CD14+CD16+ population (pro-inflammatory) (39%) while both CD14+CD16neg (55.9%) and CD14lowCD16+ (4.63%) are impoverished when compared to blood mononuclear cells from OA patients (5.89% for CD14+CD16+). MΦs in OA SF show a higher expression of HLA-DR compared to those in blood, indicating an activated state. Similarly, unlike circulating T cells, more than 70% of T cells are activated (CD69+) in KOA SF. Analysis of associations of pro-inflammatory MΦs with KOA radiographic grade (defined as early, KL=1-2 or late, KL=3-4) showed no differences based on stage, however there was a significant association (β>|0.4|) with mean KOOS, KOOS activity of daily living, quality of life and sports; mean WOMAC and WOMAC pain, function and stiffness. [Conclusions] The main leukocytes in the SF KOA environment are MΦs and T cells, both of which present an activated state, indicating the subjacent chronic inflammation in OA. CD14+CD16+ (pro-inflammatory) MΦs are highly prevalent in the KOA SF and are associated with patient symptoms.

EP3-04

Magnoflorine with Hyaluronic Acid Gel Regulate Subchondral Bone Regeneration and Attenuate Cartilage Degeneration on the Early Stage of Spontaneous Osteoarthritis

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Conflict of interest: None

[Object] Aim to address Chinese medicine magnoflorine combined with hyaluronic acid (HA) gel effectively promote trabecular bone remodeling and attenuate cartilage degeneration on the early stage of spontaneous knee osteoarthritis (OA). [Methods] The MC3T3-E1 cell (osteoblast) viability was detected by XTT. The cell proliferation was reflected by cell cycle assay. Bone formation was detected by Alizarin Red staining. The 5 month female Dunkin-Hartley guinea pig as a spontaneous OA model was made a standardized bone defection with 1mm diameter and 5mm depth on the tibial medial under cartilage. Guinea pigs were once intra-bone injected 50 ng magnoflorine, HA gel, 50 ng magnoflorine + HA gel, and null, respectively. All collected limbs were performed micro-CT (μCT) scan and histological staining at 2 month post-surgery. [Results] MC3T3-E1 cells treated with 25 μg/ml magnoflorine, the cell viability, S phase of cell cycle and degree of mineralization were significantly increased. For in vivo study, with 50 ng magnoflorine + HA gel treatment, the trabecular bone parameter changes were implied trabecular bone regeneration. Furthermore, the decreased modified Mankin's scores, higher ratio of hyaline cartilage (HC)/ calcified cartilage (CC) volume and the fractal dimension (FD), which was implied the roughness of subchondral bone plate (SBP), were reflected significant improvement of cartilage degeneration, when compared to no treatment and HA group. Finally, there was a significant positive association between FD and the volume ratio of HC/CC measured by histological staining and a significant negative association between FD and modified Mankin's scores. [Conclusions] We elucidated the potential benefit of magnoflorine combined with HA gel for trabecular bone and cartilage regeneration, and the relationship between SBP and cartilage on the early stage of OA. It also demonstrated the possibility to diagnose pathogenesis of early OA using μCT analysis for clinical assessment.

EP3-05

MicroRNA discovery in knee osteoarthritis using next generation sequencing

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Conflict of interest: None

Objective: Since there is no cure for osteoarthritis (OA), early intervention is critical to prevent disease progression. There are no biomarkers that can be used in a diagnostic, prognostic, or therapeutic manner for OA. Circulating microRNAs show promise as biomarkers for several diseases. Our lab was the first to perform global array screening of microRNAs in OA. Our current objective is to use next generation sequencing to identify circulating microRNAs as biomarker signatures to define cohorts of patients with varying severity of OA. **Methods:** Sequencing has never been applied to identifying circulating microRNAs in OA, and has the sensitivity and specificity to detect known and novel microRNAs that are unique to various cohorts. We are defining our cohorts based on Kellgren-Lawrence radiographic grading for early OA (grades 0 & 1) and late OA (grades 3 & 4). Plasma samples from 10 normal donors, 10 early OA patients, and 10 late OA patients will be subjected to next generation sequencing of microRNAs. Candidate microRNAs will be selected for validation by real-time PCR in additional cohorts of early OA (N=100), late OA (N=100), and normal donors (N=100). Bioinformatic methods will be used to predict the biological function of candidate microRNAs in OA. **Results:** Initial sequencing analysis of 5 normal donors and 5 late OA patients is complete. A list of top 20 differentially expressed microRNAs was generated based on false discovery rate < 0.05, log counts per million > 2, log fold change > 1.5, and p-value < 0.0003. Hierarchical clustering of these microRNAs revealed a distinct pattern between normal and late OA samples. Among these microRNAs is a candidate previously shown to be dysregulated in OA synovial fluid, and a novel putative microRNA that has not previously been identified. **Conclusion:** Preliminary results suggest that next generation sequencing is a useful approach for identifying known and novel circulating microRNAs as potential biomarkers for OA.

EP3-06

Presence of RANK- Osteoclast-like Cells in the Bone of Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Object] Previously, we reported that novel osteoclast-like cells (OLCs) were induced, both in vitro and in vivo, from mouse bone marrow-derived monocytes/macrophages by addition of a combination of TNFα and IL-6. Herein, we aimed to examine differentiations of OLC, which a combination of TNFα and IL-6 induced from human peripheral blood mononuclear cells (PBMCs) and to identify differences in molecular expression patterns between OLCs and conventional osteoclasts. Furthermore, we evaluated OLC presence in the bone of patients with rheumatoid arthritis (RA). **[Methods]** PBMCs from RA patients and healthy volunteers were stimulated with TNFα and IL-6 or RANKL. Quantitative PCR was used to measure mRNA expression levels of osteoclastogenesis-related genes. Decalcified frozen sections of tibia from 6 patients with RA or osteoarthritis (OA) were stained by tartrate-resistant acid phosphatase (TRAP) as an osteoclast histochemical marker, and osteoclastogenesis-related molecular expression was analyzed by immunohistochemistry. **[Results]** The number of TRAP-positive multinucleated OLCs was significantly increased from PBMC of patients with RA treated with a combination of TNFα and IL-6 compared to that of healthy volunteers. In addition, RANK mRNA expression was clearly up-regulated in osteoclasts and was obviously down-regulated in OLCs. In cancellous bone, the number of $RANK^+$ osteoclasts was significantly increased in patients with RA compared to that in patients with OA. Interestingly, numerous $RANK^-$ OLCs were present in the cancellous bone of patients with RA, while almost none were observed in the cancellous bone of patients with OA. **[Conclusions**] Human OLCs, expressing RANK low, were induced from PBMCs of patients with RA with a combination of TNFα and IL-6. $RANK^-$ OLCs were present in the bone of patients with RA. These results suggest that $RANK^+$ osteoclasts and $RANK^-$ OLCs may be involved in the pathogenic mechanism underlying inflammatory bone diseases such as RA.

EP3-07

Expressions of BAFF, its receptors and TLRs in peripheral blood B cells of patients with rheumatoid arthritis

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Conflict of interest: Yes

Objectives: B cells play important roles in rheumatoid arthritis (RA), the expression of BAFF and TLRs have been implicated in the survival and activation of B cells. We studied regulatory B cells, BAFF and its receptors, TLRs in RA and investigated their relationships with disease activity. Methods: 30 patients with RA and 15 healthy controls were selected. BAFF levels in serum were measured by ELISA. The proportions of B cells and regulatory B cells ($CD24^{hi}CD38^{hi}$, $CD24^{hi}CD27^+$) in peripheral blood were detected by flow cytometry, and the expressions of TLR7, TLR9 and three BAFF distinct receptors (TACI, BAFFR, BCMA) in B cells detected. B cells were sorted by magnetic beads, and the expressions of TLR7 and TLR9 were detected by QPCR at mRNA level. Results: The proportions of B cells and regulatory B cells were no significant difference between healthy control and RA. Compared with healthy controls, the serum BAFF levels in patients with RA were significantly increased. Flow cytometry showed that the proportion of TACI in B cells increased in patients with RA, and the MFI of TLR7 and TLR9 increased significantly. QPCR results showed that the expression of TLR9 was increased significantly, but there was no significant difference between patients and healthy controls about the expression of TLR7, The patients were divided into high disease activity group (DAS28>5.1) and low disease activity group (DAS28<5.1) according to DAS28, and TLR9-MFI was significantly higher in the high disease activity group. Conclusion: RA has no significant effect on the proportions of B cells and regulatory B cells. BAFF may promote the increase of TLR9 mainly through TACI. TLR9 is valuable in evaluating the severity of RA, and is worthy of further study.

EP3-08

Occupational Performance In Rheumatologic Diseases: Translation, Validity And Reliability of Occupational Circumstances Interview And Rating Scale (OCAIRS-S V2)

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Conflict of interest: None

[Object]: Rheumatologic diseases (RD) are chronic, disabling diseases results in progressive joint destruction with deformities and various degrees of limitation in occupational performance. Disease severity can vary considerably even from day one to the next. The aim of this study was to translate the Occupational Circumstances Interview and Rating Scale (OCAIRS-S V2) to Turkish language and assess its reliability and validity in people with Rheumatologic Diseases. [Methods] The Turkish version was obtained after a translation and back-translation process. 157 people with different rheumatologic diseases were assessed with OCAIRS-S V2. To assess its validity, they also fill the Turkish version of Community Integration Questionnaire (CIQ) and authors assessed occupational performance with Canadian Occupational Performance Measure (COPM). [Results] The internal construct validity of the OCAIRS was assessed by Rasch analysis and external construct validity by correlations with the CIQ and COPM. Reliability was tested by internal consistency and person separation index. After rescoring the disordered response categories and sub testing “short-term goals” and “long-term goals”, item set satisfied Rasch model expectations with a mean item fit of 0 (SD 0.652) and person fit of 0.626 (SD 1.2). While the unidimensionality assumption was confirmed, the subset of “long7short-term goals” showed differential item functioning in terms of education. (Those with an education level of primary school were rated lower than those with high school and university graduation). The reliability was good with Cronbach’s alpha coefficient and person separation index levels above 0.83 ($p<0.001$). The presence of the expected level of correlations between OCAIRS, CIQ and COPM has confirmed the external construct validity ($p<0.001$). [Conclusions] The results of this study show that the Turkish version of OCAIRS is reliable, valid and sensitive to change for people with rheumatologic disease.

EP3-09

Some anti-CL-beta2-GPI antibodies induce a prothrombotic state by the dual reactivity with DNA and internalization into live cells

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Conflict of interest: None

[Object] Anti-CL-β_2GPI antibodies play a pathogenic role in antiphospholipid syndrome. Although several candidate receptors have been proposed as mediators in β_2GPI-induced cell activation, the mechanism of binding of β_2GPI to live cell surface has not been fully elucidated. We generated a monoclonal antibody WB-6 which binds to CL-β_2GPI, from an (NZW x BXSB) F1 mouse, and reported that it leads to a prothrombotic state in normal mice by inducing tissue factor (TF) expression on the circulating monocytes. Later, we noticed that WB-6 also reacts with DNA, in addition, it enters live cells. This study is aimed to clarify the mechanism of interaction between WB-6 and the cells in these experiments. **[Methods]** WB-6 was purified by a protein A column. Apoptosis was induced in monocytic THP-1 cells by staurosporine, and microparticles (MPs) were isolated from the culture supernatant by differential centrifugation. THP-1 cells were incubated with WB-6 for 2 h at 37°C. After wash, fixation, permeabilization and blocking, internalized antibody was detected using fluorescence-labeled anti-mouse IgG, and

analyzed by fluorescence microscopy and flow cytometry. **[Results]** By 2 h incubation, WB-6, but not normal mouse IgG, entered the live cells. At this point, the cells showed no morphological change, or no staining with FITC-annexin V. Pre-treatment of the cells with DNase 1 diminished the entry of WB-6, suggesting that cell-surface DNA is involved in this phenomenon. On the other hand, pre-incubation of the cells with MPs enhanced the entry of WB-6. Moreover, internalization of WB-6 led to TF expression on THP-1 cells. **[Conclusion]** Since two decades ago, anti-DNA antibodies have been known to enter live cells. In the current study, we show that at least a part of anti-CL-β_2GPI antibodies possess the nature of dual-recognition between CL-β_2GPI and DNA, and can be internalized by live cells through cell surface DNA, which finally leading to TF expression on monocytic cells.

Poster Session

P1-001

Ultrasonographic findings in patients with lung cancer who developed arthritis symptoms during treatment of the immune checkpoint inhibitor Pembrolizumab

Tadashi Okano[1], Kentaro Inui[1], Yutaro Yamada[1], Koji Mandai[1], Kenji Mamoto[1], Yuko Sugioka[2], Setsuko Takeda[3], Emi Yamashita[3], Yuko Yoshida[3], Tatsuya Koike[2,4], Hiroaki Nakamura[1]
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Conflict of interest: Yes

[Object] In recent years, it has become possible to use immune checkpoint inhibitors to treat advanced cancer, but immune-related adverse events (irAE) have been reported. We have experienced various ultrasonographic (US) findings in patients with lung cancer who developed arthritis symptoms during treatment of the immune checkpoint inhibitor Pembrolizumab. [Case 1] A 57-year-old man. Joint pain appeared in hand, knees and ankle after administration of Pembrolizumab for non-small cell lung cancer (NSCLC). US showed synovial inflammation in MCP and knee, tenosynovitis in flexor tendon and enthesitis were found. Oral glucocorticoid was effective for these inflammtion. [Case 2] A 61-year-old female with rheumatoid arthritis. After administration of Pembrolizumab for NSCLC, swelling appeared on the right ring finger and the left middle finger. Synovitis was not found in the joint, but remarkable flexor tenosynovitis was observed in US examination. Glucocorticoid injection for tenosynovitis was effective. [Conclusions] Various inflammatory findings were detected by US in patients treated immune checkpoint inhibitor. It is very important to understand that irAE due to immune checkpoint inhibitors develop not only synovitis like rheumatoid arthritis but also tenosynovitis and enthesitis.

P1-002

The influence of musculoskeletal ultrasound findings at the time of achievement of clinical remission on the subsequent disease activity

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Conflict of interest: Yes

[Object] The study aimed to conduct additional examinations for change in disease activity and musculoskeletal ultrasound (MSKUS) findings at the time of achievement of remission during the following 6 months. [Subject] Of 72 cases with achievement of clinical remission in DAS28-ESR and lower disease activity in SDAI during the period one year, the study targeted 71 cases with a follow-up during the following 6 months. [Methods] 1) The course of disease was examined by calculating DAS28-ESR and SDAI for 3 months/6 months after achievement of remission. 2) The study investigated the following items as a relation between MSKUS findings at the time of achievement of remission and DAS28-ESR and SDAI after 3 months/6 months. The study items were set as PD score, GS score, and presence/absence of PD≧ 1/PD=grade 2/GS≧grade 2. [Results] 1) 56 cases indicated the maintenance. 2) For 3 months/6 months after remission, the study found there was a difference between average SDAI and SDAI at the time of remission with presence/absence of PD=grade 2. [Conclusions] According to the cases with joint findings of PD=grade 2 found by MSKUS at the time of achievement of remission, it would be required to carefully observe a progress of the subsequent disease activity.

P1-003

Diagnostic utility of detecting MTP synovitis by ultrasonography in early Rheumatoid arthritis

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Conflict of interest: None

[Object] In rheumatoid arthritis (RA), not only hand and finger joints but also the metatarsophalangeal (MTP) joints are affected site of synovitis. We investigated whether detection of MTP synovitis by ultrasonography (PDUS) is useful for diagnosis in early RA. [Methods] We enrolled 161 patients with suspected RA within 6 months of onset. We assessed articular synovium of Gray scale and power Doppler signals by semiquantitative method (grade 0 - 3) in both hand and finger joints (22 joints), as well as synovitis, bone erosion and intermetatarsal bursitis in both MTP joints (10 joints) by PDUS. [Results] Fifty-three patients were diagnosed as RA, and 108 patients were non-RA. RA patients showed PDUS synovitis in hand and finger joints (79%) and in MTP joints (55%). The frequency of MTP synovitis, bone erosion, and metatarsal bursitis were significantly higher in RA patients than in non-RA. Among RA patients without PDUS synovitis in hand and finger joints, 7 patients (64%) showed MTP synovitis and 4 patients showed asymptomatic synovitis. [Conclusions] In this study, 13% patients of RA were developed with MTP synovitis. If synovitis cannot be detected in hand and finger joints by PDUS, the scanning for MTP joints is useful for diagnosis in early RA.

P1-004

Comparative study on effectiveness of non-TNF inhibitor (Abatacept; ABT, Tocilizumab; TCZ) using joint ultrasonography (US)

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Conflict of interest: None

[Object] Rheumatoid arthritis's (RA) synovial lesion assessment of US (Gray scale; GS, Power doppler; PD) is being well-established recently. Non-TNF inhibitors (ABT, TCZ) are often selected for patients who are difficult to administer methotrexate, but there are no clear. We conducted US evaluation, examined whether it could be a tool for treatment selection. [Methods] 135 RA patients who were introduction of ABT, TCZ from September 2010 to October 2015 were observed. We evaluated the difference between ABT group (n=67) and TCZ group (n=68) by baseline characteristics, disease activity, change in serological test value, GS and PD score at baseline, 6, 12 and 24 months. [Results] At 24 months between ABT and TCZ groups, there was no significant difference in ΔDAS28-CRP (-1.89 vs. -1.73) and ΔMMP-3 (-87.80 vs. -152.09 ng/mL), but ABT group's RF titer was significantly suppressed. (ΔRF -184.10 vs. 19.55 IU/mL, P<0.05) ABT group's GS score decreased significantly at 24 months compared to baseline, but not in TCZ group. (ABT; 32.90 vs. 15.50, P<0.05, TCZ; 36.38 vs. 23.85, P=0.07) PD score showed a significant decrease in both groups. (ABT; 8.85 vs. 0.44, P<0.01, TCZ; 9.29 vs. 0.95, P<0.01) [Conclusions] ABT could be an effective therapeutic agent in cases with high joint swelling by US.

P1-005

The comparison between physical and ultrasound joint examination for the hand joints in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To establish the importance of joint examination by ultrasound (US) in clinical practice of patients with rheumatoid arthritis (RA), we compared the US findings with the joint examination findings sorted by the presence of tenderness and/or swelling in the hand joints. [Methods] A total of 208 RA patients completed clinical, laboratory and US assessments. Clinical joint assessments determined the presence of tenderness alone (T) or swelling alone (S), both (TS) or none (N) of them. US synovitis was defined as GS grade≧1 or a PD grade≧2. [Result] Arthritis based on US was 26% (50/195) in TS, 6% (11/195) in T, 19% (37/195) in S, 50% (97/195) in N. The detection of arthritis in the US was 90% (45/50) in the radial side, 96% (48/50) in the median and 96% (48/50) in the ulna side in the TS. In T,45% (5/11), 64% (7/11), 45% (5/11). In S, 54% (20/37), 78% (29/37), 59% (22/37). And in N, 42% (41/97), 76% (74/97), 48% (47/97). In TS, T, and S, there was no difference in the detection rate of arthritis in US by observation site, but in N, arthritis in US was detected more in the median than on the radial side and the ulnar side (p<0.01). [Conclusions] Based on the US, arthritis in the US was more frequent in the midline of the wrist joint when the wrist joint had neither tenderness nor swelling.

P1-006

The comparison between the EULAR response criteria and ultrasonography assessment in monitoring therapeutic response for rheumatoid arthritis

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Conflict of interest: None

[Object] To investigate the association between the EULAR response criteria and US assessment in monitoring RA activity. [Methods] Power Doppler (PD) US was performed in 24 joints (all PIP, MCP, bilateral wrist and knee joints) as comprehensive evaluation in 23 RA patients treated with certolizumab pegol or tofacitinib. Before and after treatment, PD signals and gray-scale (GS) were scored semiquantitatively in each joint. The comprehensive PD and GS scores were calculated by summing up PD and GS scores, respectively, of the 24 joints. [Results] Both change of comprehensive PD and GS scores by treatment were significantly larger in good response (GR) group of the EULAR response criteria than in no response (NR) group (p = 0.0043 and 0.011, respectively). Among the patients in the NR group, 2 (40%) and 3 (60%) showed decrease in the comprehensive PD and GS scores, respectively. Among the patients with response by the EULAR response criteria (GR and moderate response groups), 2 (11%) and 3 (17%) showed no improvement in the comprehensive PD and GS scores, respectively. Thus total 4 (17%) and 6 (26%) showed discrepancy between the EULAR response criteria and the US assessment. [Conclusions] The US assessment is important for monitoring response to treatment in individual RA patients.

P1-007

Study on usefulness of joint ultrasonography in 2015 ACR / EULAR gout classification criteria

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Conflict of interest: None

[Purpose and Object] 2015 gout classification criteria (2015 criteria) scores 8 domains and more than 8 points are classified as gout. Among domains, the double contour sign (DC) which the presence of MSU crystals by US has been given a high score of 4 points. In this study, 263 male

gout patients were scored and compared with the 1977 ACR classification criteria (1977 criteria) and the usefulness of US in 2015 criteria was examined. [Results and Conclusions] In all cases, the sensitivity of 2015 criteria was 82%, which was superior to the sensitivity of 1977 criteria of 53%. When examined in patients with 1st MTP gout, the sensitivity of 1977 criteria was 78%. the sensitivity of 2015 criteria was 64% and1977 criteria was 14% in the patients other than 1st MTP. In the examination in each domain of 2015 criteria, there was a significant difference in the involved site and US findings compared with the patients of 6 points or more in the patients with 5 or less in 1977 criteria. In 2015 criteria, there was a significant difference in involved site, typical course compared with the patients with 8 or more points in the patients of 7 points or less and no DC was observed in the patients of 7 points or less.

P1-008

Ultrasound findings of treatment for rheumatoid arthritis treated with Tofacitinib

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Conflict of interest: None

[Object] To investigate ultrasound findings of tratment for rheumatoid arthritis treated with Tofacitinib. [Subject] We performed a retrospective study of 11 patients who were treated with Tofacitinib and were estimated by using ultrasounds. We treated 4 patients by 5mg/day Tofacitinib,7 patients by 10mg/day Tofacitinib. [Method] We used Avius (urtrasounds by Hitachi). We observed the bilatelal MPjoints, PIP joints, thener MP joints, wrist joints (radial, medial, ulnar, distal radius-ulnar joint). [Estimate] We estimate for tenderness joint counts, swollen joint counts, CRP, Patients VAS, Dr VAS, DAS28 (CRP), SDAI, MMP-3, total gray scale Score (0~66) and total power dopplar score (0~66) at baseline, at 12weeks, at 24weeks. [Results] Average DAS28 (CRP), SDAI, MMP-3 were 4.98→2.81→2.31 (at baseline-12weeks-24weeks), 27.3→12.4→9.0, 480.3→212.1. Total GS scores were 15.9-12.6-10.4 (at baseline-12weeks-24weeks), Total PD scores were 15.0-8.4-6.7 (at baseline-12weeks-24weeks). There were significantly improved from baseline beetween at 12weeks,24weeks. [Conclusions] We suggest that ultrasounds findings (Total GS scores and PD scores) were improved by treatment for rheumatoid arthritis who treated by Tofacitinib.

P1-009

Correlation and diagnostic relevance between findings of musculoskeletal ultrasonography and RA classification criteria (2010ACR / EULAR) for undiagnosed patients with polyarthralgia

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Conflict of interest: None

<Objective> We evaluated relationship between RA classification criteria and musculoskeletal ultrasonographic findings. <Methods> Ultrasonographic studies of both wrists,2-5 MCP joints and painful joints were performed for undiagnosed patients with polyarthralgia, who visited our hospital from December 2015 to October 2017. We defined significant findings as fellows. 1) PD ≧ 2 in MCP joint, PIP joint, 2-5 MTP joint, or hand joint. 2) PD ≧1 in elbow or knee joint. <Results> There were 183 patients (female / male: 108/75); mean age: 66 years [53, 75]; RF positive 41.5%, ACPA positive 26.2%, bothnegative 56.3%; the interval between ultrasonography and the onset (weeks): 12 [7, 24]. The ACR / EULAR score was the most numerous (4 points (19%), followed by 7 points (17%), 5 points (16%). The ACR / EULAR score was 110 (60.1%) for 5 or less. Significant ultrasound findings were found in 44.5% of groups with 5 or less. In the group with 6 points or more, 32.8% (24cases) was the case without significant findings of echo. Among them, 6 patients (25%) was with SjS or suspected SjS. <Conclusion> Addition of sonographic exam would make the diagnosis of RA more sophisticatedly.

P1-010

Examination of ultrasound images for rheumatoid arthritis clinical remission cases

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Conflict of interest: None

[Object] Joint ultrasonography is used for the diagnosis and treatment evaluation of rheumatoid arthritis (RA), and is particularly useful for the detection of latent synovitis which is difficult to judge by clinical evaluation. Here we evaluated the presence or absence of latent synovitis in clinical remission cases with ultrasound images. [Methods] An RA patient meeting ACR / EULAR classification criteria in our hospital rheumatism internal medicine clinic. DAS - CRP 28 9 cases that met the remission criteria 98 joints. Boolean remission was 7 cases. Average age is 63.4 years (27 years old to 84 years old) 9 women. Grayscale (GS) Grade 2 and above was synovial thickening, and Powered doppler Signal (PD) was Grade 1 and above as inflammatory. Equipment used: LOGIQ e 12 L linear probe in GE company. [Results] Synovial thickening was observed in 4 cases of 5 joints (3 wrist, 1 knee, 1 PIP) and PD positive cases were 3 cases 4 joints (3 wrist, 1 PIP). In one of these cases, treatment was strengthened. [Conclusions] Even in cases diagnosed as clinical remission, PD was confirmed by joint ultrasound, suggesting that clinical remission and image remission do not necessarily match. Joint ultrasonography is useful for assessment of latent synovitis.

P1-011

Analysis of joint ultrasonography, patient background and the serologic characteristics in the rheumatoid arthritis diagnosis of patients with the joint symptoms that is not diagnosed

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Conflict of interest: None

[Object] In rheumatoid arthritis patient with the joint symptoms that is not diagnosed, I examined the association with the factors such as joint ultrasonography, patient background and the serologic characteristics. [Methods] 28 patients were enrolled. The synovitis evaluated gray scale (GS) and power doppler (PD) with 26 both hands joints. I evaluated age, sex, the number of joint pain and swelling, the serologic characteristics (CRP, ESR, CCP, RF, MMP-3). [Results] RA group which were finally diagnosed RA was 10, non RA group which was not diagnosed was 18. RA group; ACR/EULAR>6 was 4, ACR/EULAR<6 was 6. In the 6 patients, 4 patients were diagnosed with ultrasonography, and 2 patients with MRI. The main patient background age (64.8±19.3, 60.0±19.3), the sex (70%/30%, 22.2%/77.8% (M/F)) number of the joint pain (5.9±5.2, 2.6±1.9), the number of the swelling joint (3.5±4.4, 0.7±1.4) (mean±SD). As a result of single variable analysis, number of the swelling joints, CRP, RF, CCP, MMP-3, GS, PD were extracted for significant difference. For the multivariate analysis by the step Wise method, PD was extracted with a dominant difference (p=0.0001). [Conclusions] In the patient with the joint symptoms that is not diagnosed, PD was a useful tool by the diagnosis of rheumatoid arthritis.

P1-012

Usefulness of joint ultrasonography (US) in differentiation and evaluation of arthritis

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Conflict of interest: None

[Object] the opportunity for the US to be implemented as an aid for early diagnosis and activity evaluation of rheumatoid arthritis (RA) in outpatient has increased. US is useful not only for the presence or absence of synovitis but also for the diagnosis of bone erosion, calcified lesion, bursa of bursa, tendon stenosis. [Methods] Patients who complained of joint symptoms in our department from 2015 to 2017 were subject to US enforcement. Synovitis was evaluated by semi-quantitative determination (0 - 3) of GS and PD. When there were significant findings in the joints and large joints other than the wrist joint, we judged it positive by the presence or absence of PD. [Results] Even in cases where it is difficult to conclude with clinical information alone such as serologically negative atypical cases and low disease active RA, it was possible to diagnose RA early by pointing out latent synovitis did it. [Conclusions] It is impossible to improve patient outcome by making accurate diagnosis only with serological diagnosis and classification standards and we considered that US is very useful as an assistance tool for medical treatment. It is suggested that the asymptomatic PD signal may be a risk of joint destruction.

P1-013

Evaluation of new acoustic couplers in rheumatic ultrasound

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Conflict of interest: None

[Object] The Joint ultrasonography is one of the most important diagnosis tools of rheumatoid arthritis. But examiners have difficulty taking images of a joint with transformation and curvature. Acoustic coupler SF-001 was developed to avoid the difficulty in near field observation, so we describe its use experience this time. [Methods] This study was conducted with 127 joints of fingers of patients who took rheumatism examination at Hokkaido Medical Center for Rheumatic Diseases. We compared the GS Grade, the PD Grade, and vascularity value (Vs%) measured by Box method. The comparison was made by the jelly and coupler method respectively. The grading of GS and PD followed the joint imaging method echo guideline, and evaluations ware performed using Ultrasound Diagnostic Scanner: Noblus (Hitachi. Ltd). [Results] The GS and PD grades by coupler method were matched the ones by jelly method, and the correlation coefficient between each method resulted in R=1.00 (P<0.001) on GS grade, R=1.00 (P<0.001) on PD grade. For Vs% the correlation coefficient resulted in R=0.99 (P=<0.001). [Conclusions] The acoustic coupler could evaluate ultrasound images in the equivalent level as the conventional jelly method.

P1-014

Ultrasound Examination of Shoulders and Wrists in Patients with Polymyalgia Rheumatica

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Conflict of interest: None

[Object] Polymyalgia Rheumatica (PMR) is a rheumatic disease in which stiffness and pain around shoulders or hips is one of the main symptoms with elevated CRP and MMP-3. Rheumatoid factor (RF) and anti-citrullinate protein antibody (ACPA) are negative in most of patients with PMR. Differential diagnosis between PMR and RA is often difficult. In the present study, results of ultrasound (US) examination in shoulders and wrists in patients with PMR are investigated. [Methods] 32 PMR patients were included in this study. US of bilateral shoulders and wrists were performed by JCR sonographers in these patients for diagnosis before treatment and they were diagnosed as PMR by rheumatologist. Flequency of pulse doppler (PD) signals in shoulders and wrists were investigated. [Results] Mean age was 76.0 years old. 21 female and 11 male. None was ACPA positive and one was RF positive. PD at either shoulder was observed in 28 cases (88%). PD at either wrist was observed in 22 cases (69%). PD at both either shoulder and either wrist was observed in 22 cases (69%). [Conclusions] It is well known that peripheral arthritis or arthalgia is sometimes concomitant in PMR patients. PD at wrist joints are observed besides PD at shoulder joints in PMR patients in the present study.

P1-015

Influence and effects of joint ultrasound (US) examination results on suspected cases of polymyalgia rheumatica (PMR)

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Conflict of interest: None

[Object] To clarify the contribution and characteristics of US findings to the diagnosis and treatment course of suspected PMR. [Methods] We investigated 37 cases who underwent US retrospectively because clinically suspected of PMR in March 2015-May 2017. Based on the US findings, we classified them into 4 groups (1) PMR (2) rheumatoid arthritis (RA) (3) no findings (4) others, and examined the clinical diagnosis and treatment progress up to November 2017. [Results] 15 patients (40.5%) in group (1), 12 were treated with PSL only and the progress was good, 2 added methotrexate because of resistance to PSL, 1 was unknown. 12 patients (32.4%) in group (2), 8 were treated as RA, 2 were diagnosed PMR and treated with PSL only. 1 was unknown.1 improved symptoms without treatment. 5 patients (13.5%) in group (3), both patients improved symptoms without treatment. 5 patients (13.5%) in group (4), 2 were RA, 1 was pseudogout, 2 were unclassifiable. [Conclusions] Most of cases conforming to PMR in both clinical judgments and US findings were good with treatment with PSL only. On the other hand, cases in which US findings differ from clinical diagnosis occupied more than half, and treatments other than PSL were required. It was suggested that joint US is useful for decision and prediction of treatment course.

P1-016

Screening research of peripheral arthritis by ultrasonography in patients with inflammatory bowel disease

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Conflict of interest: None

[Object] Traditionally, tender and swollen joint counts were assessed by clinical assessment. To date, the modern imaging tool such as ultrasonography (US) can detect the joint and enthesial inflammation more sensitively than clinical assessment. The aim of this study was to research the utility of US screening for detection of peripheral arthritis in patients with inflammatory bowel diseases (IBD) such as ulcerative colitis (UC) and Crohn's disease (CD). [Methods] Total 42 patients including 27 patients with UC and 15 patients with CD were underwent gray-scale (GS) and power Doppler (PD) US examination in MCP, PIP, DIP and wrist joints in both hands. GS and PD were scored on a semi-quantitative scale for each joint. [Results] In the clinical assessment, 12 patients with UC and 7 patients with CD had joint symptoms. US active synovitis (GS Grade≧2 · PD Grade≧1) was found in 8 patients with UC and 6 patients with CD. The concordance rate between clinical findings and US findings was relatively low in UC and high in CD patients. [Conclusions] The peripheral arthritis findings in patients with IBD was compared between clinical and US examination. The presence rate of subclinical synovitis was not high, thus US screening might not useful in patients with IBD without arthritis symptom.

P1-017

Sonographic evaluation of hands and shoulders in patients with remitting symmetrical synovitis with pitting edema: Comparison with polymyalgia rheumatica

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Conflict of interest: None

Objective. To compare ultrasound (US) findings of hands and shoulders in patients with remitting symmetrical synovitis with pitting edema (RS3PE) with polymyalgia rheumatica (PMR). *Methods.* US images of untreated 9 RS3PE and 15 PMR patients were retrospectively analyzed. Synovitis was assessed in wrists and 2nd MCP using OMERACT-EULAR composite US score. Presence of abnormality was assessed in shoulders regarding following findings: long head of biceps (LHB), subacromial bursa (SAB), glenohumeral joint (GHJ), subscapularis tendon (SST). *Results.* All RS3PE patients had symmetrical pitting edema on hands, feet, or both which was confirmed by US. Eight out of 9 RS3PE patients had pain and limited range of motion in the shoulders. RS3PE patients had higher wrist synovitis score than PMR. However, there was no difference between groups when patients without any sings of synovitis were excluded. One RS3PE patient had synovitis in MCP joint whereas no PMR did. PMR patients had higher prevalence of LHB tenosynovitis, whereas no difference between groups was observed in other shoulder findings (LHB:86.7 vs 38.9% (p=0.0005), SAB:30.0 vs 22.2%, GHJ:50.0 vs 44.4%, SST:33.3 vs 16.7%). *Conclusion.* US identified little difference between RS3PE and PMR in hands and shoulders.

P1-018

Gout with double contour sign in all 40 joints: a case report

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Conflict of interest: None

A 58-year-old man was referred to our hospital complaining of acute development of polyarthritis. Despite NSAIDs, colchicine, and febuxostat treatment at the previous hospital, arthritis deteriorated day by day and he could not move by himself. His past history showed that he was diagnosed as hyperuricemia at the age of 40 and gout in left MTP joint at 45. Since then, he had been suffering from gout attacks every 2 years. Physical examination revealed swellings and tenderness in all joints, and also found subcutaneous nodules which suggest gouty tophus. X-ray demonstrated bone erosion and overhanging margin in fingers and toes. Musculoskeletal ultrasound examination showed double contour sign in all 40 joints examined. Synovitis with tophus-like lesion and hyperechoic spots were also detected by ultrasound. We confirmed acicular crystal in tophus by needle aspiration biopsy and diagnosed as polyarthritis by gout. Since he had chronic renal failure, we treated him with prednisolone 30mg/day. His symptoms were significantly improved by the treatment.

P1-019

Up-date OMERACT RA MRI scoring system (RAMRIS) for assessing the efficacy of biologics in the treatment of rheumatoid arthritis

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Conflict of interest: None

[Background] In 2016, the OMERACT RAMRIS (rheumatoid arthritis MRI scoring system) was updated to include scores for joint space narrowing and tenosynovitis. [Object] To assess the efficacy of biologics in the treatment of RA using the OMERACT 2016 RAMRIS. [Subjects] Subjects were 17 RA patients at a mean age of 46.8 years. [Methods] Simple and contrast MRI examinations were performed on the hand of patients before and one year after treatment with biologics. The OMERACT 2016 RAMRIS was used to score bone erosion (full score: 250), joint space narrowing (88), osteitis (75), synovitis (24), and tenosynovitis (42). [Results] Mean scores before and after treatment with biologics were 11.6 and 16.9 for bone erosion, 15.1 and 17.4 for joint space narrowing, 10.1 and 6.4 for osteitis, 7.8 and 4.9 for synovitis, and 7.2 and 2.8 for tenosynovitis, respectively. Scores for bone erosion and joint space narrowing worsened in 12 and 8 of 17 patients, respectively, whereas scores for osteitis, synovitis, and tenosynovitis improved in 12, 14, and 15, respectively. Patients with high baseline tenosynovitis scores had worsened bone erosion scores after treatment with biologics. [Conclusions] The OMERACT 2016 RAMRIS is useful for assessing the efficacy of treatment and predicting prognoses.

P1-020

Two cases of anti-CCP antibody (ACPA) positive arthritis which showed remarkable decrease of trabecular bone at distal radius by analysis with high resolution peripheral Quantitative CT (HR-pQCT)

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Conflict of interest: None

HR-pQCT (Xtream CT II Scanco Medical) can quantitatively analyze the microstructure of bone cortex and trabecular bone. We report 2 cases of ACPA positive which showed the interesting change in the microstructure. [Case 1] A 36-year-old female had bilateral joint pain, ACPA was positive at 65.8 U / mL, bone erosion was not observed in XP, and synovitis was not observed in US. Arthralgia disappeared after 2 months. [Case 2] A 56-year-old female had pain in the MTP joint 6 weeks ago, ACPA was positive at 1200 U / mL, XP had a bone erosion in the MTP joint, and US also had synovitis in the MTP joint and MCP joint in the US. [Results] The microstructure of the distal end of the right and left radius was evaluated by HR-pQCT. There was no change in cortical bone in 2 cases. On the other hand, inner trabecular volumetoric BMD and the trabecular number decreased in comparison with the average of 21 cases of the same age females. [Conclusions] The microstructure of trabecular deteriorated in patients with ACPA-positive transient arthritis and RA patients immediately after onset.

P1-021

Quantitative analysis of metacarpophalangeal joint space volume in rheumatoid arthritis on HR-pQCT imaging

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Conflict of interest: None

[Object] We developed a volumetric measurement technique of the metacarpophalangeal (MCP) joints on high resolution peripheral quantitative CT (HR-pQCT). The purpose of the study is to evaluate the feasibility of this technique for the evaluation of the MCP joints in rheumatoid arthritis (RA). [Methods] A total of 18 RA patients underwent HR-pQCT of the 2nd and 3rd MCP joints of dominant hands. A dedicated software was used for segmentation and calculation of the joint space volume (JSV) and average joint space width (AJSW) of the MCP joints. Radiographic grading of the joint spaces was based on the modified total Sharp score. The minimal and maximum widths of the 2nd and 3rd MCP joint spaces were measured on radiography. These radiographic values were compared with the results of volumetric measurement using HR-pQCT. [Results] There is no significant correlation between JSV/AJSW and the

radiographic grading. JSV was not correlated with the joint space width measured on radiography. AJSW was significantly correlated ($p<0.0001$) with the maximal, minimal and average joint space widths measured on radiography: r= 0.698; r= 0.619; r= 0.740, respectively. [Conclusions] The volumetric analysis using HR-pQCT was feasible in evaluating the joint space width of the MCP joints of the hand.

P1-022

Relationship between lessor toe dislocation and flexor tendon in rheumatoid arthritis

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Conflict of interest: None

Purpose: Multi-slice computed tomography (CT) is frequently used to assess bone morphology and bone arrangement, among other items. 3D volume rendering (3D-VR) enables three-dimensional rendering of soft tissue such as skin, tendons, and ligaments by arbitrarily changing CT values. Therefore, the relationship between dislocation and the flexor tendon was investigated in RA patients using 3D-VR. **Methods:** A total of 31 feet was examined in 24 patients. Preoperative CT scans were taken without loading. Volume Analyzer SYNAPSE VINCENT was used for 3D-VR reconstructions. CT values were then gradually changed, and the relationships between flexor tendons and the bone and joints were examined. **Results:** MTP joint dislocation was observed in 80 toes (complete dislocation: 63, subluxation: 17). The flexor tendon was dislocated 27 (inside 15, outside 12) at 2nd toe, 27 (inside 21, outside 6) at 3rd toe, 16 (inside 15, outside 1) at 4th toe. **Conclusion:** MTP joints dislocate result in loosening of the ligament and joint capsule after joint arthritis. 3D-VR is useful in assessing joint dislocation and flexor tendons.

P1-023

The development of the automatic measurement of joint space distance of the metacarpophalangeal joint of the rheumatoid arthritis patient by the super-resolution image processing

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Conflict of interest: None

[Background] We reported that the measurement of joint space distance (JSD) using the curve fitting method and super-resolution image processing for detecting the radiographic progression. [Object] To develop the algorithm of automatic measurement of JSD for the purpose of saving the time. [Methods] We prepared bilateral 2nd -5th metacarpophalangeal (MCP) joint X-ray images of rheumatoid arthritis patients. Super resolution process for improving accuracy, Robert filtering to detect edges, the reduction of artifacts, Bwtraceboundary mapping to trace edges and measurement JSD by the curve fitting method were performed automatically. We compared the difference between automatic measurement and manual operation. [Results] In 21 joints of 40 joints (52.5%) in both 2-5 finger MCP joint, the difference of measurement value between automation and manual operation was less than 0.1mm. In 29 joints of 40 joints, (72.5%) it was less than 0.2mm. In index and middle finger, 14 joints (70.0%) were less than 0.1mm. 16 joints (80.0%) were less than 0.2mm. In ring and little finger, 7 joints (35.0%), 13 joints (65.0%) were respectively. [Conclusions] We tried the automation of the measurement of the joint space distance. We developed the method that the measurement value was calculated in several seconds.

P1-024

The analysis of the relation between physical examinations at the first visit and future joint destructions

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Conflict of interest: None

[Object] We don't have enough time and manpower to do ultrasonography or MRI in all cases of RA at usuall clinical practice. Therefore we analyzed the ability of the physical examination to predict the future joint destruction (JD). [Methods] We enrolled 80 patients examined within a year from onset of RA. The average age at the first visit was 58 years, and the follow-up period was 65 months. We defined the JD with the Larsen grade, and classified the joints under from A to H group. Swollen (S)+Tender (T)+ joints were classified as Group A, S+T- as B, S-T+ as C, and A+B+C as Group D. We used Mulder sign as the physical test, and ++ was classified as Group E, + as F, ≧+- as G. [Results] The number of JD were 45 (hand), and 15 (foot). The sensitivities for JD were 51% (Group D), 33% (Group G) in hands and were 33% (D), 67% (G) in feet. The positive predictive values (PPV) for JD were 9% (Group A), 25% (Group E) in hands and were 0% (A), 21% (E) in feet. There were the significant differences about sensitivity of JD among hand groups, and foot groups (P=0.006, P=0.00009). [Conclusions] The sensitivities and PPV for JD were low for hand groups. Therefore we need imaging tests of hand periodically. In addition, Mulder sign had greater sensitivity and PPV than swelling or tenderness for feet.

P1-025

Radiological evaluation of distal interphalangeal joint in patients with rheumatoid arthritis

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Conflict of interest: Yes

[Object] To evaluate the frequency of radiological deformity of DIP joint in patients with RA. [Methods] This study reviewed 136 RA patients. Radiologically, the deformities of MP, thumb IP, PIP and wrist joints as well as DIP joint, were investigated. Clinically, the duration of disease, disease activity (DAS28-CRP), therapeutic drugs were investigated. All 136 patients were classified into three groups according to the radiological DIP deformity (1. RA deformity, 2. OA [Heberden] deformity, 3. normal). [Results] Radiological deformity of DIP joints was observed in 37 of 136 patients (27%). Among them, RA deformity was observed in 22 patients (16%) and OA deformity in 15 (11%). The mean duration of disease (18.7 years) in patients with RA deformity was significantly longer than that in patients without RA deformity (8.9 years) ($P<0.01$). The frequencies of deformities of MP, IP, PIP and wrist joints in patients with RA deformity of DIP were significantly higher than those in patients without RA deformity of DIP ($P<0.01$). [Conclusions] The results of our study indicate that the radiological RA deformity of DIP joint is partially observed in patients with RA, in addition to MP, IP, PIP and wrist joints.

P1-026

Spinal lesion in Rheumatoid Arthritis

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Conflict of interest: None

[Object] To clarify the relationship between joint lesion and spinal

lesion leading to serious dysfunction. [Methods] 194 cases visited our outpatient clinic for more than 1 year were investigated. The average visit period of 194 cases is 6 years and 8 months, the age at the time of first visit is 16 to 91 years old, 50 males and 144 females. The relationship between joint lesion and spinal lesion were examined. [Results] 112 of 194 patients underwent a simple x-ray examination of the spine, with 69 cervical and 82 thoraolumbar spine. Contents of cervical lesion were vertical subluxation 3, atlanto-axial subluxation 16, etc. Thoracolumbar lesion was vertebral fracture 38, lumbar slippimg 21 and so on. All of the above cervical lesions were observed only in seropositive cases, and lumbar slipping was seropositive in 18 of 21 cases. Many of severe spinal lesions were stage IV. In 12 patients underwent surgery, thoracolumbar fracture 4, atlanto-axial subluxation 2, dens fracture 2, etc. [Conclusions] In cases with poor prognostic factors, there are many severe spinal lesions leading to surgery such as atlanto-axial dislocation and lumbar slippimg. It is necessary to evaluate periodic spinal lesions like joint lesions.

P1-027

Gingival Bleeding and Periodontitis in Japanese Patients with Rheumatoid Arthritis: Results from the IORRA Cohort Study

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Conflict of interest: None

Objective: Periodontitis is a potential risk factor for rheumatoid arthritis (RA) and many patients with RA complicated periodontitis. This study aimed to evaluate periodontitis in RA patients using our IORRA cohort. **Methods:** Patients with RA enrolled in the IORRA cohort completed self-administered questionnaires as part of the 2016 IORRA surveys, which included gingival bleeding during tooth brushing and periodontitis. Logistic regression analyses were used. **Results:** Among 5660 Japanese patients with RA who participated in the cohort (median age, 62 years old; females, 86%), 29% and 27% reported having gingival bleeding during tooth brushing in the previous 6 months and history of periodontitis, respectively. Younger age, fracture history, and JHAQ-DI were significantly associated with gingival bleeding during tooth brushing, and older age, female sex, ever-smoker status, fracture history, JHAQ-DI, and use of diabetes medications were significantly correlated with past history of periodontitis. **Conclusion:** In Japanese patients with RA, many patients experienced gingival bleeding during tooth brushing and were diagnosed with periodontitis. Age, female sex, ever-smoker status, fracture history, disability, diabetes may be associated with periodontitis in Japanese patients with RA.

P1-028

Contribution of multiple bacterial pathogens in the pathogenesis of rheumatoid arthritis: Bacterial pathogens overwhelming antibody responses evoke serological disease markers and aggravate disease activity in rheumatoid arthritis

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Conflict of interest: None

(Purpose and Methods) To study a possible involvement of bacterial pathogens in the pathogenesis of rheumatoid arthritis, IgG and IgA antibodies against three bacterial pathogens, Escherichia coli-lipopolysaccharide (E. coli-LPS), Porphyromonas gingivalis-LPS (Pg-LPS) and peptidoglycan polysaccharide (PG-PS) from Streptococcus pyogenes, were determined by an improved ELISA system for sera from two groups of patients with rheumatoid arthritis (RA), who met rapid radiographic progression (RRP) criteria and non-RRP, and compared to normal (NL) controls. (Results) Among the patients with RA, lower IgG or higher IgA and consequent higher IgA/IgG antibody ratio among the patients with RA related to disease marker levels and disease activity. Especially, the IgA/IgG anti-Pg-LPS antibody ratio strongly correlated not only with RF, but also ESR, CRP and DAS28-ESR in the RRP group. In contrast, the IgA/IgG anti-E. coli-LPS and anti-PG-PS antibody ratio correlated or tended to correlate with RF, ESR, CRP, and DAS28-ESR in the non-RRP group (Conclusion) Multiple bacterial pathogens, which overwhelm the host antibody defense function, contribute independently or concomitantly to evoking disease makers and aggravating disease activity, and affect disease outcomes.

P1-029

What are the risk factors for developing sarcopenia in patients with rheumatoid arthritis - from CHIKARA study -

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Conflict of interest: None

[Object] Rheumatoid arthritis (RA) is often associated with sarcopenia due to joint dysfunction and chronic inflammation. We investigated risk factors for developing sarcopenia in patients with RA. [Methods] 100 patients (78 female, average age 68 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 condition. Patients with sarcopenia onset at 1 year were detected and their characteristics were analyzed. Predictors for developing sarcopenia were also investigated by uni- and multivariate analysis. [Results] 9 patients developed sarcopenia during 1 year. Their glucocorticoid (GC) use was significantly higher ($p=0.036$). Univariate analysis revealed that GC use ($r=0.217$, $p=0.035$), body fat mass at baseline ($r=-0.211$, $p=0.040$) and change in CRP at 1 year ($r=-0.205$, $p=0.046$) had significant associations with sarcopenia onset. GC use more than 2mg (OR 8.0, 95%CI 1.2-54.8, $p=0.034$) and body fat mass (OR 0.78, 95%CI 0.61-0.98, $p=0.037$) were detected as significant factors by multivariate analysis. [Conclusions] RA patients with GC use >2mg or low fat mass were more likely to develop sarcopenia.

P1-030

Sarcopenia could not predict falls in RA patients

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Conflict of interest: None

[Object] We reported that prevalence of sarcopenia was 28% and locomotive syndrome (locomo) was 52% in rheumatoid arthritis patients. We investigated the events of fall and fracture, and predictive factors influence for those events. [Methods] We used the date from prospective observational study (CHIKARA study). We investigated the number of patients and events per year about fall and fracture. The predictive factors influence for those events were analyzed. [Results] Fall occurred in 21 patients and 33 events (mean 2 times/person). Fracture occurred in 4 patients and 5 events. The predictive factors for fall events were height, bone mass index, trunk muscle mass, obesity revel, fat percentage, grip strength, and locomo at baseline. Whereas, there were no relations between fall and CRP, DAS28, skeletal muscle mass, sarcopenia. Height (odds ratio: 0.912, $p=0.003$) and obesity revel (odds ratio: 1.04, $p=0.006$) were independent predictive factors by multivariate analysis. About fracture events, fall was an only predictive factor ($r=0.469$, $p=0.001$). [Conclusions] It was reported that fall was significantly higher in sarcopenia. However, there was no relationship between fall and sarcopenia. We may need to evaluate not only skeletal muscle mass, but also muscle function to predict fall.

P1-031

A cross-sectional analysis of the association of fatigue with disease activity and clinical remission in Japanese patients with rheumatoid arthritis based on the IORRA cohort

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Conflict of interest: None

[Object] To investigate fatigue severity and how fatigue is related to disease activity and clinical remission in Japanese patients with rheumatoid arthritis (RA). [Methods] Among Japanese patients with RA in the IORRA study in April 2015, fatigue was measured by the Checklist Individual Strength 8R (CIS 8R): normal, CIS 8R≦26; heightened fatigue, 27≦CIS 8R≦34; severe fatigue, CIS 8R≧35. We performed a cross-sectional investigation of the association between fatigue severity and RA clinical factors with an ordered logistic regression analysis. We also analyzed the contribution of RA clinical factors to fatigue severity by an analysis of variance. [Results] Among 5,024 RA patients, fatigue severity was normal in 2,152 (37.9%), heightened in 1,489 (26.2%) and severe in 1,383 (24.4%). The 28-joint Disease Activity Score (DAS28) was associated with fatigue severity (P = 0.04). The DAS28 remission rate decreased with fatigue severity (P < 0. 01). Of the four components of the DAS28 score, only patient global assessment (PGA) was associated with fatigue severity (P < 0. 01). PGA made the strongest contribution to fatigue severity (81.0%). [Conclusions] Fatigue was strongly associated with PGA and affected the evaluation of disease activity and clinical remission in patients with RA.

P1-032

Effect of sodium intake on disease activity of rheumatoid arthritis

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Conflict of interest: None

[Object] It was reported that increased salt intake was the risk factor of pathogenesis of rheumatoid arthritis. We assessed the association between salt intake and disease activity in RA patients. [Methods] The study group consisted of 192 RA patients. We calculated salt intake every three months by equations from guidelines of the Japanese Society of Hypertension. We classified the patients in the groups which was higher than higher than targeted values of salt intake according to the Japanese Ministry of Health, Labour and Welfare (≧9g, male, ≧7.5g, female) (group A), and the lower (group B). Using a propensity score-matched patients, we calculated the amounts of the change of the disease activity 3, 6, and 9 months after observation starting time. [Results] We identified 82 patients (group A: n=41, group B: n=41). The average salt intake in RA patients was 8.26±2.42 g/day. We did not recognized the significant differences to the amounts of the change of the disease activity 3, 6, and 9 months after observation starting time between both groups. [Conclusions] We were unable to confirm the association between salt intake and RA disease activity. It was thought that there was the need that we increased number of cases and examined.

P1-033

Investigation of primary factors in the causes of rheumatoid arthritis by multiple center cohort study (Part I) -Japanese clinician biologics research group-

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Conflict of interest: Yes

[Object] It has long been known that RA is caused by genetic factors, and stressors, such as gum disease and smoking as causes of the disease have been reported. There is little data from Japan, therefore we carried out a multi-facility survey. [Methods] 22 RA specialist facilities and 205 outpatients participated in the survey. Questioned patients regarding disease onset, the period leading up to diagnosis, whether or not they had stress and gum disease, history of gynecological ailments, whether they smoked or not, family history, surgical history among others. [Results] Average age was 64, 84% were female. 85% reported having stress, and the causes were various. Although 75% of patients reported no history of smoking, but 75% of their family had smoking history. Their history of disease are gum disease (31%), gastrointestinal problems (40%), and gynecological ailments (28%). 38% reported a history of surgery before onset of RA. Family history of RA showed 12% percent had a parent with RA and grand-parent 10%. [Conclusions] Patients generally remembered the history of their RA onset, but none of them attributed onset to stress. Further studies are required, but epidemiological surveys such as this are critical to the understanding of disease onset factors in the Japanese.

P1-034

An inflammation mechanism and treatment of Rheumatoid Arthritis (RA) considered by statistical analysis of the antinuclear antibody

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Conflict of interest: None

[Object] To consider an inflammation mechanism and treatment of RA by an analysis of the indirect fluorescent antibody method (FANA). [Methods] 1545 patients with RA are divided into three groups by FANA titer 40,80, above160 and analyzed relations of FANA and CRP,1/Fe, MMP-3, Granulocyte (Gra), Lymphocyte (Lym), Platelet (Plt), gammaglobulin (g-glb), IgG, IgA, IgM, Complement (CH50) and of CH50 and CRP,1/Fe, MMP-3, Gra, Lym, Plt, g-glb, IgG, IgA, IgM next by an U test, rank correlation coefficient, multiple regression analysis. [Results] FANA was unrelated to Proinflammatory cytokine. In any FANA titer above80, MMP-3, Gra, Lym, Plt decreased, so the arthritis ameliorated but g-glb, IgG, IgA, IgM increased and CH50 decreased, so the acquired immunity and complement system activated. IgG increased than IgM by FANA but IgM for IgG increased more. Only IgM had a negative correlation with CH50 and related to the activation of the complement. [Conclusions] Why FANA ameliorates arthritis and decreases Gra, Lym, Plt is unknown, but the elevated acquired immunity and complement may inhibit bone marrow. We suppose that Steroid is an effective and necessary treatment of RA because it inhibits an IgM-complement system without lowering too much the acquired immunity by a different reaction of IgG, IgM to FANA and to CH50.

P1-035

Investigation of oldest old rheumatoid arthritis patients aged over 90

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Conflict of interest: None

[Object] Patients with rheumatoid arthritis (RA) are getting older with the improvement of treatment outcomes. However there was no study or report on oldest old RA patients aged over 90, the current status of these patients in our hospital was investigated. [Methods] We conducted investigation of oldest old RA patients aged over 90 in our hospital from October 2016 to October 2017. [Results] Oldest old RA patients aged over 90 in our hospital were 29 cases. The mean age at investigation and diagnosis were 92.7 and 72.7. The mean of disease duration was 19.9

years, and 22 cases were elderly onset RA. In the evaluation of disease activity by DAS 28-CRP, 11 cases were remission, 6 cases were low disease activity, 12 cases were moderate. The mean of HAQ-DI was 2.26, The mean number of DMARDs was 1.62, and the medications were MTX (8 cases, mean 5.25 mg/week), BU (3 cases), SASPEN (5 cases), TAC (7 cases) and IGU (1 case), respectively. 20 cases were treated with PSL (mean 4.15 mg/day). Biological DMARDs (GLM, ABT, TCZ) administer to 3 cases. 5 cases were treated with PSL alone and 4 cases without DMARDs. [Conclusions] We need to be careful in the management of oldest old RA patients, because they have many complications.

P1-036

Correlation between changes of serum 25(OH)D level and disease activity from baseline in patients with rheumatoid arthritis: TOMORROW study

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Conflict of interest: None

[Object] Serum 25(OH)D concentration (VitD) is known to be low in patients with rheumatoid arthritis (RA). In this study, we examined factors related to 7-year variation of VitD. [Methods] TOMORROW research (prospective cohort study targeting 208 RA outpatients and 202 healthy volunteers (Vo) group matched by age and sex) in 2010 (at registration: BL) and 2017 data was selected. We examined the association between variation of 7-year VitD (ΔVitD) and each BL factor and variation of Disease Activity score (DAS). [Results] The VitD levels were significantly lower ($p<0.001$) in RA group than in Vo group over time and ΔVitD was also significantly lower in RA group ($p=0.007$). In the anti-citrullinated peptide antibody and rheumatoid factor positive group, there was no significant difference between VitD levels and ΔVitD as compared with the negative groups. Although there was no significant correlation between ΔVitD and ΔDAS, there was a negative correlation ($r=-0.072$, $p=0.341$). Multiple regression analysis revealed that BL-DAS was not associated with ΔVitD. [Conclusions] The VitD levels were significantly lower in patients with RA than Vo and the variation of VitD was also significantly lower in RA patients. There was no significant association between variation of VitD and disease activity in RA.

P1-037

Pivotal role of IL-33 in pathology of rheumatoid arthritis

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Conflict of interest: None

[Background] IL-33 belongs to IL-1 family of cytokines. IL-33 acts directly on human eosinophils, basophils, mast cells and the other cells. IL-33 is related to type-2 associated reaction, cardiovascular disease, nerve system and immunologic deseases. It is suggested that IL-33 is the exacerbation factor of rheumatoid arthritis, but the mechanistic insights remain largely elusive. [Objectives] We investigate the function of IL-33 on pathology of rheumatoid arthritis. [Method] Expression of IL-33 receptor was investigated on human white blood cell subsets. Levels of RANKL and inflammatory cytokines mRNA and protein were evaluated using quantitative RT-PCR and flow cytometry. The osteoclast formation was assessed in the co-culture systems using RAW 264 cells. [Results] IL-33 receptor was markedly expressing on human basophils. IL-3 stimulation of basophils induced RANKL and TNF-α expression, and further additional of IL-33 synergistically enlarge that expression. Furthermore, basophils induced osteoclast formation, which is further enhanced by addition of IL-3. [conclusion] Our current findings suggest that IL-3 and IL-33 stimulation of basophils induced RANKL and inflammatory cytokines production, which is related to the pathology of rheumatoid arthritis.

P1-038

Resistin upregulates chemokine production by fibroblast-like synoviocytes from patients with rheumatoid arthritis

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Conflict of interest: None

[Object] The aim of this study is to elucidate the effects of resistin on fibroblast-like synoviocytes (FLSs). [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. Expression of CAP1 was examined by RT-PCR and Western blotting. The gene expression profile of FLSs treated with resistin was analyzed by RNA sequencing. Chemokine level in the culture supernatant was determined by ELISA. FLSs were transfected with CAP1 siRNA. [Results] Resistin and CAP1 was highly expressed in the RA synovium compared to OA. Resistin was expressed by macrophages and CAP1 was expressed macrophages, FLSs, and endothelial cells. *In vitro*, CAP1 was expressed by FLSs. RNA sequencing revealed that expressions of 18 genes, including 7 chemokines (CXCL1, CXCL2, CXCL3, CXCL5, CXCL6, CXCL8 and CCL2), were increased more than 2 fold by resistin-stimulated FLSs. CXCL8 and CCL2 levels in the culture supernatant were increased by resistin. Resistin-induced CXCL8 production was inhibited by the abrogation of CAP1. [Conclusions] Resistin might play an important role in the pathogenesis of RA via up-regulation of chemokine expression in the synovial tissue.

P1-039

ISG15 expression in CD4-possitive T cells is up-regulated in early-onset and untreated rheumatoid arthritis (RA) patients

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Conflict of interest: None

[Background] Interferon stimulated gene 15kDa (ISG15) is a ubiquitin-like protein induced by interferon stimulation. ISG15 is strongly induced by type-I interferons. The patients with ISG15 gene mutation presents type-I interferonopathy including autoantibodies production (Science 2012). Recently, it has been reported that ISG15 expression is up-regulated in whole blood samples in RA patients (Front Immunol 2017); however, it is unclear which cells produce ISG15 in RA. [Objective] To measure the expression of ISG15 in CD4-positive T cells and CD14-positive monocytes with early-onset and untreated RA. [Methods] CD4-positive T cells and CD14-positive monocytes from early-onset and untreated RA and healthy controls were sorted. ISG15 mRNA expression was measured by RT-PCR. [Results] ISG15 mRNA expression in CD4 T cells with RA patients was significantly up-regulated compared to healthy controls. Interestingly, in healthy controls, ISG15 mRNA expression was significantly higher in unstimulated CD4 T cells than in stimulated CD4 T cells. In CD14-positive monocytes, ISG15 mRNA expression was not changed between RA and healthy controls. [Conclusion] These findings suggest that ISG15 has an important role for pathogenesis in early-onset and untreated RA.

P1-040

ADAM-17 is expressed on vascular endothelial cells in rheumatoid arthritis synovial tissues and is involved in production of cytokine in vascular endothelial cells

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Conflict of interest: None

[Object] A disintegrin and metalloproteinase 17 (ADAM-17) is involved in a number of inflammatory conditions. We have reported to be expressed on rheumatoid arthritis (RA) synovial fibroblasts and be involved in inflammatory of RA. We examined the expression of ADAM-17 in RA vascular endothelial cells and HUVEC. We investigated whether ADAM-17 is related to production of cytokine in HUVEC. [Methods] ADAM-17 expression on vascular endothelial cell in RA synovial tissue and was measured by immunofluorescence. ADAM-17 expression on HUVEC was examined by immunostaining. HUVEC were transfected with siRNA against of ADAM-17. The levels of cytokines in ADAM-17 siRNA transfected HUVEC-conditioned medium were measured. [Results] ADAM-17 was expressed on vascular endothelial cell in RA synovial tissue. ADAM-17 was also expressed on HUVEC. MCP-1/CCL2, RANTES/CCL5, fractalkine/CX3CL1, ENA-78/CXCL5, IL-8/CXCL8, CXCL16, and VCAM-1 in ADAM-17 siRNA transfected HUVEC-conditioned medium is higher compared with in control siRNA transfected HUVEC-conditioned medium. [Conclusions] ADAM-17 was expressed on vascular endothelial cell in RA synovial tissue, and is related to production of cytokine in HUVEC. This study is suggested that ADAM-17 is involved in RA inflammation.

P1-041

Regulation of epigenome-modulator in CD4+ T Cell under inflammatory conditions

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Conflict of interest: None

[Object] In rheumatoid arthritis, ectopic lymphoid-like structures have been observed in the synovitis, where the level of C-X-C motif chemokine 13 (CXCL13) is elevated. PD-1^{hi} CXCR5^{-}CD4^{+} T Cells were reported to produce CXCL13 in inflamed joints. In PD-1^{hi} cells, the level of Enhancer of Zeste Homologue 2 (EZH2) is reportedly elevated. In this presentation, we investigated the relationship between EZH2 and PD-1^{hi} CXCR5^{-}CD4^{+} T Cells. [Methods] We stimulated CD4^{+} T Cell with anti-CD3/CD28 antibodies in the presence of several inflammatory cytokines and investigated the expression of EZH2. Then, we lentivirally transduced shRNA against EZH2 into CD4^{+} T Cell and cultured them with similar conditions. The levels of PD-1, CXCR5, and CXCL13 are evaluated on day 5. [Results] CD3/28 stimulation upregulated the expression of EZH2, which reached a peak one day after the stimulation and gradually decreased. The presence of proinflammatory citokines upregulates the level of EZH2. Knockdown of EZH2 upregulated the level of PD-1 and CXCL13 and downregulated the level of CXCR5. [Conclusions] Inflammatory cytokines upregulate the level of EZH2, knockdown of which gene upregulated the number of CXCL13^{+} PD-1^{hi} CXCR5^{-} T Cells, implying that EZH2 may suppress inflammation in RA as a negative regulator.

P1-042

Effect of SPACIA1/SAAL1 knockdown on TNF-alpha-induced CDK6 expression in vitro

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Conflict of interest: None

[Object] SPACIA1/SAAL1 (SPACIA1) is a gene associated with the aberrant proliferation of RA synovial fibroblasts (RASFs). We have reported that SPACIA1-deficient mice developed collagen-induced arthritis (CIA), as did wild-type mice. Deletion of SPACIA1 had only mild effects on the progression of CIA. We previously identified functional expression of CDK6 is controlled by SPACIA1 in RASFs proliferation. Recently, it was reported that CDK6 is involved in the signaling pathway of inflammatory cytokines such as TNF-α. In this study, we investigated the potential role of SPACIA1 in TNF-α-induced CDK6 gene expression in vitro. [Methods] RASFs were transfected with SPACIA1 siRNA for 48h and then exposed to TNF-α for 6h. The inhibitory effect of SPACIA1 gene-silencing on CDK6 expression was determined by real-time PCR. [Results] CDK6 expression was reduced by half with SPACIA1 siRNA in static condition. After 6h of TNF-α stimulation, CDK6 mRNA levels were upregulated by 2.5-fold. However, SPACIA1 knockdown was not totally abolished TNF-α-induced CDK6 expression. [Conclusions] SPACIA1 partially inhibited TNF-α-induced CDK6 expression. TNF-α-signals in RASFs regulate the expression of the CDK6 gene, suggesting that CDK6 could be a crucial factor in the pathophysiology of rheumatoid arthritis.

P1-043

Study of the factor which has on influence on the rheumatoid arthritis synovium

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Conflict of interest: None

[Object] In late years disease control of the rheumatoid arthritis (following RA) is improved drastically by the spread of biological preparation. It is not a rare case which only a single joint pain remains in even if we gave the medical treatment with any drug are not only rare. Because I weighed the factor which has an influence on the synovium in in the arms joint of RA and the lower leg joint this time, I report it. [Methods] The synovial membrane samples were obtained from 15 wrist joints undergoing wrist synovectomy surgery and 15 knee joints undergoing knee arthroplasty. The evaluation of the RA synovium checks many cell surface antigens emerging on Rooney score and the antigen presenting cell surface. [Results] There was no significant difference CD1, CD2, CD4, CD10, CD11, CD41 and CD68 between two groups except CD56. Only CD34 only found a meaningful tendency between two groups. [Conclusions] It has been already reported that sustained positive of the bloodstream in the intraarticular synovium appears from the early stage when joint swelling is not apparent to there being an association between progress of a bone, the joint destruction and it and the bloodstream in the synovium. It is thought that a further study will be necessary in future based on this findings.

P1-044

Attempt of early detection of rheumatoid arthritis (RA) using ultrasound (US) in general populations

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Conflict of interest: None

[Background/Object] The major pathology of RA is synovitis and bone destruction at an early stage. Therefore, patients at risk of RA need to be identified and treated as early as possible. US is useful for detecting synovitis and bone erosion early in the course of RA. We aimed to investigate the possibility of screening early RA by using joint US. [Methods] The study included 843 general residents who participated in preventive medical examination in Ishikawa prefecture from 2013 to 2016. Physical

examination, US, screening blood sampling test of RA were performed on them with joint symptoms in the hand region. [Results] 114 (13.5%) had joint symptoms and underwent joint US. Among them, 32 (3.7%) had US findings, of whom Two had power Doppler ≧2, 15 had greyscale ≧2, and 27 had bone erosion in hands. None of them fulfilled 2010 ACR/EULAR classification criteria, nevertheless one showed high titer of anti-citrullinated protein antibody and three had a history of RA treatment. [Conclusions] Positive findings of US examination for general residents with painful joints did not lead to diagnosis of RA by current classification criteria. We will continue to follow up the citizen with US findings.

P1-045

Change in RF Titers didn't Reflects RA Disease Activity and didn't Predicts Therapeutic Response during Abatacept Therapy

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Conflict of interest: Yes

[Object] To determine whether change of RF levels reflects RA disease activity and predicts therapeutic response in RA treated with Abatacept (ABT). [Methods] Subjects were 23 RA patients who filled ACR RA criteria 1987 or 2010, were treated with ABT, and had moderate to high disease activity and high titer of serum RF (≧100 IU/ml). Their medical records were reviewed retrospectively. Serum RF levels were measured 0, 4 and 12 month during ABT treatment. When RF levels were changed more than 10%, the change was judged as "significant". RA disease activity was measured by DAS28-CRP. [Results] ABT didn't decrease serum RF levels at 12Mo, but reduced DAS28-CRP. Change in RF levels during first 4Mo ABT therapy showed "significant decrease" in 91.3% and "no decrease" in only 8.7%, but exhibited "significant decrease" in only 28.6% and "no decrease" in 71.4% during 4-12Mo. Significant decrease of RF levels during both 0-4Mo and 4-12Mo had no correlation with reduction of RA disease activity at 12Mo. Change in RF levels during ABT therapy didn't reflect RA disease activity and failed to predict therapeutic response at 12Mo. [Conclusions] Change in RF titers didn't reflects RA disease activity and didn't predicts therapeutic response during ABT therapy.

P1-046

Reduced rate of rheumatoid factor reflects rheumatoid arthritis disease activity

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Conflict of interest: None

Rheumatoid factor (RF) is involved in the pathology of rheumatoid arthritis (RA), though its blood concentration varies during the course of treatment. We examined the relationship between RF change rate and disease activity in 287 RA patients (mean age 62.3 years, mean disease duration 13.1 years) treated at our hospital between 2015 and 2017. Three groups were classified according to RF change rate for over a 1-year period; decreasing, less than 80% (n=92), unchanged, 80% to 119% (n=114), and increasing, 120% or more (n=81). We evaluated disease activity using the simplified disease activity index (SDAI). The drugs used were MTX (mean dosage 3.81 mg) in 63.1%, PSL (mean dosage 1.47 mg) in 37.3%, and biologics in 48.8%. Mean disease activity change (delta SDAI) in 1 year was -0.88 (range 6.90-6.02). The median RF concentration at baseline was 76 (27.5-178.5) and median RF change rate was 96% (71.5-125%), with delta SDAI significantly improved in the decreasing group (-1.97, 0.005, -0.04, p=0.0011). The counts for swollen and tender joints, as well as evaluator's global assessment and CRP were also significantly improved in the decreasing group. Although RF concentration did not decrease in all cases, our findings suggest that RF reduction rate reflects disease activity.

P1-047

Relationship between HLA-DRB1 and therapeutic response to biologics in rheumatoid arthritis

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Conflict of interest: None

[Objective] Shared epitope (SE) of HLA-DRB1 is the major genetic susceptibility locus of rheumatoid arthritis. Some data suggest positivity of SE is related to efficacy of biologics, but results have been conflicting. Here, we analyzed correlation of the presence or the copy number of SE with therapeutic response to biologics. [Methods] We analyzed DAS28 (CRP) of 39 patients whose HLA-DRB1 allele are already genotyped and disease activity of 6 months after starting first biologics can be obtained. Patients were divided into 3 groups, a group with 2 copies of SE (SE2+), with 1 copy of SE (SE1+) and with no SE (SE-). Data were analyzed by a two-way ANOVA with repeated measures. [Results] There were no significant interaction between DAS28 (CRP) of SE positive (n=28, 3.98 to 3.01) and SE negative (n=11, 3.99 to 3.09). Also, no significant interaction was observed between SE2+ (n=9, 3.64 to 3.24), SE1+ (n=19, 4.14 to 2.91) and SE-. Similar analysis was performed in abatacept administered cases (n=28), but no interaction was observed. [Conclusion] In this study, there was no relationship of the presence or the copy number of SE with therapeutic response to biologics. We plan to increase the number of cases and examine again.

P1-048

Investigation of differences between remission criteria of rheumatoid arthritis using NinJa2016 database

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Conflict of interest: None

The first aim of treat to target of rheumatoid arthritis is to achieve clinical remission. Although criteria of remission was readjusted, there are still differences between criteria. [Object] We investigated the differences of RA disease activity scores. [Methods] We made the investigation by using clinical data on National Database of Rheumatic Disease by iRnet in Japan (*NinJa*) study. We examined differences of decision of remission between, SDAI, CDAI, Boolean, DAS28, DAS28-CRP. [Results] Percentage of Remission/Non-remission and Non-remision/Remission are Boolean vs SDAI: 1.4% and 10.1%, Boolean vs DAS28-CRP: 0.5% and 29.9%, SDAI vs DAS28-CRP: 0.2% and 20.9%, respectively. [Conclusions] Boolean criteria is strict, and about 10-30% of patients in remission judged by other criteria are Non-remission judged by Boolean criteria.

P1-049

Relationship between the blood concentration of adalimumab and maintenance of remission in patients with rheumatoid arthritis

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Conflict of interest: None

[object] We examined the relationship between the state of disease control and blood concentration of adalimumab (ADA). [Methods] The subject were 40 patients with RA who had received ADA. The clinical effects were compared using the DAS28-CRP to investigate changes for 5 years. The blood concentration of ADA was measured using adalimumab ELISA (SHIKARI Q-ADA, Matriks Biotek, Ankara, Turkey). [Results] The mean age at the start of administration was 52.5 years. The mean du-

ration of disease was 8.2 years. The mean doses of methotrexate and prednisolone were 8.3 mg/week and 4.6 mg/day, respectively. The DAS28-CRP at the start of administration and after 5 years were 5.38 and 3.33, respectively, showing a significant reduction in disease activity. The DAS28-CRP remission rate after 5 years was 34.0%, and the drug retention rates at 2 and 5 years were 60.8 and 43.7%, respectively. In 24 blood samples from 12 patients in whom remission was maintained (mean 2.6±1.6 years, range: 1.0 to 5.2 years), the trough levels of ADA were detectable, ranging from 1.14 to 10.00 μg/ml (mean: 6.57±3.07 μg/ml). [Conclusions] The results showed that ADA blood concentration was maintained in patients with long term remission.

P1-050

Sufficient treatment for early rheumatoid arthritis can help overcome poor prognostic factors for radiographic progression

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Conflict of interest: None

[Object] To compare the impact of poor prognostic factors of radiographic damage between untreated early rheumatoid arthritis (RA) and early RA after 12 months of treatment. [Methods] This study included 100 consecutive outpatients with a disease duration of <1 year (median, 3.6 months; 74% women). The outcome was assessed on the basis of the presence or absence of radiological progression of RA in the hand, wrist, and foot at 12 months. [Results] At baseline, 33% of the patients already had a bone lesion. One year later, 24.7% of the patients developed a new bone lesion. For the baseline bone lesion, presence of anti-cyclic citrullinated peptide (CCP) antibody (odds ratio [OR], 3.33; 95% confidence interval [CI]=1.09-10.14), high disease activity at baseline (OR, 1.48; 95% CI, 1.04-2.10), and delayed diagnosis/treatment initiation (OR, 1.43; 95% CI, 1.16-1.76) were associated. In contrast, only baseline radiographic damage (OR, 3.9; 95% CI, 1.1-14.0) and high disease activity at 12 months (OR, 1.9; 95% CI, 1.03-3.8) were associated with newly developed bone lesion at 12 months after treatment. [Conclusions] To prevent structural damage, initiation of treatment before the appearance of a bone lesion and controlling disease activity within 12 months are important.

P1-051

Factors associated with needs for supports of the Long-term care Insurance system in elderly patients with rheumatoid arthritis

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Conflict of interest: None

To evaluate the factors maintaining healthy long-life in patients with RA we prospectively analyzed the therapeutic process and patients backgrounds. Methods: elderly RA 152 patients, age over 70 years ago, prospectively follow up from 2015-2016, 33 elderly RA patients who support by long-term care insurance system or need to living support services by comprehensive community Support Centers in long-term care Insurance system. We measured the cognitive assessment tools (MMSE or Moca-J) and clinical findings, RA disease activity assessment by comprehensive disease activity score, HAQ-DI, bone Xray changes. Results: These patients are mean age 81years ago, 33 elderly RA patients who support by long-term care insurance system. Dementia was 22cases (mean MMSE 18), Mean DAS28 was 4.81±1.51 (before treatment), 2.95±1.4 (at care support center). These patients take corticosteroids 82%, MTX 48%, Biologics22%. Several infection was associated with hospitalization of care center. Factors associated with support by long-term care insurance system is low HAQ-DI, Corticosteroids use, bone change, and respiratory comorbidities. Conclusions: These data suggested that it should be noted RA care and treatment in Long-Term Care Insurance system inJapanese super-aging society.

P1-052

Aiming for optimal treatment of rheumatoid arthritis

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Conflict of interest: None

[Object] Treatment of rheumatoid arthritis came to aim for remission using biological products. Drug selection in daily clinical practice is difficult, and there is no indicator that makes it easy to select the optimal drug. We investigated whether disease activity in each biologics preparation can be predicted from the clinical index at the start of administration of biologics 3 months and 1 year after starting administration. [Methods] Using the clinical indicator at the start of the administration of the biological preparation, using the multiple disease regression analysis after 3 months and 1 year after the total 109 treatments of 61 patients who started the administration of the biological preparation. The therapeutic effect was predicted using the CDAI score and ΔCDAI score. After discontinuation due to ineffectiveness or adverse event, analysis was performed with ΔCDAI = 0. [Results] Significant predictive values were obtained 3 months and 1 year after administration was started with tocilizumab, avatacept, etanercept, golimumab, infliximab. [Conclusions] It is possible to select a drug predicted to have a greater therapeutic effect before starting administration.

P1-053

Association analysis of ultrasound global score and various cytokines in patients treated with biologics

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Conflict of interest: None

[objective] Previously, we reported US examination is useful with complement of physical examination findings in rheumatoid arthritis patients (RA) treated with biologics (Bio). In this study, we measured various serum cytokines, and examined the usefulness of the US global score in patients treated with biologics. [Methods] Twelve cases started tocilizumab (TCZ) were registered. We have performed US tests on the 40 joints and evaluated by semi-quantitative method using GS/PD along with CDAI, CRP, ESR, MMP-3 at the baseline and 24 weeks. In addition, we measured 27 inflammatory cytokines. [Results] CDAI, total GS/PD score decreased significantly at week 24. At baseline, total GS/PD score, MMP-3 correlated with various cytokines. MMP-3 still correlated significantly with various cytokines at week 24, but the correlation between US global score and cytokines decreased. [Conclusions] It was suggested that the US global score may not reflect the inflammatory cytokine and immune serologic activity in patients treated with TCZ or patients with low disease activity. As previously reported, it is considered that the Utilization method under Bio administration is not a multi-joint parts and global score but a few and local evaluation.

P1-054

Impact of treat to target strategy on real world: Radiographic outcomes in early rheumatoid arthritis over the past decade

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Conflict of interest: None

Objectives: To compare radiographic progression of early RA patients starting treatment 10 years ago vs more recently in daily clinical practice. Methods: We reviewed the medical records of RA patients in a single center retrospectively. 70 patients who were diagnosed with RA during 2003-2005 were included in the first cohort (2000s) and 71 patients during 2013-2015 were in the second cohort (2010s). Radiographs of hands were assessed at baseline and 1 year after. Results: Mean chang-

es for joint space narrowing score, erosion score, total radiographic score were higher in 2000s than 2010s (p=0.010, p=0.390, p=0.015). MTX was frequently used for initial treatment in 2010s than 2000s (p=<0.001), and dose of MTX were higher in 2010s than 2000s (p=<0.001). The mean duration from symptom onset to diagnosis was earlier in 2010s than 2000s (p=0.001). CRP at baseline and 1 year after were lower in 2010s than in 2000s (p=0.001, p=0.03). There were no significant differences in sex, age, positive rate of RF and ACPA, the Sharp score at baseline, steroid, and biological agents between two cohorts. Conclusions: In recent 10 years, early diagnosis and appropriate MTX use led to prevent joint destruction of RA patients in daily clinical practice based on treat to target strategy.

P1-055

Can Clinical Parameters Predict Residual Power Doppler Signals of Ultrasonography in Rheumatoid Arthritis?

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Conflict of interest: None

[Object] Several composite measures in rheumatoid arthritis (RA) define criteria of remission. However definitions of remission by clinical criteria do not always equate complete absence of inflammation. Recently, residual power doppler (PD) in joint ultrasonography (US) is taken notice of because it may indicate active histological inflammation. However it is not practicable to perform thorough joint US in clinical practice. MMP-3 has also been pointed out to be possibly useful in predicting remission. Here we examined the clinical parameters such as MMP-3 if they could predict residual PD signal. [Methods] joint ultrasonography was performed to 50 female patients who fulfilled DAS28-CRP remission. We assessed commonly used clinical parameters including MMP-3 between patients who had residual PD signal and patients without any residual signal. [Results] MMP-3 for group with and without residual PD signal were 54.2±17.3ng/mL, 49.9±14.5ng/mL respectively, no significant difference between groups (p=0.3446). There were also no significant difference for another clinical parameters. [Conclusions] Residual PD signal was not correlated with commonly used clinical parameters including MMP-3. PD ultrasonography may be an independent activity evaluation for RA to these clinical parameters.

P1-056

Clinical outcome with poor prognostic factors of 2 years' treatment of early phase rheumatoid arthritis

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Conflict of interest: None

[Objective] To retrospectively investigate outcomes after 2 years' treatment begun within 12 months of onset of early rheumatoid arthritis in Japanese patients. [Methods] Of 1,663 patients registered in the Akita Orthopedic Group on Rheumatoid Arthritis registry, 66 were treated within the first year of rheumatoid arthritis appearance. Forty-four patients were followed up for 2 years and enrolled in this study. [Results] There were 9 males and 35 females. Mean age and disease duration were 60.3 (21-85) years and 7.6 (3-11) months, respectively. According to 28-joint disease activity score-C-reactive protein (DAS28-CRP) criteria, 27 (61%), 7 (16%), 8 (18%) and 2 (5%) patients were classified into remission (REM), low disease activity (LDA), moderate disease activity (MDA) and high disease activity (HDA) at 2 years. The average pretreatment DAS28-CRP (3.2) was significantly lower after 2 years of treatment (2.2) ($p < 0.05$). The MDA and HDA groups had higher baseline age ($p = 0.005$), stage ($p = 0.025$), and DAS28-CRP ($p = 0.016$) than REM and LDA groups. [Conclusion] After 2 years, 61% of patients were classified into REM according to DAS28-CRP. Baseline age, Steinbrocker's stage, and DAS28-CRP were higher in association with MDA or HDA than REM or LDA.

P1-057

The examination of the disease activity evaluation by the ultrasonography about the late-elderly with rheumatoid arthritis

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Conflict of interest: None

[Object] We often experience the overestimation by the clinical evaluation against the elderly patients with RA. On the other hand, It is reported that the ultrasonographic disease activity evaluation is more available than clinical disease activity evaluation in the examination of the rheumatoid arthritis (RA). We investigate the patient data to consider the availability of the ultrasonography in the elder patients with RA. [Methods] We classified the 37 RA patients who underwent the musculoskeletal ultrasonography test by October 2017 (total 48 counts) to the group A under 75 years of age and the group B over 75 years of age, and investigated the relationship statistically between the ultrasonographic evaluation (total gray scale score and total power Doppler score) and the clinical evaluation (DAS28CRP, CDAI, SDAI). [Results] In the group A, the ultrasonographic evaluation related to clinical evaluation significantly. But in the group B, so-called the late elderly, there are no relationship between these two evaluation methods. [Conclusions] The ultrasonographic evaluation may deviate from the clinical evaluation about the late elderly with RA. When we estimate the disease activity of the late elderly, we should use these two evaluations comprehensively.

P1-058

Is DAS28-CRP 20percet improvement a useful measure for predicting outcome of annual treatment using biologics?

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Conflict of interest: None

[Object] To reveal whether or not DAS28-CRP 20 percent improvement, a useful measure for predicting outcome of annual treatment using biologics at our hospital. [Methods] All 46 patients who started biologics at our hospital and were able to follow up a year, whether or not biologics were continued, were included. DAS28-CRP improvement rate was evaluated at one, two and three month after starting biologics. Patients who achieved DAS28-CRP 20% improvement two or three times were classified in to good prognosis group. Zero or one time achievement was classified to bad prognosis group. Patients who were able to use the same biologics for a year and annual disease activity by DAS28-CRP revealed remission or low were described good clinical course. Others whose disease activity that were moderate or high, had stopped using the same biologics were described in bad clinical course. [Results] Abatacept were used in 27 cases, Eternercept in 10, Tocilizumab in 5, Golimumab in 4. 35 cases were classified in good prognosis group, 11 were in bad prognosis group. 30 cases were in good clinical course in a year and 16 were not. 74% of the cases were able to predict the annual clinical course. [Conclusions] DAS28-CRP 20% improvement might be a good measure for annual biologics use.

P1-059

Factors that correlates with EQ5D in rheumatoid arthritis patient

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Conflict of interest: None

(Object) It is well known that Euro QOL 5 Dimension (EQ5D) has close correlation with Quality of Life (QOL) in rheumatoid arthritis (RA) patient. Then, correlation of EQ5D with indices that are used in RA treatment was investigated statistically. (Methods) 327 RA patients were picked up, in whom EQ5D, modified Health Assessment Questionnaire (mHAQ), 28-joints disease activity score with C-reactive protein (DAS28), Sharp/van der Heijde Score (SHS), pain score with visual analogue score (PS) were monitored. Correlation between each parameter of EQ5D and the other indices at first consult (BL) and last time (LT) was evaluated with multiple linear regression analysis (MLR) and Paired T-test (PTT). Significant level was set within 5%. (Results) Most significant index was mHAQ, so that demonstrated significant correlation with all parameter of EQ5D both for MLR and PTT. Next was DAS28, and that demonstrated significant correlation in MLR, but not significant in PTT. The other indices demonstrated no statistical significance. (Conclusions) mHAQ demonstrated close correlation with QOL in through EQ5D. And DAS28 also suggested to have correlation with QOL.

P1-060

Studies on scoring methods of disease activities on rheumatoid arthritis (RA) in our hospital

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Conflict of interest: None

[Background] Disease control of RA improved with MTX or/and biologic disease modifying anti-rheumatic drugs (bDMARDs). Some patients can get remission only with MTX, but it is hard for some patients with several DMARDs. We report that clinical background and therapies of these refractory cases. [Methods] 1181 RA patients, who underwent evaluation of 28 joints swelling and tenderness, patients' and doctors' VAS from October 2013 to October 2017, were included. The database includes 19706 evaluations. We selected CDAI to avoid influence of tocilizumab. [Results] 301 cases experienced high disease activity (HDA, CDAI>=22). 32 cases suffered from more than 8 times HDA. 7 males and 25 females, average 69.7 year-old (median 74). Average disease duration was 14.7 years (median 12), but it was less than 3 years for 6 cases. In Steinbrocker classification, Stage1 19%, Stage2 25%, Stage3 25%, Stage4 31%. Anti CCP antibodies were detected in 24 cases (75%) with average titer 225U/ml (median 25.3). MTX was administered in 71.9% cases, and bDMARDs in 61.9% cases. Some of them suffered from HDA for a long time with progression of joint destruction. 9 cases were refractory in early stage. Only 1 case, 25 year-long RA in Stage4, showed frequent HDA with low objective, but high subjective assesment.

P1-061

The longitudinal follow-up of rheumatoid arthritis patients with lung disease

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Conflict of interest: None

[Background] Subclinical and overt lung diseases in rheumatoid arthritis (RA-LD) are prevalent seen in 30-50% of patients. However, the mortality of patients with RA-LD remains unclear. [Object] To clarify the prognosis of RA patients with RA-LD and RA patients without LD (non RA-LD). [Methods] This retrospective study comprised 103 RA patients who underwent CT scan of their lungs regardless of their respiratory symptoms in 2009. Events were defined as death, serious infections and other events (admission due to bone fracture, and ischemic heart disease). Kaplan-Meier method was introduced to define risk factors for the events. [Results] Of 103 subjects, 31 (30%) had RA-LD. Mean observation period was 9.1 years. Ten-year survival rate (SR) was 92% and 10-year event free survival rate (EFS) 69%. Each rate was significantly lower than non RA-LD (SR p=0.0008, EFS p=0.008). The causes of death were infection (55%), malignant tumor (27%), interstitial pneumonia (9%), and the other (9%). The adverse events included infection (41%), malignant tumor (21%), bone fracture (15%), cardiac disease (10%), and the other causes (13%). Infection (p<0.0001, HR 26.7) was identified as a risk factor for deaths. [Conclusion] RA-LD is related with a high mortality compared with non RA-LD.

P1-062

Treatment of refractory rheumatoid pleuritis with methotrexate and abatacept

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Conflict of interest: Yes

A-61-year-old man, in whom rheumatoid arthritis (RA) had been diagnosed 5 months previously, was referred to our clinic with right pleural effusion. He had received methotrexate and etanercept for RA, which was discontinued considering the possibility of side effects or adverse events. A thoracocentesis revealed a sterile exudate with elevated adenosine deaminase level of 136 IU/l and normal cytology. He was initially treated with 40 mg/day prednisolone (PSL), but this treatment did not improve the effusion. The dose of PSL was tapered to 15 mg/day. We performed thoracoscopic biopsy of the right pleura, and histopathology revealed fibrotic tissue with infiltration of lymphocytes. A diagnosis of rheumatoid pleuritic was made. He was started on abatacept with resuming methotrexate. These treatments were effective, and the pleural effusion was reduced. Six months later, the patient remains well with continuous treatment of abatacept, methotrexate, and PSL 8 mg/day. Clinical significance: Pleural effusion is a common manifestation in RA patients. Pleural effusion is generally responsive to corticosteroid therapy, but refractory cases require clinicians to select second-line therapy. Abatacept can be a treatment option in cases of refractory rheumatic pleuritis.

P1-063

The positivity of Anti-ARS antibody related to lung involvement of rheumatoid arthritis

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Conflict of interest: None

[Object] To reveal the risk factors in RA-associated lung diseases. [Methods] We performed a retrospective study of RA patients presented to our department from April 2015 to December 2016. Patient data such as medical histories, medications and laboratory data were collected through medical charts and were compared between patients with and without lung diseases (L and I group, respectively.). [Results] We investigated 175 patients (female:127, average age: 56yo, average disease duration: 113 months). Lung diseases were detected in 26% (46 cases) with Chest X-ray or CT scan, including interstitial lung diseases in 29 cases. There were significant difference in population of male (41% vs. 22%), disease duration (average 158 months vs. 96 months), positive RF (74% vs. 50%) and RF titer (192 IU/ml vs. 68 IU/ml) between L and I group, respectively. Anti-ARS antibody was also more likely to be positive in L group than I group (9% vs. 1%, *p=0.0056*). [Conclusions] Male, longer disease duration of RA, positive RF, high RF titer and positive anti-CCP antibody were associated with lung diseases, like previous studies. Additionally, our study suggested anti-ARS antibody can be one of the risk factors.

P1-064

Clinical features of pleuritis in RA: A few cases show clinical characteristics described in textbooks

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Conflict of interest: None

[Object] To clarify the clinical features of pleuritis in RA [Methods] Subjects were 19 RA patients in 476 cases received diagnostic thoracoscopy for pleural effusion from 2005 to 2017. Clinical features, pleural effusion (PE) characteristics and pathological findings were analyzed. [Results] Subjects were 7 male and 12 female with mean age of 66 years. RA preceded pleuritis in 12, developed simultaneously with pleuritis in 4, and followed pleuritis in 2 cases. Arthritis was found in 14 cases. PE was exudative with lymphoid or neutrophil dominance in all cases. Decreased glucose levels, low PH, and elevated ADH levels in PE, characteristics of RA pleurisy, were found in 7 (36%), 7 (36%) and 9 cases (47%), respectively. Empyema was a 1 case. On endoscopic examination, non-specific inflammation was found in most cases and 2 cases reveled small nodules in the pleura. Pathologic examination showed lymphocytic pleuritis in 5 (2 had marked lymphoid follicles) and granulomatous lesion resembling RA nodules in 2 cases, although non-specific pleuritis was mostly found. Glucocorticoid was given 14 cases and improved 13cases. [Conclusions] Pleuritis in RA shows a variety of clinical features and only a few cases revealed the characteristics of pleural effusion described in textbooks.

P1-065

A case or RA with multiple rheumatoid nodules with cavities in both lungs

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Conflict of interest: None

[Case] A 73-year-old woman had been diagnosed with rheumatoid arthritis (RA) 25 years earlier. She had been treated with PSL, SASP, tacrolimus, and ETN. In February 2017, she developed a cough and hemoptysis. Chest computed tomography revealed multiple nodules with cavities in both lungs, which were diagnosed as rheumatoid nodules pathologically. The ETN was stopped. An increase in the PSL dose had only a temporary effect and golimumab, abatacept, and tofacitinib were ineffective. She was admitted to our hospital in October. Laboratory data revealed elevated CRP, RF, and IgG-RF levels, as well as an ESR rate. Complement and ANCA were within the normal range. After increasing the dosage of PSL to 40 mg and adding IVCY, her symptoms and laboratory data improved rapidly. **[Discussion]** Rheumatoid nodules are extra-articular findings that occasionally appear in refractory RA cases; most develop at the elbow or in occipital and sacral regions. Rheumatoid nodules in the lungs are rare, occurring in 0.18-0.30% of refractory RA cases; 38.4% of these are reported with cavities. DMARDs, including TNF blockers, are reported to induce RA nodules in some cases. We report a patient who developed RA nodules with cavities during ETN treatment, and who improved with IVCY.

P1-066

A case of rheumatoid arthritis with skin rash like rheumatoid nodules improved after the administration of IGU

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Conflict of interest: None

A 73-year-old female was diagnosed as rheumatoid arthritis (RA) in 2007. She was administrated to MTX and PSL but stopped MTX due to MTX-induced Interstitial Pneumonia (IP). Therefore, we initially treated with TAC because of Non-Specific Interstitial Pneumonia (NSIP) but her disease activity was increased. We finally changed TAC to MZB and added PSL20mg. Her disease activity was improved and we decreased a dose of PSL. She had multiple of skin rash in the articular surface on the fingers of both hands with pain and itching under ministration of PSL12.5mg and MZB50mg. Skin biopsy was done but there were no typical granulomatous changes. Dermatologist suggested that skin rash was to be consistent with rheumatoid nodules because of the fibrosis of dermis layer. We stopped MZB and changed to SASP but a multiple of skin rash were not changed. We added IGU because of aggravation of disease activity in 2017, so we recognized the prominent improvement of skin rash. Finally we deareased a dose of PSL, and skin rash were improved. This is the first report of RA patients with skin rash like rheumatoid nodule improved after the administration of IGU.

P1-067

A case of rheumatoid arthritis accompanied with nontuberculosis mycobacteriosis which was treated effectively with tacrolimus

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Conflict of interest: None

A case of rheumatoid arthritis accompanied with nontuberculosis mycobacteriosis which was treated effectively with tacrolimus A 70-year-old male developed rheumatoid arthritis ten years ago. He was treated with methotrexate (MTX) 8 mg every week, thereafter his disease activity remained in remission. He had a wet cough, general malaise, and fever one year ago. As a result of a CT scan and sputum examination, he was diagnosed with mycobacterium-avium complex disease. He started treatment with clarithromycin, ethambutol, and rifampicin. MTX was continued for rheumatoid arthritis, but swelling and pain appeared in multiple joints, including in both of his hands (DAS 28 (CRP) 5.2). Tacrolimus (1.5 mg per day) was introduced after MTX was discontinued. As a result, disease activity decreased (DAS 28 (CRP) 2.5) in four weeks. Pulmonary lesions also remained stable during this period. Tacrolimus is useful for patients for whom MTX is not adequately effective. Furthermore, it may be effective for patients with rheumatoid arthritis accompanied by pulmonary complications.

P1-068

Investigation of factors influencing the period from the start of Methotrexate administration to onset of Lymphoproliferative disease

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Conflict of interest: None

[Object] Under MTX administration, factors affecting the period up to onset of LPD will be clarified. [Methods] We targeted 38 RAs who received MTX in the subject from 2002 to 2017 and developed LPD. Retrospectively, in addition to patient background such as age and gender, presence of concurrent use of folic acid (FA), csDMARDs, use / non-use of biological products, presence of SjS Risk factors for early onset of LPD were extracted from factors using multivariate analysis. [Results] The average age of 38 subjects was 64.2 years, the RA mean disease duration was 137 months, ACPA or RF prevalence was about 80%. The average period from the start of MTX administration to onset of LPD was about 81 months. 14 cases without folic acid, 14 cases combined with csDMARDs, 4 cases combined with bDMARDs and 5 cases with SjS combination. The time to onset of LPD was significantly shorter in FA non-combination group and csDMARDs combination group. ($P < 0.05$). No use of FA and with csDMARDs group were extracted as independent risk factors for early onset of LPD ($P < 0.05$). [Conclusions] It was suggested that concomitant no use of FA and use csDMARDs may be a risk factor for early onset of LPD in RA patients with MTX administration.

P1-069

A case of oculomotor nerve palsy, panhypopituitarism, and multiple subcutaneous nodules with methotrexate-associated lymphoproliferative disorder in a patient with rheumatoid arthritis

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Conflict of interest: None

A 65-year-old woman with rheumatoid arthritis had been treated with weekly methotrexate (MTX) for 10 years. She gradually suffered from facial hypoesthesia, abduction of eyeball, and ptosis of the right side, and was regarded as oculomotor nerve palsy (ONP). Computed tomography showed multiple tumors in the right orbit, the paranasal sinus, the mediastinum, the bilateral lungs, and the right kidney. Magnetic resonance imaging also revealed a tumor in Turkish saddle. Endcrinological tolerance test demonstrated the complication of panhypopituitarism. Biopsy specimens showed the infiltration of atypical lymphoid cells in the paranasal sinus, the mediastinum, and a subcutaneous nodule in left upper arm. Immunohistological studies indicated that those cells were positive for CD20, CD79a, and EBER-ISH but not for CD3. Therefore, she was diagnosed with EB virus-associated lymphoproliferative disorder (LPD) by MTX treatment. Withdrawal of MTX resulted in regression of all lesions and lead to functional recovery of ONP within 8 weeks. This case illustrates the rare occurrence of multiple MTX-LPD-induced dysfunction. It is advisable to perform tumor biopsy as soon as possible to facilitate differential diagnosis because cessation of MTX can primarily be a most important therapeutic option.

P1-070

A case of extranodal NK/T cell lymphoma nasal type developing in rheumatoid arthritis patient treated with MTX

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Conflict of interest: None

Introduction Methotrexate-associated lymphoproliferative disorder (MTX-LPD) is a lymphoproliferative disease developing in patients treated with MTX. Only a few cases of NK/T cell lymphoma have ever been reported. Case A 79-years old woman having RA treated with MTX complained oral pain and nasal occlusion from early February X. Multiple painful oral and pharyngeal erosion accompanied by tongue fur and purulent necrotic tissue in the nasal cavity were found. The pain worsened and she was hospitalized. From admission MTXcessation, leucovorin rescue, micafungin and ampicillin was started with suspicion of MTX mucosal damage, candida and bacterial infection. Infiltration of CD3 (+) CD56 (+) CD20 (-) EBER (+) lymphocytes were observed from the nasal biopsy tissue, she was diagnosed as extra-nodal NK/T cell lymphoma nasal type. Purulent necrotic tissue disappeared with only MTX cessation. Significance It has been reported that the clinical features of MTX-LPD undergoing spontaneous regression are EBER (+), a rapid increase peripheral blood lymphocytes after MTXcessation. This case shows EBER (+), a rapid increase in lymphocytes count after MTXcessation and suggests the factors mentioned above are associated with spontaneous regression tendency in NK/T cell lymphoma type.

P1-071

The Significance of axillary lymphnode enlargement as a Marker of clinical features in Rheumatoid Arthritis

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Conflict of interest: None

<Object>The present study was conducted to evaluate the association with axillary lymph nodes (ALN) enlargement and Rheumatoid Arthritis (RA) clinical features. <Methods>This was a retrospective observational study performed at our institute on outpatients from October 2014 to September 2017. All 49 untreated RA patients (age 73 ± 10 years olds) were performed by chest computed tomography scanning (CT), the maximum length and the maximum short diameter of left and right ALN were measured from the CT image, either the left or right ALN larger values was adopted. <Results> In multivariate analysis, the maximum length of the ALN was independently associated with MMP3, and the maximum short diameter of ALN independently correlated with RF (β = 0.38, P <0.05). Both the maximum length and the maximum short diameter of ALN were significantly longer in subjects above 6 months of RA diseased period than in subjects below 6 months of that (P <0.05). <Conclusion> ALN diameter seems to reflect diseased period in untreated RA, and ALN diameter is associated with MMP 3 or RF, which is a prognostic predictor of RA. It is suggests that ALN enlargement may be an indicator suggesting diseased periods and the progression of joint destruction in patients with untreated RA.

P1-072

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, pathological findings in renal tissue, and clinical parameters in AA and AL amyloidosis. [Methods] One-hundred nineteen patients with AA and AL amyloidosis were participated. For statistical analyses, the percentage area of amyloid deposition was transformed to a common logarithmic value. In addition, renal pathological findings were evaluated. [Results] Results of sex-, age-, and Log_{10}%amyloid-adjusted analyses showed that 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. As for renal tubulus and interstitium, inflammatory cells infiltration was not observed and there was no difference in the frequency of the deposition in AA and AL. [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. These differences could be mainly attributed to the pattern of glomerular amyloid deposition.

P1-073

Prognosis of amyloid A amyloidosis secondary to rheumatoid arthritis: ANSWER cohort

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Conflict of interest: None

[Object] Systemic amyloid A (AA) amyloidosis secondary to rheumatoid arthritis is a serious complication, often leading to end-stage renal disease or death. Therapeutic intervention with biologic agents may improve the prognosis. [Methods] Among patients with rheumatoid arthritis in ANSWER Cohort in Japan, patients with histologically-proven AA amyloidosis were identified. [Results] Eleven patients (F 10: M 1) were identified. Median age was 64 years and median duration from the onset of rheumatoid arthritis was 16 years (range 1-28). Affected organs were intestine (n=8), kidney (n=7) and/or heart (n=2). Median period of observation was 4.2 years (range 0.3-9.3) and 3 patients died. Three of 7 pa-

tients with renal involvement died, while all 4 patients with only intestinal involvement or all 7 patients treated with biologics survived. End-stage renal disease occurred in 5 patients, of whom 4 patients had never been treated with biologics. Median duration from the onset of rheumatoid arthritis was 21 years in patients with poor prognosis, while 13 years in patients with good prognosis. [Conclusions] Prognosis was associated with duration from the onset of rheumatoid arthritis, advanced renal dysfunction and insufficient anti-inflammatory treatment.

P1-074

Relationship between abnormal body composition and various disease parameters in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To clarify the prevalence of skeletal muscle atrophy in RA patients by cross-sectional studies, and to investigate the association with disease activity, dysfunction, joint destruction, and osteopenia. [Methods] Direct segmental multifrequency bioelectorical inpedance analysis was performed on 91 patients with RA, and skeltal muscles mass index (SMI) and bone mineral content (BMC) were measured. As a simple representative value of joint destruction, the average value of the Carpal Height Ratio (CHR) was measured. Subjects in whom SMI is less than 7.0kg/m^2 for male and less than 5.7kg/m^2 for female was defined as skeletal muscle reduction. The relationships between SMI, DAS28ESR, mHAQ, and BMC were investigated using the Pearson`s correlation coefficient. [Results] We identified 39 cases (42.9%) as skeletal muscle reduction, and 21 cases (23.1%) as bone mineral depletion. There was a positive correlation was found between SMI and CHR (R=0.464, P=0.000). SMI correlated strongly with BMC (R=0.832, P=0.000). [Conclusions] Many patients with RA suffer skeletal muscle loss. The extent of bone destruction is related to the reduction of SMI. There is also a close relationship between skeletal muscle loss and bone mineral density reduction.

P1-075

Increased homocysteine level for 7 years in patients with rheumatoid arthritis: TOMORROW study

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Conflict of interest: Yes

[Objectives] Osteoporosis is a disease in which the density and quality of bone are reduced and rheumatoid arthritis (RA) patients are proved at higher risk of osteoporosis. In this study, we evaluated homocysteine (Hcy) concentration as a bone quality marker in RA patients for 7 years and compared Hcy of RA with Hcy of healthy volunteer (Vo). [Methods] 202 RA patients and 202 age-, sex-matched Vo were enrolled. Laboratory data of bone metabolism as well as baseline characteristics data were collected. These data were compared between RA and Vo, then only in RA, we analyzed changes of Hcy between 2010 and 2017 in relation with baseline data. [Results] The level of Hcy increased over time from 2010 to 2017 in both groups ($p<0.0001$, repeated measure ANOVA), and "RA" and "time" interacted each other ($p=2.58e-7$, repeated measure ANOVA). Multiple regression analysis of BL data revealed the relationship between the level of Hcy and MTX dose ($p=0.048$). [Conclusions] MTX intake in RA patients will lead to folate deficiency, which will increase Hcy. Aging is another significant factor related to Hcy increase.

P1-076

Remarkable effectiveness of intravenous immunoglobulin therapy for intractable lower leg ulcers in rheumatoid vasculitis

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Conflict of interest: None

[Case 1] A 69-year old female diagnosed with rheumatoid arthritis (RA) in 1967 suffered skin ulcers of her legs from 2005. Skin biopsy revealed vasculitis and diagnosis as rheumatoid vasculitis. Leukocytapheresis therapy (L-CAP) was performed 5 times, but the effect was limited. Additionally, high dose corticosteroids including pulse therapy, cyclophosphamide, methotrexate (MTX), and azathioprine was not effective. The severe leg ulcers were worse, and foot paralysis was appeared. Finally, intravenous immunoglobulin (IVIG) therapy remarkably improved the lesions. [Case 2] A 76-year-old female diagnosed with RA in 1987 suffered leg ulcers under treatment with salazosulfapyridine, iguratimod, and MTX. Skin biopsy revealed vasculitis in 2016. The leg ulcers deteriorated and developed cellulitis with sepsis. IVIG therapy followed by antibiotics improved the lesions.

P1-077

Development of Dental Risk Reduction System for Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Object] Periodontitis (PD) plays a potential role in rheumatoid arthritis (RA) development. RA treatment influences PD activity. Bidirectional relationships between PD and RA exist. Herein, medical-dental collaboration (MD), a novel method for assessing PD, was developed and its effectiveness in reducing dental risk was evaluated. [Methods] All RA patients who visited the hospital after April 2013 when dental hygiene screening (DS) for RA underwent in the hospital were included. Patients were categorized into two groups based on whether DS was performed (DS+) or not (DS-). Patients who visited the hospital before and after MD development were categorized into MD- and MD+, respectively. Dental incidents were analyzed among all groups. [Results] In total, 212 patients were included (MD-: 194, MD+: 18) and DS was performed in 41 (MD-: 28, MD+: 13). Based on DS, 24 patients (MD-: 18, MD+: 6) were advised to visit a dentist; however, only 13 visited (MD-: 8, MD+: 5). There were three incidents in the MD- and DS- group. However, there was no incident in the MD+ or DS+ groups. [Conclusions] DS and MD are effective in reducing dental risk.

P1-078

Prevalence of and factors associated with renal dysfunction in rheumatoid arthritis patients: a cross sectional study in community hospitals

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Conflict of interest: None

[Object] To determine the prevalence of renal dysfunction (RD) in RA patients, and to identify factors associated with RD. [Methods] Between October 2014 to May 2015, we consecutively recruited RA patients of community hospitals. Each patient's absolute and BSA-indexed estimated glomerular filtration rate (eGFR) values were measured. RD was defined as absolute eGFR or BSA-indexed eGFR< 60. Associations between RD and possible risk factors were examined by multivariate lo-

gistic regression analysis. [Results] A total of 1908 outpatients with RA were included. The prevalence of RD base on absolute and BSA-indexed eGFR was 33.8 and 18.6%, respectively. Advanced age (odds ratio [OR] 7.24 p<0.001), female sex (OR 3.12 p<0.001), hypertension (OR 2.22 p<0.001) and obesity (OR 0.59 p<0.001) were independently associated with the risk of absolute eGFR based RD. Advanced age (OR 5.19 p<0.001) and hypertension (OR 3.05 p<0.001) also had associations with BSA-indexed eGFR based RD. RA duration, stages, severity were considered significant risk factors in univariate analysis, but their associations were less potent after adjustment for other covariate. [Conclusions] RD is relatively common in RA patients and is mainly associated with advanced age and hypertension but not with RA-related factors.

P1-079

Thermal dispersion among fingers in connective disease patients

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Conflict of interest: None

[Object] In collagen disease, blood flow disorder is frequently observed in both limbs and internal organs. When seeing it in the periphery of the fingers, I have observed that there is a difference for each finger. This is evaluated by thermographic inspection (thermo). [Methods] In collagen disease patient, thermo was applied to 10 collagen disease patients. 10 seconds in 10 ° C water, dipped, observe in minutes after drawing out. The observation site is the nail bed of the first to fifth fingers of the right hand. [Results] In healthy subjects the coefficient of variation was 0.0075 before load, 0.0330 after 1 minute, 0.0144 after 3 minutes, 0.0079 after 5 minutes and returned to the state before loading after 5 minutes. The mean of the coefficient of variation of 10 collagen disease patients was 0.0357 before the loading, 0.0553 after 1 minute 0.0537, 0.0537 after 0.05 minutes 0.0535, 0.0480 after 10 minutes, 0.0404 after 20 minutes, 0.0354 after 30 minutes, the bulge was high from before loading, and it took 30 minutes to return to the state before loading. [Conclusions] In patients with collagen diseases, there are many cases in which the burrs are recognized before the low temperature loading, the burrs are reinforced after the loading and hard to improve until after 30 minutes.

P1-080

Cognitive function in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] We investigated the cognitive function in patients with RA and compared it with the cognitive function of elderly residents. We also examined the relationship between the cognitive function and disease activity of patients with RA. [Methods] 29 cases of RA (RA group) and 65 elderly people living in the community (Control group) were recruited. The age of the RA group was 70.2 ± 14.0 years old, and the age of the control group was 70.5 ± 3.7 years. For evaluation of cognitive function, Japanese version of Montreal Cognitive Assessment (MoCA-J) was used. DAS 28-CRP was also used to evaluate the disease activity of RA. [Results] The total points of MoCA-J in the RA group and the control group were not significant at 22.4 ± 5.5 points and 22.8 ± 3.6 points, respectively. There were no significant differences between 20 cases (69%) and 48 cases (73%) judged as mild cognitive impairment, respectively. In the cognitive function, the visual space / executive function significantly decreased (p <0.05) in the RA group and the abstraction significantly decreased (p <0.001) in the control group. There was no significant correlation between cognitive function and DAS 28-CRP in the RA group. [Conclusions] It seems necessary to further examine the cognitive function of RA patients.

P1-081

The efficacy of treatment of add-on iguratimod in patients with rheumatoid arthritis inadequately responding to tocilizumab

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Conflict of interest: None

[Object] We report 24-week outcome of treatment of add-on iguratimod (IGU) in patients with rheumatoid arthritis (RA) inadequately responding to tocilizumab (TCZ). [Methods] 10 cases were used from Toyohashi RA Database (TRAD). We compared DAS28-CRP, CDAI and MMP-3 (ng/mL) at 4, 8, 12 and 24 weeks from baseline by Wilcoxon signed-rank test, respectively. We investigated adverse events. Every data is shown by mean. [Results] As baseline demographics, age was 57.7, disease duration was 16.4 years, DAS28-CRP was 3.35, CDAI was 16.8, MMP-3 was 105.2, 1 case was treated with methotrexate, 5 cases were treated with steroid (3.6mg) and 4 cases had past history of lung disease. DAS28-CRP, CDAI, MMP-3 at 4, 8, 12 and 24 weeks were 2.85 (p=0.009), 2.41 (p=0.021), 2.18 (p=0.008) and 2.23 (p=0.011); 11.4 (p=0.005), 8.2 (p=0.008), 7.4 (p=0.008) and 8.1 (p=0.008); and 87.6 (p=0.241), 77.2 (p=0.008), 76.0 (p=0.008) and 69.6 (p=0.051). 1 case of hepatic disorder leaded to the discontinuation of IGU. 3 cases of stomatitis and 1 case of pharyngalgia did not lead to the discontinuation of IGU. [Conclusions] Combined use of TCZ and IGU was effective. While TCZ inhibits JAK/STAT pathway, IGU inhibits NFκB pathway. They inhibit different pathway each other so that inflammation might be reduced more strongly.

P1-082

The efficacy of additional administration of tacrolimus in patients with rheumatoid arthritis of an inadequate response to abatacept

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Conflict of interest: None

[Object] We tend to select abatacept (ABT) when there are some risk of complications in patienes with RA. Therefore, even when ABT is insufficiently effective, switching to other biological DMARDs may be difficult. In this study, we examined the effectiveness and safety of additional administration of tacrolimus (TAC) targeting T cells as well as ABT. [Methods] 21 patients added TAC after using ABT by TBCR. The mean age was 65 years, the duration of disease was 14 years, the duration of ABT administration until the addition of TAC was 1.6 years. The clinical outcome at 24 weeks after TAC combination start was examined. [Results] The average DAS28-ESR was 4.35 at the time of addition of TAC, but 3.36 at 24 weeks (P <0.01). MMP-3 was 150.6 ng/ml, but 91.3ng/ml at 24 weeks (P <0.05). EULAR response rate (over moderate response) at 24 weeks was 14 cases. TAC dose was 1.7mg/day and the continuation rate of ABT was 90.5% at 24 weeks. Adverse events were not observed. [Conclusions] For patients with inadequate effect of ABT, good response was recognized by addition of TAC. If switching to other biological products is difficult, additional combination of TAC was considered a useful treatment option.

P1-083

Efficacy and influence to renal function of iguratimod in rheumatoid arthritis

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Conflict of interest: None

[Object] We aimed to examine the efficacy of iguratimod (IGU) and its influence on renal function in patients with rheumatoid arthritis (RA). [Methods] 77 patients with RA treated by IGU were identified from local registries at two hospitals. We collected patients' back ground, DAS28-CRP, eGFR at 0, 3, and 6-month time point after IGU treatment. [Results] Median age was 68 years. 51 cases was female (66.2%), Median disease duration was 2 years. Co-medication of glucocorticoid was found in 21cases (27.3%), any csDMARDs in 60 cases (77.9%), NSAIDs in 36 cases (46.8%), biologics in 17 cases (22.1%). Mean levels of DAS28-CRP and eGFR before IGU treatment was 3.62 and 76.1, respectively. DAS28-CRP levels at 3-months and 6-months following IGU treatment were markedly reduced to 2.94 (p<0.01) and 2.7 (p<0.01). GFR was significantly decreased to 68.1 (p<0.01) at 3-months and 68.5 (p<0.01) at 6-months. The number of concomitant csDMARDs was detected as a risk factor of eGFR deterioration. Bucillamine and salazosulfapyridine were detected as a risk factor of GFR reduction. Decrease in eGFR was almost fully recovered following the discontinuation of IGU. [Conclusions] Combination therapy of IGU with DMARDs could lead to the eGFR reduction, careful attention should be paid on the renal function.

P1-084

Analysis of cases with methotrexate discontinuation

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Conflict of interest: None

[Object] To analyze the factor causing MTX discontinuation and the influence after MTX discontinuation. [Methods] A total of 170 patients with rheumatoid arthritis who were stopped administering methotrexate between 2015 and 2016 were included. The clinical characteristics were investigated from medical records. We compared DAS28 between before and 6 months after MTX discontinuance. [Results] The causes of MTX discontinuation were infection in 11.2%, interstitial pneumoniae, MTX associated lymphoproliferative disorder, bone marrow suppression in 8.8%, gastrointestinal symptoms in 8.5% and remission in 4.1% of cases. The dose of MTX just before discontinuation was 6.0±3.1mg/week and less than 4.0mg/week in 42.4% of cases. After discontinuation of MTX, no additional treatment was added in 34.7%, csDMARDs were added in 15.9%, dose of prednisolone was increased in 15.9% and bDMARDs were added in 10.9%. DAS 28 was not ameliorated after 6 months of MTX discontinuation (2.9±1.2 v.s. 2.6±1.1, p=0.002). [Conclusions] There were various reasons to result in MTX discontinuation. Disease activity was not worsened at least in short period of time after MTX discontinuation.

P1-085

The impact of the combination therapy of conventional synthetic disease-modifying anti-rheumatic drug with anchor drug, MTX in the Japanese large cohort, NinJa2016 (National Database of Rheumatic Diseases by iR-net in Japan)

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Conflict of interest: None

[Object] To evaluate the impact of the combination therapy of conventional synthetic disease-modifying anti-rheumatic drug with anchor drug, MTX in the Japanese patients with RA. [Methods] In 15343 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 22% from these therapies showed MTX+BUC+TAC, MTX+SSZ, MTX+TAC, BUC+TAC that had high efficacy. In addition, from the point of view of safety, the hospitalization rate of each combination was generally around 5%. However, two combination therapy, SSZ+IGU and SSZ+BUC+TAC was higher rate of annual hospitalization than the rate in the overall NinJa. [Conclusions] In NinJa2016, the combination therapy with csDMARD in which 2 or 3 drugs are selected from 5 drugs of SSZ, BUC, TAC, IGU and mainly MTX has been actively performed also in Japan. Especially, MTX and SSZ evaluated as strongly recommended in Guidelines for the management of RA. Iguratimod is increasing as new DMARD as combination drug in RA.

P1-086

Comparison of efficacy between combination therapy with Tacrolimus and Sulfasalazine with Methotrexate in Japanese patients with Rheumatoid Arthritis: propensity score analysis

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Conflict of interest: None

[Object] To clarify the efficacy of combination therapy with Tac in comparison with that of SSZ with MTX in typical clinical practice. [Methods] We analyzed data from RA patients registered in a large database (NinJa: National Database of Rheumatic Diseases by iR-net in Japan) from April 2011to March 2016. In this study, we compared the two groups who received Tac or SSZ in addition to methotrexate in the earlier year. We excluded patients who started receiving biologic DMARDs, and Tac or SSZ the year prior to the study period. The predicted probability of Tac treatment was calculated by fitting a logistic regression model using all clinically relevant variables. The outcome was remission rate with disease activity score 28 CRP (DAS28-CRP) in the year after initiation of Tac or SSZ therapy. [Results] The group that received Tac in addition to MTX included 100 patients; the other group that received SSZ in addition to MTX included 120 patients. 74 patients were compared in each group after score matching. The remission rates of DAS28-CRP in the following year was 56.8% and 52.7% (P=0.741) in the Tac and SSZ groups, respectively. [Conclusions] Combination therapy with Tac or SSZ and methotrexate for rheumatoid arthritis did not show a significant difference in disease activity.

P1-087

Efficacy of iguratimod in combination with biologics

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Conflict of interest: None

[Object] Numerous reports on the efficacy and safety of Iguratimod (IGT) have been reported. However, there are not many reports on the effectiveness of IGT with biologics. Therefore, we examined the effectiveness of IGT for patients with rheumatoid arthritis using each biologicals in our hospital. [Methods] Twenty-one patients with rheumatoid arthritis who were able to continue Iguratimod for 12 weeks or more after continuing the biologics for 3 months or longer. We examined the age, morbidity history, Stage, Class, MTX combination rate, MTX dose, PSL combination rate, PSL dose, DAS 28 - ESR, CDAI, using LDA achieve-

ment rate and CDAI change amount at 12 weeks and 24 weeks. [Results] Average age 66.3 years, disease duration 15. 9 years, MTX combination rate 33.3%, MTX average dose 8 mg, PSL combined rate 57%, PSL average 3 mg, Stage 3.04, Class 1.71. CDAI before combination with IGT was 16.3 ± 8.56, 12.1 ± 11.6 after 12 weeks and 11.7 ± 12.4 after 24 weeks. The LDA achievement rate before IGT combination was 28.6%, 61% at the 12th week and 81% at the 24th week. There was no significant difference in effectiveness between biologics [Conclusions] Improvement of disease activity can be expected by using IGT in combination with insufficient effect of biologics.

P1-088

The Evaluation of Disease Activity and Radiographic Efficacy by Adding Iguratimod for Treating 89 Rheumatoid Arthritis Patients with Inactive Response to conventional therapy

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Conflict of interest: None

OBJECTIVES: To obtain 2-year disease activity and radiographic efficacy about adding iguratimod (IGU) on RA patients with poor response to conventional therapy in 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=33), respectively. We evaluated which factors are important in determining a prognosis of clinical response and mTSS for 2years. **RESULTS:** 89 RA patients were recruited and male was 25% (n=17). Mean age was 61.2 years old and mean of disease duration was 96 months. Main csDMARDs were MTX (72%). The mean dose of MTX was 6.4mg/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 6months ($P < 0.0001$). Yearly mTSS was 0.60 and rate of structural remission was 87%. Rapid Radiographic Progression (RRP) was 30.3% in one year, but RRP in next one year was 3.3%. **CONCLUSIONS:** Adding IGU to csDMARDs with poor response in RA patients is effective and might suppress the progression of TSS after 2 years. This result showed effectiveness for patients who could not have been treated with biological products for various reason.

P1-089

The efficacy of the persistence in the biological agents with the combination of csDMARDs

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Conflict of interest: None

[Object] To compare the efficacy of different concomitant disease modifying antirheumatic drugs (DMARDs) on the persistence with anti-TNF inhibitor, anti-IL-6R antibody, and human cytotoxic T lymphocyte-associated molecule 4 connected to a modified Fc region of human immunoglobulin G-1. [Methods] This analysis included 319 patients with RA enrolled, an observational study, who were starting their anti-TNF, tocilizumab (TCZ), and abatacept (ABT) therapy and were receiving one of the following DMARD treatments at baseline: TNFi (n=70)/TCZ (n=64)/ABT (n=67). Kaplan-Meier survival analysis was used to study the persistence with these therapies in each DMARD subgroup up to 3 years. [Results] 3-year drug survival for TNFi therapy with no csDMARDs was 38% and it was the significant lower compared with that with 2 (62%) and 3 csDMARDs (72%). 3-year drug survival for TCZ therapy with no csDMARDs was 82% and it was the high compared with that with 2 (57%) and 3 csDMARDs (86%). 3-year drug survival for ABT therapy with no csDMARDs was 67% and it was the significant lower compared with that with 2 csDMARDs (82%). [Conclusions] These results support the continued use of background DMARD combinations with biological agents. True monotherapy with the TNFi without csDMARDs is infrequent.

P1-090

Background of nonopioid analgesics use in rheumatoid arthritis patients

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Conflict of interest: None

[Object] It was reported that tight control of rheumatoid arthritis (RA) activity had been possible with cs DMARDs and biological DMARDs, but more than half cases received NSAIDs. The purpose of this study was to examine the background of patients requiring nonopioid analgesics. [Methods] Based on the medical record visited between April and June 2017, we collected the data that whether or not nonopioid analgesics were used and the patients background (sex, age, RF, anti-CCP, MTX, Biologics, PSL, DAS28). Logistic regression analysis on the use of nonopioid analgesics was performed. [Results] Nonopioid analgesics were used in 104 patients (30.1%). Based on logistic regression analysis, DAS28 was involved in the use of nonopioid analgesics (OR:1.87). In addition, the number of tender joints counts (OR: 1.2) and pain VAS (OR:1.02) were related to the use of nonopioid analgesics. [Conclusions] In the United States, it was reported that opioid analgesics were prescribed in 40% of RA patients, while the proportion of nonopioid analgesics use in our study was lower than in the past in Japan. The reduction of tender joint counts and pain VAS may lead dose reduction of nonopioid analgesics.

P1-091

Continuation rate of the Iguratimod with conventional synthetic DMARDs 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 69 RA patients who were treated with IGU from September 2014 to September 2016 were observed. 24 patients treated with MTX (mean dose 7.0 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. The average dose of MTX was 7mg/week, and the IGU continuation rate in the high-dose MTX group and the low-dose MTX group was examined. Patients with IGU was discontinued in 4 cases with MTX, 12 cases without MTX, 5 cases (42%) each with liver disorder/invariance or exacerbation. (Results) DAS28-CRP decreased -1.53 in all cases at 54 weeks compared with that at baseline. The change in DAS-28 was significantly improved in the IGU monotherapy-1.27, with MTX -1.35, ($P<0.05$). Continuation rate of patients treated with IGU for 24 weeks were 77.9%, with MTX were 83.3% (high-dose group 90.9%, and low-dose group 75%, $P=0.3$), had no significantly high rate in the combined with MTX. (Conclusions) IGU with MTX therapy in patients with RA may not be affected by continuation rate.

P1-092

Efficacy of Iguratimod and Predictive Factors of its Effect (including Autoantibodies)

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Conflict of interest: None

Object: To examined the efficacy of iguratimod (IGU) and predictive factors of its effect (including autoantibodies). Methods: We examined 117 RA patients receiving IGU between Sept 2012 and Sept 2016. Of these, 76 who received the treatment for at least six months, or whose treatment was discontinued due to an insufficient effect were selected for this study. To assess efficacy, the patients were divided into remission group and non-remission group based on DAS28CRP score after six months. We also examined the relationship between clinical remission and autoantibodies in a further 46 patients who gave their consent. Results: In the patient backgrounds, treatment duration, proportion of patients also receiving methotrexate, and pre-treatment DAS28CRP score (2.75vs3.54) differed significantly between remission group and non-remission group. Multivariate analysis revealed that pre-treatment DAS-28CRP score was an independent predictive factor of effect. IGU efficacy appeared to be greater in patients that were positive for, or with high titers of, anti-SS-A antibodies and anti-SS-B antibodies and anti-thyroid TPO antibodies. Conclusions: Low pre-treatment DAS28CRP score predicted IGU effect. IGU efficacy appeared to be related to anti-SS-A, anti-SS- B, and anti-TPO antibodies.

P1-093

Treatment of Japanese early rheumatoid arthritis patients with low-dose and short period prednisolone therapy leads to earlier improvement of disease activity and patient's satisfaction with early improvement of pain

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Conflict of interest: None

[Object] We investigated the changes of each factors of disease activity index and patient's satisfaction after low-dose and short period predonisolone (GC) therapy. [Methods] We classified patients into two groups, one was group treated with DMARDs alone (N group; n=39) and the other with ≦5 mg of GC for maximum 1 year along with DMARDs (GC group; n=45). We evaluated the changes of number of swollen joints and tender joints, CRP, VAS of pain and patient's global assessment (PGA) scores for 3 years, and evaluated patient's satisfaction by questionnaire. [Results] There were no significant differences in DAS28-CRP scores at baseline. In the GC group, the mean GC dose and administration period were 2.63 mg/day and 20.2 weeks, respectively. At 1 month after treatment, there was a significant difference in the improvement rate of the number of swollen joint, CRP, VAS and PGA in the GC group compared with the N group. No significant difference was observed between the two groups at 3 months or more post-treatment. In questionnaire, patients in GC group were satisfied with the improvement of pain more than patients in N group. [Conclusions] We suggest that the treatment enable us to build good relationship with patients.

P1-094

BSA and body weight involved igratimod-induced renal dysfunction

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Conflict of interest: None

[Object] To examine factors influenced to renal function induced by igratimod (IGU) in rheumatoid arthritis (RA). [Methods] We enrolled all cases that received IGU therapy for RA (n=58) in Okayama City Hospital from Sep 2012 to Oct 2017. We excluded cases that did not continued to receive IGU therapy. [Results] 33 patients (27 females, mean age 64 yo, mean disease duration 130 months). The average of DAS28ESR were 4.4. ΔeGFR from 0 to 24w, was decreased (-6.8, p = 0.0005). We classified cases to Group I (ΔeGFR at 24w > -5; 10 cases) and Group 2 (23 cases), and analyzed. Male patients in group 1 were more (50% v.s. 4%). Cases in group 1 had heavy body weight (62 kg v.s. 50kg, p = 0.0186) and wide BSA (p = 0.0050), and were younger (56 yo v.s. 68 yo). There was no difference in anti-rheumatic drugs, anti-hypertensive agents and clinical parameters of baseline, except for dosage of corticosteroid. At 24 weeks after initiation, there was no difference of drugs taken in each group, but ΔDAS28ESR was lower in group (-1.1, v.s.0.1 in group 1). [Conclusions] IGU influenced renal function. This study revealed that body weight and BSA influenced to IGU-induced dysfunction. It indicated that usual dose of IGU in our country were too much in patients with renal dysfunction induced by IGU.

P1-095

Cost and effectiveness analysis of DMARDs therapy (annual report from Ninja 2016) -the cost of biologics stopped to increase and decreased-

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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 2002-2016 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 480,000 yen / patient in 2016, 10,000 yen lower than the cost in 2015. The rate of the cost of biologics was 74 % and consistently decreased in two years. The usage rates of IFX, ETN and ADA decreased. [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 is strong and continued in 2016. This tendency was thought to be caused by the increase of the usage of cheaper biologics, The cost of DMARDs might have hit the ceiling.

P1-096

Combined effect of iguratimod and biologics in non-responders to biologics

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Conflict of interest: Yes

Object: We investigated the effect of combined therapy with iguratimod (IGU) and biologics in non-responders to biologics. Patients and Methods: IGU was additionally administered to 26 patients with rheumatoid arthritis who could not achieve low disease activity (LDA) with biologics. Tender joint counts, swollen joint counts, CRP, DAS28-ESR, and the HAQ-DI in these patients were evaluated during 52 weeks of combined treatment. Results: The CRP and DAS28-ESR before additional administration of IGU were 1.5 (±2.4) mg/mL and 4.2 (±1.2), respectively, indicating moderate disease activity. However, after 52 weeks, these values decreased to 0.3 (±0.6) mg/mL and 2.9 (±1.2), respectively, indicating LDA. As for the improvement rate of DAS, the proportion of patients with LDA at week 0 was 15%, but it rose to 46% at week 24 and to 57% at week 52. The remission in the cases of Bio + MTX combination was 55%, higher than 33% without MTX combination at week 52. The HAQ-DI changed from 1.0 (±0.9) at week 0 to 0.7 (±0.7) at week 52. No adverse events were observed. Conclusions: Additional administration of IGU to non-responders to biologics may help achieve LDA, suggesting that this combined treatment may be worth trying before switching biologics.

P1-097

Factors associated with gastrointestinal disorders in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To investigate factors associated with gastrointestinal disorders in patients with RA. [Methods] A total of 376 patients with RA treated with MTX were included in this cross-sectional study. Gastrointestinal Symptom Rating Scale (GSRS) was used to evaluate gastrointestinal disorders. The GSRS has five subscales (Reflux, Abdominal pain, Indigestion, Diarrhea and Constipation) and a seven-point graded Likert-type scale. Symptomatic was defined as a score of ≧ 2 on GSRS subscale. [Results] Patients were predominantly female (80%), and had a mean age of 62 years, BMI of 22 kg/m^2, disease duration of 13 years, DAS28-CRP of 2.1, and MTX dose of 8.5 mg/week. The proportion of patients receiving folic acid, glucocorticoids, NSAIDs, and proton pump inhibitors (PPIs) was 86%, 31%, 27%, and 22%, respectively. The prevalence rate of reflux, abdominal pain, indigestion, diarrhea, and constipation was 27%, 22%, 27%, 26%, and 43%, respectively. Multivariate analysis revealed that independent associated factors were as follows: for reflux, female, NSAID use, and higher BMI; for abdominal pain, female and higher MTX dose; for indigestion, PPI use; and for diarrhea, glucocorticoid use and drinking. [Conclusions] The drugs used can cause gastrointestinal disorders in patients with RA.

P1-098

Clinical features of methotrexate-associated lymphoproliferative disorder

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Conflict of interest: None

[Objectives] To investigate the clinical features of methotrexate-associated lymphoproliferative disorder (MTX-LPD). [Methods] We examined 6 patients diagnosed with MTX-LPD between January 2011 and January 2017. We retrospectively investigated 1) patient characteristics, 2) pathological findings and 3) therapeutic course. [Results] 1) All 6 patients (67.3±6.7 years old, 1 male/5 females) were rheumatic arthritis (duration: 14.3±9.9 years). MTX dose was 8.3±2.1mg/week, and total cumulative dose was 2538±1279mg for 5.7±3.6 years. Anti-CCP antibody was positive in all cases, and high titer (>300U/mL) was seen in 3 cases. RF was positive in 5 cases, and they all showed high titer (>100U/mL). 2) LPD developed in lymph nodes from 4 cases, and in extra nodal organs from 2 cases. Pathological findings included 2 DLBCL, 2 Hodgkin lymphomas, 1 MALT lymphoma and 1 undifferentiated lymphoma. 3) Although 3 patients reached remission after MTX withdrawal, 1 patient relapsed and resulted in death. Three patients who did not improve after MTX withdrawal were given chemotherapy. [Conclusions] Relapse after LPD remission was observed, indicating that careful observation after remission was necessary. We need further research about the relation between LPD and the high titer of RF and anti-CCP antibody.

P1-099

Correlation between renal function and the dose of weekly MTX in patients with RA

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Conflict of interest: None

[Objective] To clarify correlation between renal function and the dose of weekly MTX in patients with RA, we retrospectively studied the outcomes of reduction and discontinuation of MTX in patients with RA. [Methods] One hundred and one RA patients who fulfilled ACR criteria of RA, who were thought to need for MTX therapy, were included in this study. Patients were divided into 5 groups by level of renal function. G1 group (eGFR≧90) 15 patients, G2 group (60≦eGFR≦89) 49 patients, G3a group (45≦eGFR≦59) 19 patients, G3b group (30≦eGFR≦44) 14 patients G4 group (15≦eGFR≦29) 4 patients. We investigated age, the dose of weekly MTX, the dose of daily prednisolone, CRP, ESR, DAS28-CRP, DAS28-ESR, CDAI and SDAI. Data were analyzed statistically. [Results] age (years old): G1 (52) G2 (67) G3a (72) G3b (73) G4 (83) dose of MTX (mg/week) G1 (8.3) G2 (7.3) G3 (6.3) G4 (4.9), dose of prednisolone (mg/day) G1 (1.6) G2 (2.2) G3a (2.7) G3b (3.7) G4 (4.0), Reduction and cessation of MTX G1 (0/15) G2 (1/48) G3a (3/19) G3b (9/14). [Conclusion] Significant correlation between renal function and the dose of weekly MTX were observed. Reduction and discontinuation of MTX were frequently observed in G3b Group.

P1-100

Efficacy and safety of iguratimod for the patients with rheumatoid arthritis in daily clinical practice

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Conflict of interest: None

[Object] To clarify efficacy and safety of iguratimod (IGU) in patients with rheumatoid arthritis (RA) in daily clinical practice. [Methods] We identified 88 cases treated with IGU in University of Tsukuba hospital, and retrospectively analyzed their 1) baseline characteristics, 2) efficacy and the factors influencing efficacy, and 3) continuation rate and adverse events. [Results] 1) At the start of IGU, mean age was 62 years old, and mean disease duration of RA was 14.6 years. The rate of cases treated with biological agents, methotrexate, or glucocorticoid was 23%, 39%, or 70%, respectively. 2) CRP was significantly decreased at 3 months after initiation of IGU compared with before treatment. The efficacy rate of IGU was significantly higher in cases without concomitant use of glucocorticoid than cases with it. 3) Cumulative continuation rate was 63% at 12 months. Twenty-eight cases discontinued IGU, because of lack of efficacy in 9 cases, and adverse events in 16 cases; liver injury in 4 case, and gastrointestinal dysfunction in 3 cases. [Conclusions] IGU might be effective even in cases with long-standing RA, and also in patients without concomitant use of glucocorticoid. Liver injury and gastrointestinal dysfunction should be paid attention during the treatment with IGU.

P1-101

Iguratimod significantly decrease serum levels of RF and MMP-3 in RA patients with inadequate response to DMARDs

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Conflict of interest: None

[Object] To evaluate the efficacy and safety of iguratimod (IGU) in RA patients with inadequate response to DMARDs. [Methods] We retrospectively investigated 121 RA patients treated with IGU in our hospital from April 2014 to July 2017. Administration of IGU was examined about dosage, prior DMARDs, continuation period and rate, and adverse events. Clinical response was evaluated by DAS28-CRP. Serum levels of RF and MMP-3 were examined. [Results] The mean age was 65.6 years. Disease duration was 140 months in average. Patients recieved PSL in 56.5% (5.2mg/day), MTX in 54.5% (9mg/week), tacrolimus (TAC) in 29.8% (1.7mg/day), SASP in 46.3%, and BUC in 37.2%. Biological DMARDs were used in 17 patients. After administration of IGU the serum levels of RF and MMP-3 significantly decreased from baseline to 12 week ($p<0.01$) and to 24 week ($p<0.01$) together with DAS28-CRP improvement. The continuation rate of IGU was 81% at 6 months, 69% at 12 months, and 69% at 24 months. [Conclusions] IGU is known to have suppressive effect on inflammatory cytokine production by inhibiting NF-κB. MMP-3 is known as an important enzyme to destroy joint cartilage and bone at synovitis in RA. Our results suggested the usefulness of IGU to inhibit joint destruction.

P1-102

RA treated with DMARDs and its flare-up due to complicated PMR

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Conflict of interest: None

[Object] In cases of flare-up in controlled RA, it is generally called as the escape phenomenon or secondary ineffectiveness. In the cases treated with csDMARDs and bDMARDs, appearance of P-glycoprotein and autoantibodies to the biologics, respectively, may be involved in this mechanism. To avoid this phenomenon, increase of the drug dose, combined use of P-glycoprotein inhibitor, and switching and/or add-on to other csDMARDs or bDMRADs have been suggested. [Methods] 14 cases of seropositive RA (7 with csDMARDs, 7 with bDMARDs), in which aggravated joint pain was found to be due to complicated PMR. PMR combined with RA is difficult to be distinguished from RA exacerbation. During the treatment with tocilizumab, diagnosis of PMR would be more difficult since the inflammatory response can be masked. [Conclusions] A similar case has been reported as follows by Iwadate et al. in 2002. "Seronegatve" is the principle issue for diagnosing PMR, but it is not surprising that it merges with elderly RA. Steroid administration is the basic therapy for PMR. However, the strategy may be changed considering the continuation of DMARDs, biologics or MTx. Thus, it is necessary to differentiate PMR, when the RA symptoms rapidly deteriorated during DMARDs treatment.

P1-103

Bezafibrate for methotrexate-induced liver injury in patients with rheumatoid arthritis; comparison with an increased dose of folic acid

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Conflict of interest: None

[Object] We investigated the efficacy of bezafibrate (BZ) for improving methotrexate (MTX) -induced liver injury. **[Methods]** Twenty patients with rheumatoid arthritis who were treated with MTX and exhibited liver function abnormalities in two consecutive outpatient settings were randomly assigned to the BZ group (400 mg per day) or FA group (increasing dose to 10 mg/week) and prospectively followed up for six months for AST and ALT values. We also compared persistence rates in the treatment groups. **[Results]** AST values in the BZ group (11 patients, mean age 62±13) and FA group (9 patients, mean age 61.0±13) at the time of enrollment were 60.5±22.6 IU/L and 54.1±15.8 IU/L, respectively, and these values decreased to 28.3±13.4 and 41.0±24., respectively, 6 months after enrollment (p<0.05 and p=0.07, versus values at the time of enrollment). ALT values in the BZ groupand FA group were 72.6±24.1 U/L and 65.0±15.9 IU/L, respectively, at the time of enrollment, and decreased to 28.3±13.4 and 41.0±24.3, respectively, 6 months later (p<0.05 and p=0.07, versus values at the time of enrollment). A Kaplan-Meier analysis revealed a better persistence rate in the BZ group (p=0.10). **[Conclusions]** BZ is a promising option for MTX-related liver injury in patients with rheumatoid arthritis.

P1-104

Analysis for serum and blood extermination DATA of 25cases suffering from elderly-onset rheumatoid arthritis (EORA) treated with methotrexate (MTX) for one year

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Conflict of interest: None

[Object] According to guideline 2016, recipe for MTX recommend to start 2-4 mg/week for the elderly. EORA patients consider retrospective liver and renal function and blood cell disorder in one year after MTX treatment. [Methods] 27cases suffering from EORA, over 60-years-old, observed in our hospital from 9/2013 to 9/2016. 2 cases prohibited to use MTX. 25 cases are considered as hematology and serum. GOT (AST), GPT (ALT), renal function (eGFR) and blood lymphocyte counts are studied before administration and one year. GOT40U/L, GPT45U/L, eGFR60, lymphatic ball number 500 / μ-litter are thought as a reference value limit. [Results] Average age are 70.08 years, average time-rag from on-set to 1st visit is 4.4 months. DMARDs introduce up to average 0.7 months. ACPA positive 13/25 RF positive 16/25 male 12 casees. Befor MTX introduction, DAS28ESR is average 4.71, HDA 7, MDA 16, LDA 2 cases. MTX initial introduction dose is 4mg 6, 6mg 14, 8mg 5cases. administered after, GOT abnormal value 4 cases, GPT abnormal value is 4, 50% deterioration happened 56%. CKDstageIII increases 5 to 9cases. The lymphocyte count reduction, less than 500/micro-litter, happened in 3cases. [Conclusions] Liver and renal function and blood cell disorder in one year after MTX treatment must be attention for EORA.

P1-105

Changes in various markers when adding iguratimod to rheumatoid arthritis patients using biological DMARDs

Koji Hashimoto
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Conflict of interest: None

[Object] Iguratimod is said to show anti-rheumatic action by suppression of inflammatory cytokine due to monocyte and the macrophage, and production inhibition of immunoglobulin due to B cells. This time we examined the clinical effects of adding iguratimod to biological DMARDs. [Method] For 10 rheumatoid arthritis patients who were additionally administered iguratimod during the use of biological DMARDs in our department, we evaluate their backgrounds and serologic evaluation (CRP, erythrocyte sedimentation rate 1 hour value, MMP-3, Leukocytes, lymphocyte count, rheumatoid factors) and clinical evaluation (DAS 28-ESR) for 24 weeks. [Result] After using iguratimod in combination, inflammatory markers, rheumatoid factor and DAS28-ESR showed a declining tendency. Although liver function had transient rise, it eventually declined. No significant changes were observed in the number of lymphocytes. No new serious side effects were observed. [Conclusion] Not only the reduction of inflammatoty markers by combining iguratimod with biological DMARDs, suppression of antibody producing (rheumatoid factor) was admitted. In addition, it is necessary to stack the cases, it was suggested that it can be a depper remission, especially a drug taht helps to maintain immunological remission.

P1-106

The effect of various treatments on diabetic control in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] We examined medical records of patients with RA complicated with glucose intolerance to measure HbA1c, body weight and DAS28-ESR. [Methods] Newly registered 20 RA patients complicated with glucose intolerance (HbA1c ≧ 5.6%) at our hospital from May 2013 to December 2015, have treated with as follows; Treatment with infliximab, golimumab, and etanercept in combination with 4-12mg/w of MTX (group A; 6 cases, TNF + MTX), MTX (4-10 mg/w) alone (group B; 8 cases). The other DMARDs (group C; 6 cases) had been registered. We have compared the changes of HbA1c levels, body weight and DAS 28-ESR from the beginning of the treatments and 6 and 12 months later. We analyzed these results with paired and unpaired t test using JMP12.2.0. [Results] Groups A and B showed significant improvement of DAS 28-ESR after treatment with 12 months ($P < 0.001$), but no significant difference in group C. The mean reduction in HbA1c showed a significantly decreases only in the group B ($P < 0.001$). There were no significant differences in body weight between the each group. [Conclusions] In this study, MTX was thought to contribute not only to suppress chronic inflammation but also to improve the glucose tolerance as compared with TNF inhibitors plus MTX and other DMARDs.

P1-107

The improvement of Ultrasonographic findings for 24 weeks may predict remission at 52 weeks in Japanese rheumatoid arthritis patients treated with Iguratimod therapy

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Conflict of interest: None

[Objectives] To evaluate the clinical efficacy of IGU therapy patients with rheumatoid arthritis (RA) using ultrasonography (US). [Methods] We used IGU treated 63 RA patients more than 52 weeks. We evaluated the improvement of gray scale (GS) and power doppler (PD) score from baseline to week 24. [Results] The patients included 18 males and 45 females. The mean age was 65.1±13.7 years and the number of MTX combination, other DMARD excluded combination, IGU monotherapy and Biologics combination were each 36, 14, 8 and 5 cases. Clinical findings related to RA were as follows: CRP, 1.0±1.2 mg/dL; ESR, 29.7±17.6 mm/h; DAS28-ESR, 4.30±0.90 and SDAI, 16.1±6.9. In the achieved remission for DAS28-ESR at Week52 (n=18) and not achieved or discontinued IGU patients (n = 45), the respective changes in GS and PD scores from baseline to 12 or 24 weeks were as follows: ΔGS score: -3.4± 4.9 vs 0.1 ± 6.3 (p=0.051) at 12 weeks and -5.7± 5.4 vs -0.5 ± 9.5 (p=0.007) at 24 weeks; and ΔPD score: -3.4± 5.2 vs -1.0 ± 4.8 (p = 0.021) at 12 weeks and -5.1± 6.0 vs -0.8 ± 6.1 (p = 0.002) at 24 weeks. [Conclusion] The present study provides evidence supporting t the improvement of GS and PD score from baseline to week 24 may predict whether the achieved remission or not at Week 52.

P1-108

Usage status of MTX for patients with rheumatoid arthritis

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Conflict of interest: None

[Object] We decided to consider MTX usage status in rheumatoid arthritis (RA) treatment. [Methods] We examined the maximum dose of MTX in 194 RA patients (42 male, 152 female) who had MTX prescription history from 2012 to 2017. In addition, it was classified into two groups (group with increased weight until maximal effect of MTX (extended group) and group that was not able to increase by side effect etc. (non-extended group), and age, sex, BMI, Duration of disease, Steinbroker staging, CRP, RF, MMP-3, MTX course and combination therapy were studied. [Results] The maximum MTX dose of 8 mg / week accounted for 45.9% of the total, and for elderly people aged 65 years or older, the average was 8 mg / week and was significantly less than 65 years old or less. 120 cases in the extended group and 74 cases in the non-extended group, comparison of the combination therapy change before and after MTX increase between the 2 groups showed significant combination of csDMARDs and the biological preparation in the non-extended group It started. [Conclusions] We studied 194 patients with RA who undergo MTX therapy, and the maximum dose of MTX was significantly less than 65 years old. In the insufficient effect period MTX was reduced or stopped at 38% of the total.

P1-109

A case of methotrexate (MTX) induced non-alcoholic fatty liver disease with severe lipid deposition

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Conflict of interest: None

Background Liver dysfunction were described in up to 20% of patients with rheumatic arthritis receiving MTX therapy. Liver abnormalities have not been considered a significant liver damage as they usually resolve with daily folic acid or drug discontinuation. However, we experienced a case with persistent liver toxicity occurred even after discontinuation of MTX that led to severe non-alcoholic fatty liver disease confirmed with liver biopy. Case A 47-year-old thin woman with BMI of 16.8 presented to our hospital with a 2-year-history of arthralgia and morning stiffness. On the basis of her history, physical exam, and L/D, she was diagnosed as RA. We started MTX and achieved complete remission in 3 months with 12mg per week. 1 year later, her LFT started to increase. We administered daily folic acid and discontinued MTX. However, the elevated LFT never normalized after that. We perfomed liver biopsy The specimen revealed non-alcoholic fatty liver with severe lipid deposition. 3 months after initiation of FA and discontinuation of MTX, her liver dysfunction still continued. Conclusion Her cumulative dose of MTX was 666mg in total. We consider that her liver damage occurred because the liver toxicity of MTX was superimposed by her potential liver failure due to chronic malnutrition.

P1-110

Regional Differences of Rheumatoid Arthritis Clinical Practice Within Akita Prefecture

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Conflict of interest: None

[Object] The aging rate, disease activity and treatment of RA patients may differ depending on the area within Akita Prefecture. The purpose of this study is to investigate whether there are regional differences in clinical practice of RA treatment. [Methods] 1,778 RA patients who were registered in the AORA Registry in 2016 were investigated. 1,106 patients who visited the hospital around Akita City were classified in Group A, and 672 patients who visited other regional hospitals were classified in Group B. The aging rate, disease activity, physical function evaluation and type of medical treatment were investigated. [Results] The aging rate of Group A was significantly lower than Group B. Significant differences were observed in DAS28ESR between the two groups, but there were no significant differences in SDAI. HAQ was significantly lower in Group A. There were no significant differences between the two groups in the prescription rate of MTX and biological DMARDS. [Conclusions] Due to differences in the aging rate of the area, the aging rate of RA patients was also different. DAS28ESR and HAQ showed significant differences between the areas. ESR and HAQ are known as parameters affected by age, and the differences were thought to be caused by the difference in aging rate.

P1-111

The cases using golimumab as second biologic agent in rheumatoid arthritis

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Conflict of interest: None

[Object] To investigate the cases using golimumab (GLM) as second biologics in rheumatoid arthritis (RA). [Methods] 6 cases (male 1, female 5, mean age 56.3, history of RA for 11.8 years) who treated with GLM was second biologics. We investigated the first biologics, the reason of switching, concomitant medication, DAS28CRP, complications. [Results] All of the cases were used as the second agent, the first bio was infliximab 3, etanercept 2, adalimumab 1. The reasons of switching were infusion reaction 1, vascular pain 1, relapse after bio-free 1, secondary ineffective 2 and difficult of self injection 1. On average DAS28CRP at the

time of introduction of GLM was 3.78, concomitant medication was methotrexate 6 (average 8.7 mg/week), and PSL 3 (average 5.8 mg/day). All cases were introduced from 50 mg/4 weeks, 2 cases were insufficiently effective and increased to 100 mg/4 weeks. The rate of continuation in one year after switching was 83.3% (5/6 cases), the rate of remission was 80.0% (4/5 cases, DAS28CRP average 2.26). During GLM administration, there were 1 femoral shaft fracture due to falls and 1 clipping operation to the cerebral aneurysm. [Conclusion] From the viewpoint of continuation and remission rate, switching to GLM may useful application as the second biologic agent.

P1-112

Analysis of DMARDs selection in methotrexate-related lymphoproliferative disorder in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] Though MTX-related LPD is an uncommon medical condition, clinical course and therapies in the patients with LPD still not found. [Methods] We analyzed clinical characteristics and course of MTX-related LPD in Japanese RA. [Results] Among 1502 RA patients, 32 (6 male and 26 female) patients were enrolled in this study. The age at the diagnosis of LPD was 68.7+/-10.0 years old, and the duration of RA was 131.1+/-82.4 months. All of 32 patients were treated with MTX and average dose at the diagnosis of LPD was 9.2+/-3.6mg/week. MTX-LPD were showed in extra-nodal sites, with spine, skin, gastrointestinal tract and lung. Lymphoproliferative lesions were improved spontaneously by discontinuation of MTX in 28 cases. Although improving of lymphoproliferative lesions, activity of RA were worsened in 22 patients, These patients were treated with SASP 15cases, BUC 6cases, mizoribine 16cases, abatacept 1cases.4 out of 32 cases showed relapse either RA and lymphoproliferative lesions. These 4patients were treated with chemotherapy, R-CHOP. [Conclusions] Cessation of MTX may be a therapeutic option in patients with MTX- LPD. Further study is needed to evaluate the safety for using DMARDs in RA with MTX-LPD.

P1-113

Outcome of RA patients complicated with cancer found by screening examination before starting biologic DMARDs - from data of 2671 patients with RA at University of Occupational and Environmental Health -

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The First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan

Conflict of interest: None

[Objectives] To clarify the outcome of RA patients complicated with cancer. [Methods] 2671 RA patients were screened using CT scan before starting biologics in our hospital between January 2005 to October 2017. We assessed the outcome of RA patients who were found to have cancer. [Results] In the wake of CT scan, cancer was diagnosed in 26 patients (lung cancer; 11, malignant lymphoma (ML); 5, breast cancer; 2, uterine cancer; 1, gallbladder cancer; 1, thyroid cancer; 1, bladder cancer; 1, prostate cancer; 1, liposarcoma; 1, kidney cancer; 1, gastrointestinal stromal tumor (GIST); 1). 13 patients with early lung cancer underwent curative surgery. 10 of them were treated with biologics, the others were treated with MTX. All 13 patients had been kept RA in LDA without recurrence of cancer. [Conclusion] Screening CT before starting biologics was useful for early detection and rapid cure of lung cancer. After curative surgery, patients could be treated with MTX and/or biologics and be kept RA in LDA without recurrence.

P1-114

Serious adverse events associated with biologic DMARDs under our multi-disciplinary medical care for Rheumatology

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Conflict of interest: Yes

[Object] To study the incidence of serious adverse events associated with biologic DMARDs in patients under our multi-disciplinary medical care for Rheumatology. [Methods] We reviewed the medical records of the consecutive 183 patients who were treated with biologic DMARDs since July, 2012. [Results] Abatacept was used in 104 cases (mean age 65 yo), etanercept in 50 (57), and other biologics in 29 (59). The concomitant MTX and PSL were used in 53% and 29%, respectively. Mean doses of MTX and PSL were not significantly different among 3 groups. The mean follow-up period was 21 months. Kaplan-Meyer life table methods revealed the 2-years event-free survival rates of 85% in the abatacept, 60% in the etanercept and 62% in the others. The 2 years cumulative rate of adverse events were 4% in the abatacept, 22% in the etanercept and 31% in the others. Serious adverse events included 7 infection, 2 malignancy, 2 cardiovascular events and 1 interstitial lung disease. The incidence of serious infection per 100 person-year was 1.04 in the abatacept, 3.16 in the etanercept and 4.3 in the others. [Conclusions] Serious infection remained a critical issue in patients who were treated with biologic DMARDs even under the multi-disciplinary medical care in our clinic. Abatacept seems relatively safe.

P1-115

Abatacept (ABT) seems to be safely used for patients with rheumatoid arthritis (RA) with interstitial lung disease (ILD) of more than moderate degrees

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Conflict of interest: None

[Object] ILD is an important prognostic factor. One of the causes of ILD exacerbation is drug, and we have experienced 3 cases died of exacerbation of ILD during use of bDMARDS. In these cases, TNF-inhibitors were used and the degree of ILD was more than moderate degree. In this study, we studied the effects of ABT on ILD of more than moderate degrees in RA patients. [Methods] Subjects were 25 patients with RA (male/female = 12/13) associated with ILD with the mean age of 75.2 years (60 - 86). The grading of ILD was done according to our previous work in BMJ open 2014. Evaluation of ILD was done by chest CT, and grade 2/3 was regarded as more than moderate degrees. [Results] ILD grades were 2 in 18 patients and 3 in 7, respectively. The median duration of ABT administration was 19.6 months (6 - 66). There were no patients whose ILD grade increased, and 1 patient showed decrease in ILD grade from 2 to 1. The mean KL-6 values at the start and the last administration of ABT were 684U/ml (+/- 575) and 627U/ml (+/- 413), respectively. The mean DAS28ESR decreased significantly from 4.66 (+/- 1.78) to 2.65 (+/- 0.82). The dose of PSL also tended to decrease. [Conclusions] ABT seems to be safely used for patients with RA with ILD of more than moderate degrees.

P1-116

Analysis of 6 cases in MTX-LPD with RA: including the case of intrapulmonary origin

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Conflict of interest: None

69 years old woman was diagnosed with rheumatoid arthritis 40

years ago and treated with MTX (methotrexate) from 10 years ago. In January, many tubercles of both lung fields in CT has been pointed out. In April C-reactive protein was rising and in May she had right chest pain. The tumor became huge. We suspected MTX-LPD by the histologic of CT guided biopsy that is diffuse large B-cell lymphooma with EB virus and abrod treating with MTX. After that, the tubercles and the tumor decreased. MTX-LPD frequently inprove spontaneously by cessation of the drug. We experienced six cases in our hospital and the three case improve spontaneously. It is reported that an increase in lymphocyte count of >220/μl at 2 weeks after MTX cessation could predict spontaneous LPD regression. The three cases have increases in lymphocyte count. A lympohocyte count is important to consider spontaneous regression and treatment early.

P1-117

Analysis of patients with rheumatoid arthritis requiring hospitalization for infection during biological treatment

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Conflict of interest: None

[Object] We aimed to determine the clinical features of rheumatoid arthritis (RA) requiring hospitalization for infection during biological treatment. [Methods] We retrospectively analyzed 68 patients hospitalized for infection while receiving biological treatment between April 2012 and October 2017. [Results] Among the 68 patients, 32, 20, and 16 were hospitalized during therapy with TNF inhibitor, TCZ, and ABT, respectively. The reasons were infections of respiratory organs, skin, urinary tract, digestive organs, and joints in 32, 10, 6, 6, and 4 patients, respectively. Fourteen patients had respiratory failure, and one died of bacterial pneumonia during TCZ therapy. Causes of respiratory infection were *Pneumocystis jirovetii*, *Haemophilus influenzae*, *Pseudomonas aeruginosa*, *Moraxella catarrhalis*, *Staphylococcus aureus*, and influenza virus in 5, 4, 2, 1, 1, and 1 patient, respectively. Causes in the other 15 patients remained unknown after various culture assays. Any patients who developed *Pneumocystis jirovetii* pneumonia (PCP) did not receive prophylaxis. [Conclusions] Respiratory infections were the most common reasons for hospitalization among patients with RA undergoing biological therapy, as previously reported. PCP accounted for 15.6% of the respiratory infections.

P1-118

Claims Data Analysis of opportunistic infections during bio-DMARDs from CISA database

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Conflict of interest: None

By using CISA data in 7 years we calculated the occurrence of opportunistic infections in 6,137 RA patients treated with bio-DMARDs. CISA is the database from claims data accumulated from 12 national university hospitals in Japan. We judged the cases of opportunistic infections by administrated drugs for each patient. The average occurrence of three infections is 3.2%, and pneumocystis pneumonia 0.85%, tuberculosis 0.44%, herpes zoster 2.57%, respectively. The highest occurrence is tofacitinib (7.4%) while the lowest is golimumab (1.3%). The median period of occurrence of the infections are pneumocystis pneumonia 263.5 days, tuberculosis 388 days, herpes zoster 422 days, respectively. In this RWD analysis, occurrence of the infections has differences beween bio-DMARDs and the median occurrence data is earlier in pneumonitis pneumonia than in tuberculosis and herpes zoster.

P1-119

Clinical features of rheumatoid arthritis treated with immunosuppressive therapy and complicated by lymphoproliferative disorders

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Conflict of interest: None

Objective: Among patients with rheumatoid arthritis (RA) on immunosuppressive therapy, a few develop lymphoproliferative disorders (LPD). We aimed to determine the features of patients with RA complicated by LPD. **Methods:** We analyzed 20 patients with RA (male, n=8; female, n=12; median age at diagnosis with LPD, 70 years; median duration of RA, 10.5 years) who were treated with immunosuppressive therapies and complicated by LPD at Ohta-Nishinouchi Hospital between October 2007 and September 2017. **Results:** Eighteen patients were treated with methotrexate (MTX) for a median duration of 5.5 years, six were treated with biological agents, and 10 had extra-nodular lesions. The histological findings were diffuse large B-cell lymphoma (n=9), mucosa-associated lymphoid tissue lymphoma (n=3), and Hodgkin lymphoma (n=2). LPD treatment comprised chemotherapy (n=13) and surgery (n=4), and two patients stopped treatment with MTX. Seventeen of 20 patients achieved remission of LPD. After treatment for LPD, RA became exacerbated in three patients, of whom two improved with steroid therapy and one remained refractory to various therapies. **Conclusion:** Patients with RA under immunosuppressive therapy who develop LPD tended to have extra-nodular lesions, which might complicate early diagnosis of LPD.

P1-120

Retrospective study of MTX-LPD in our hospital

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Conflict of interest: None

[Object] Methotrexate-associated lymphoproliferative disorder (MTX-LPD) is a rare complication in treatment of rheumatoid arthritis (RA). We conducted retrospective review of patients in this study. [Methods] We retrospectively analyzed background of patients, histology of LPD, treatment and disease activity of RA in 19 patients with MTX-LPD in our hospital between 2008 and 2017. [Results] Our cases included 4 males and 15 females, and the median age of MTX-LPD onset was 70.3 years old. Average dose and period of MTX administration were 8.9 mg / week, 9.3 years. Mean DAS28-CRP and CDAI at MTX-LPD diagnosis was 1.63 and 1.57, respectively. In all cases, disease activities of RA were low or less. Chemotherapy (CTx) was required in Eight patientsThe proportion of patients associated with Sjögren's syndrome (SS) was significantly larger in CTx+ group (55.5 % v.s. 0 %, p=0.004). Soluble IL-2 receptor was significantly larger in CTx+ group (3360U/ml v.s. 1185U/ml, p=0.05) [Conclusions] Absence of SS and high level of soluble IL-2 receptor were supposed to be associated with spontaneous remission of MTX-LPD.

P1-121

Changes in interstitial lung disease (ILD) after the administration of tocilizumab (TCZ) for patients with rheumatoid arthritis (RA)

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Conflict of interest: None

[Object] ILD is an important prognostic factor. One of the causes of ILD exacerbation is drug, and we have experienced 3 cases died of exacerbation of ILD during use of bDMARDS. In these cases, TNF-inhibitors were used. In this study, we studied the effects of TCZ on ILD in RA patients. [Methods] Patients were 55 patients with RA (male/female = 15/40) associated with ILD with the mean age of 67.2 years (43 - 86). The grading of ILD was done according to our previous work in BMJ open 2014. Evaluation of ILD was done by chest CT, which was done yearly and at the time needed. At the start of TCZ, PSL and MTX had been administrated in majority of patients. [Results] The median duration of TCZ administration was 11.5 months (2 - 81). The types of ILD were NSIP in 37, UIP in 4, and OP in 14, respectively. The ILD grades were 1 in 41, grade 2 in 2, and grade 3 in 3, respectively. The status of ILD changed in 5 patients after TCZ, i.e., exacerbation in 3 and improvement in 2. ILD grade changed in 3 patients, i.e., 2 decreased and 1 increased,

but nobody discontinued because of ILD exacerbation since the change was subtle. The mean KL-6 value changed from 301U/ml (+/- 152) to 287U/ml (+/- 111). [Conclusions] TCZ seems to be used safely in RA patients with ILD.

P1-122

Recognition of understanding about MTX and steroid on sick day, andeffectiveness of explanation with the leaflet

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Conflict of interest: None

Object MTX is effective drug, but sometimes induces side effects, including OIIA-LPD. Diabetes patients learn "sick day". "Sick day" means poor physical condition sometimes with fever or loss of appetite. In their sick days, they have to stop some medicines.I assume that RA patients also need to learn their "Sick day" (RA sick day). We checked their understanding of drug side effects, their skill to cope RA sick day, and effectiveness of our education. **Method** We asked some questions to check their understanding of side effects of MTX and PSL, and their skill to cope with "RA sick day". We also explain "RA sick day" using the leaflet "For the patients who take MTX". After a few months, we surveyed their understanding of what we had explained. **Result** We asked 92 patients. Q) Do you know about MTX's any side effects? A) Nothing-42.Q) Do you take MTX on sick day? A) Yes-8 No-49 No idea-35. We asked 44 patients who also take PSL. Q) Do you take PSL on sick day? A) Yes-24 No-10 No idea-10. Few months after our explanation, we questioned 54 patients whether they take MTX on sick day, and 51 answered no. In regards to those who are taking PSL,14 answered yes.9 answered no, and4 answered no idea. **Conclusion** Many patients did not know how to deal with "RA sick day". It was worth handing leaflets for education.

P1-123

Three cases of rheumatoid arthritis with lymphatic proliferative disease

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Conflict of interest: None

[Purpose] RA patients have high risk of developing malignant tumors. Also it has been shown that the merger frequency by Methotrexate (MTX). Three cases of RA with lymphatic proliferative disease (LPD) are examined. [Case 1] 76-year-old woman. RA for the 2010 onset. Started introducing MTX in 2011. In 2014, malt lymphoma onset. But MTX is not discontinued because it is judged mainly as a clinical Helicobacter pylori infection. Treatment is only Helicobacter pylori removal and then continue to follow the progress of MTX now without increasing evil. [Case 2] 84-year-old woman. RA for the 2015 onset. There has been a history of resection of lung malt lymphoma in 2006. As RA treatment, Salazosulfapyridine + PSL are used. Lymphoma is no degradation. [Case 3] 69-year-old man. RA for the 2008 onset. MTX started in June 2009. Infliximab (IFX) introduced from August of the same year. In August 2017, the right cervical lymph node swelling and it was diagnosed malignant lymphoma. ABVD started therapy. During the course of observation only Ifx and MTX aborted PSL oral. [Study] There are various reports of the effect on the onset of lymphoma by MTX-LPD and bio, and the subsequent treatment transition, and the report is added to the three cases based on this document consideration.

P1-124

A Strategy of stringent control of side-effects prevent the incidence of methotrexate related lymphoproliferative disorders in rheumatoid arthritis

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Conflict of interest: None

[Object] We establish the hypothesis that strategy of stringent control of side-effects (S-3) that maintains lymphocyte counts at 1000/mm ^{3} or more and ALT at 30IU/L or less is an incidence of methotrexate related lymphoproliferative disorder (MTX-LPD) in rheumatoid arthritis (RA). [Methods] In 581 RA patients who were treated from 2002 to 2011 (2002 group) (80% female, age 61 years, disease duration 2 years, MTX use rate 56%, MTX dose 6.6 mg/week, prednisolone (PSL) use rate 16%, PSL use 2.7 mg/day, the biological anti rheumatic disease drugs (bDMARDs) use rate 44%), the LPD incidence rate of 8/3783 person-years and the RA patient (2012 group) introduced S-3 from 2012 are compared. At least once every 3 months, ALT 30IU/L or less, treatment medicine was changed to keep lymphocyte count at over 1000/mm^3. [Results] As of November 6, 2017, there were 282 RA patients in the 2012 group (69% of females, 67 years of age, 0.5 years of disease duration, MTX use rate of 59%, MTX use of 6.5 mg/week, PSL use rate 19%, dose of PSL 2.3 mg/day, sDMARDs use rate of 53%, JAK inhibitor use rate of 1%), 637 person-years, LPD has not occurred. [Conclusions] Although it is an intermediate analysis, S-3 is highly likely to be an extremely effective therapeutic strategy for prevention of MTX-LPD in RA.

P1-125

Research of discontinued cases of biological agents due to adverse events in RA

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Conflict of interest: None

[Object] We investigated RA patients discontinued of biological agents due to adverse events in our hospital. [Methods] April 2012 or later, we have used the biological products in 98 cases in our hospital, and 18 patients discontinued by adverse events. We investigated the used drugs, type and outcome of adverse events, and present disease activity in each case. [Results] Adverse events canceled biologics were abatacept six cases, tocilizumab five cases, eternercept three cases, adalimumab two cases and certolizumab pegol two case. Breakdown of adverse events were four cases of pneumocystis pneumonia, three cases of bacterial pneumonia, three cases of lung cancer, two cases of skin rush, one case of prosthetic joint infection, renal abscess, bacterial synovitis, malignant lymphoma, ovarian tumor, heart failure, liver dysfunction, and tamper bleeding. 10 cases were resumed biologics after discontinuation adverse events, and 7 cases used abatacept. [Conclusions] Abatacept was considered a possible re-administered biologics after discontinuation adverse events. And regularly chest CT examination is very useful for early detection of lung cancer.

P1-126

Factors which affect the adherence to methotrexate therapy in rheumatoid Arthritis

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Conflict of interest: None

[Objective] Methotrexate (MTX) is the anchor-drug of rheumatoid arthritis (RA). In order to keep its efficacy, high level of adherence to MTX (adh) must be kept for long term. Pharmacists have important role in education of patients to keep the adh. In order to perform effective education, factors affecting adh should be elucidated. Herein, we analyzed such factors. [Method] Twenty two RA patients who were taking MTX were picked up. Questionnaire survey was performed from Sep. 2017 to Nov. 2017. Treatment was continued by attending physician who are blind to the result of questionnaire survey. [Result] Mean dose of MTX was 8.09±2.98mg/week. Nine patients (40.9%) skipped taking MTX at least once per 3 month. Middle age, high level of knowledge about RA treatment, low dose MTX intake, and lower disease activity tended to be associated with bad adh. On the other hand, neither adverse effect, liver damage, nor choice of generic drug were associated with adh. [Conclu-

sion] It was implied that higher level of knowledge about RA does not improve adh, and bad adh was not connected to bad disease activity. Not only simple teaching, but also another technic are required for improving adh. And pharmacists should think of the approach to improve the outcome of RA.

P1-127

Experience with hepatitis treatment on patients with rheumatoid arthritis combined with bio use and hepatitis B / C

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Conflict of interest: None

<Introduction> The treatment of hepatitis C is approved for DAA preparation in 2015, the treatment outcome has greatly improved. <Case> 81-year-old female. RA developed at the age of 75. Hepatitis C carrier, hepatitis B has been an infection. MTX ceased due to elevation of liver enzymes. SASP 1000 mg is also inadequate control. We introduced 50 mg / week ETN from age 76 and improved RA control. The amount of hepatitis B DNA was not detected and was detected less than 20 IU/ml and slightly increased, but it did not reach 20 IU/ml and was not adapted for the introduction of nucleic acid analog preparations. We reviewed the introduction of DAA preparation against hepatitis C in 2015 as approved. Liver reserve capacity was kept as child A, but renal function was 1.1 mg/dl of Cr and somewhat decreased as estimated GFR 34. There is taking Ca antagonist. Considering renal function, concomitant medication, age, we decided not to introduce the DAA formulation this time and to consider the application of the next bile excretion type DAA formulation. <Discussion> In September 2017, DAA formulation of biliary excretion type was newly approved. It is also expected that adaptation will spread.

P1-128

Sustained long-term clinical remission after added iguratimod during biological DMARDs use in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To examine the long-term clinical course of rheumatoid arthritis (RA) patients who added iguratimod (IGU) during biological DMARDs (bDMARDs) use. [Methods] In this study, 44 RA patients who treated with IGU and bDMARDs for 24 weeks were investigated. [Results] The mean age was 65.6±13.3 years, women were 86.4%, mean disease duration was 8.5±7.8 years, and mean duration of bDMARD treatment was 1.9±1.7 years (ETN/ADA/GLM/CZP/TCZ/ABT, 8/7/8/1/6/14). Of the 44 patients, 20 patients were remission at 24 weeks after IGU administration (remission group). Of these patients, 16 patients maintained remission at 72 weeks. DAS28-ESR in the remission group was 1.75±0.58 after 24 weeks of IGU administration and 1.83±0.60 after 72 weeks (p=0.794). Of 16 patients who sustainted remission, 9 patients were able to reduce or discontinue methotrexate and/or prednisolone. There was no difference in the patient's characteristics between treatment tapering group and treatment maintenance group. Of 24 patients in the non-remission group, 7 patients achieved remission at 72 weeks. [Conclusions] RA patients who have added iguratimod during bDMARDs use and who achieved remission after 24 weeks are able to maintain long-term remission, and may be able to reduce treatment.

P1-129

Investigation of safety and efficacy of switching Japanese rheumatoid arthritis patients on long-term original infliximab product to a generic infliximab product

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Conflict of interest: Yes

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. 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.

P1-130

Clinical evaluation of abatacept or golimumab in patients with rheumatoid arthritis in our department

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Conflict of interest: None

[Objectives] To investigate the efficacy and the adherence of abatacept (ABT) or 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), Bio-naïve: 6/11. [Methods] Efficacy of ABT and GLM was evaluated by DAS28-ESR4, CDAI and SDAI for 208 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 156 weeks in both groups.2) The adherence at 52 weeks showed more than 80% in both groups and, that at 104 weeks 69.2%, that at 156 weeks 61.5% in ABT, that at 104 weeks 56.0% and that at 156 weeks 40.0% 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 4/7, cancer1/1, organizing pneumonia 0/1, pneumonia 1/1, EBV reactivation 1/1, remission1/0 and so on. [Conclusion] The efficacy and the adherence of ABT and GLM were similar.

P1-131

The clinical feature of elderly patient with rheumatoid arthritis

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Conflict of interest: None

(Objective) Along with aging of the populations, the number of elderly patients with RA patients is increasing. We investigated a clinical feature of elderly RA patients. (Method) We compared patients over the age of 70 years as of April 2017 with patients under the age of 70 for the characteristic. The drug retention rate of MTX, biologics was investigated. (Result) We investigated 50 RA patients who were over 70 years old. The disease duration was 12.5 years and the RF positive rate was 70.0%. It was Steinbrocker's class, the rate of MTX, PSL use, DAS 28 CRP that showed a significant difference compared with patients under the age of 70 in the patient characteristic. There was no difference in the dosage of MTX and the rate of biologics use. 5 year retention rate of MTX, biologics was 84%, 77%. Disease activity was worse when compared with April 2016. (Conclusion) We showed that the use rate of MTX was low, and relying on the use of steroid. The retention rate of MTX, biologics

was good, which was thought to be due to selection of the patient. Even in elderly RA patients, the treatment similar to that for young people is performed, but there is no clear guideline on how aggressive treatment should be taken in the future and it can be said to be a future task.

P1-132

Efficacy and Safety of Biosimilar Infliximab (CT-P13) in patients with rheumatoid arthritis at our hospital

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Conflict of interest: None

[Object] We have clinically studied the efficacy and safety of Biosimilar Infliximab (CT-P13) in patients with RA at our hospital. [Subjects] 17 cases were administered,7 male,10 females,9 naïve and 8 switches from other biologics. [Results] Effective in 7 of naïve cases, switch to TCZ due to ineffectiveness in 2 casaes. In one patient who was ineffective, rash showed on both lower limbs at 5 months of administration. Among the 8 switch cases, until just before, Originator IFX was administered in 6 cases, switch from GLM was 2 cases. On those 8 cases, CT-P13 were effective except one case. One case was complicated by herpes zoster from the left lower limb to the buttocks at the 7th week of administration. [Discussion & Conclusions] In cases of CT-P13 naïve, most patients who had economic circumstances, desired earnestly Biofree as commpared with cases of Originator IFX, when low diseases activity or remission is reached. Overall, CT-P13 was judged to be inferior to Originator IFX in efficacy and safety, and it was considered that it can contribute to medical economics in the future.

P1-133

Improvement of Anemia by Tocilizumab Treatment in Patients with Rheumatoid Arthritis in Clinical Setting

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Conflict of interest: Yes

[Objectives] Hepcidin is produced from hepatic cells by inflammatory cytokines such as IL-6 and one of the major causes of anemia in RA patients. Tocilizumab (TCZ) inhibits effects of IL-6 and improves anemia. Improvement of anemia in RA patients treated with TCZ was investigated in this study. [Methods] Data from Toyohashi RA Database (TRAD) was used. 31 cases who continued TCZ for 2 years and more were used for detailed analysis. [Results] Baseline Characteristics (n=31): Mean age 56 yo, Female 74.2%, RA duration 6.6y, MTX concomitant 74.2%, PSL concomitant 64.5% and bio-naïve 29.0%. In 31 RA patients who continued TCZ for 2 years and more, DAS28-CRP, CDAI and mHAQ had significantly decreased over time (baseline-1year-2year). 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, and PSL 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. Hb (g/dL) and Ht (%) ware also significantly improved (11.6-13.0-13.2, 36.8-39.9-40.1), respectively. [Conclusions] In RA patients who continued TCZ for 2 years and more, MTX and PSL was decreased. Although concomitant drugs were decreased, anemia was improved over time.

P1-134

The efficacy of Golimumab to RA patients for mid-term results

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Conflict of interest: None

[Object] To evaluate Golimumab (GLM) to RA patients. for mid-term results. [Methods] From April 2012, forty-two cases treated with GLM were evaluated by recording DAS28 (CRP). The average amount of GLM was 58.3mg. [Results] DAS28 was 4.5 and decreased to 2.0 at 48 month, CRP was also reduced from 1.3 to 0.5 at 48 month. Survival rate on Kaplan-Meier at 48 month was 80.1%. [Conclusion] The therapy of GLM was effective for mid-term results.

P1-135

Effectiveness of switching between tocilizumab and abatacept in rheumatoid arthritis

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Conflict of interest: None

[Object] To examine the clinical characteristics of patients with rheumatoid arthritis (RA) having switched between tocilizumab (TCZ) and abatacept (ABT). [Methods] We retrospectively investigated 38 RA patients who had difficulty in using either TCZ or ABT and were introduced the other between 2010 and 2016. [Results] The group in which ABT was introduced after discontinuation of TCZ consisted of 24 patients (16 females). The mean age was 67 years and the mean disease duration was 13 years. In this group, prevalence of pulmonary involvement was 42% and methotrexate (MTX) was concomitantly used 54%. The continuation rate at week 52 after the start of ABT was 75%. Among this patients, the proportion of patients achieving remission or a low disease activity (SDAI≦11) at week 52 was 72%. On the other hand, the group in which TCZ was introduced after discontinuation of ABT consisted of 14 patients (13 females). The mean age was 61 years and the mean disease duration was 13 years. Prevalence of pulmonary involvement was 57% and MTX was concomitantly used 57%. The continuation rate at week 52 was 93%. The proportion of patients achieving SDAI≦11 was 62%. [Conclusions] Even if either TCZ or ABT is difficult to continue, it may be possible to better control RA by switching to the other.

P1-136

Evaluation of the therapeutic outcome of abatacept from changes in CD4+/CD25+high fraction

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Conflict of interest: Yes

[Objective] The aim of this study was to analyze the effect of abatacept (ABT) on the CD4+/CD25+^{high} fraction. [Subjects and methods] The subjects were 32 rheumatoid arthritis (RA) patients treated with ABT therapy. The age of patients was ranging from 39 to 81 years (mean: 62±12 years.). Sixteen patients were switched from other biologics, and 16 patients were ABT naive. Changes in CD4+/CD25+^{high} expression levels in blood tests prior to ABT administration were determined by using flow cytometry in 5 points: 0 (prior to first ABT administration), 4, 12, 24, and 52 weeks. [Results] CD4+/CD25+^{high} distribution revealed that in the naive group, an interim decline occurred at week 52, but significant elevations were observed in the switched group starting at week 12. Analysis of the responders (10 cases) and non-responders (6 cases) to ABT in the switched group indicated that the responders showed significant declines in CD4+/CD25+^{high} levels between weeks 12 and 52, as did the cases in the naive group. However, the non-responders showed significant elevations in this fraction from initial ABT administration until week 52. [Conclusion] Based on these results, changes in the CD4+/CD25+^{high} fraction can be used to measure the therapeutic efficacy for RA from the perspective of CTLA-4.

P1-137

Use of abatacept monotherapy in elderly rheumatoid arthritis

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Conflict of interest: None

[Objective] In our hospital, approximately 80% of RA patients is over 60 years old. We report three cases of elderly RA treated with ABT monotherapy. [Case 1] A 79-year-old man was treated with ABT monotherapy because of MTX-induced liver injury. DAS 28 was remission and could last for 4 years. ABT was canceled at the request. Tow months later, RA relapsed and therefore ABT was reintroduced. He is now in remission. [Case 2] A 79-year-old woman was treated with ABT monotherapy. DAS 28 reached remission and could last for 19 months. LDA has been maintained after discontinuation of ABT for more than half a year. [Case 3] A 74-year-old woman was treated with ABT monotherapy because of MTX-induced liver injury. DAS 28 has reached remission for 5 years. [Results] In elderly RA, MTX often is difficult to use due to various complications. ABT monotherapy could maintain remission for average 26 months in cases who could not be used MTX. In 2 cases who discontinued ABT after remission, one relapsed but remission was obtained by reintroduction. In the other case, LDA has been maintained for more than half a year. [Discussion] ABT monotherapy can obtain remission even in elderly RA and leads to improvement of ADL. It can be one of options in elderly RA treatment.

P1-138

Drug retention rates of biological DMARDs and targeted synthetic DMARDs on methotrexate or without methotrexate

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Conflict of interest: None

[Object] There are some reports that drug retention rates of biologic agents (bDMARDs) for rheumatoid arthritis (RA). The purpose of this study was to explore drug retention rates of bDMARDs and targeted synthetic DMARDs (tsDMSRDs) in patients with RA on methotrexate (MTX) or without MTX. [Methods] RA patients treated with bDMARDs and/or tsDMARDs at Kitasato University Medical Center were investigated. Overall bDMARDs and tsDMARDs maximum 700-week drug retention was evaluated. Drug survival rates were calculated using the Kaplan-Meier method and compared by log-rank test. [Results] Of 284 patients, 117 were treated with a combination of tumor necrosis factor inhibitor (TNFi) and MTX (TNF+MTX), 41 with TNFi without MTX (TNF-MTX), 72 with a combination of non-TNF bDMARDs (non-T) and MTX (nonT+MTX), and 54 with non-T without MTX (nonT-MTX). The overall 700-week drug survival rate was 15.7%. The results showed no significant difference among the retention rates of each group. The persistence rate of the second-line and more biologic therapy with MTX were significantly higher with nonT+MTX, than TNF+MTX ($p=0.0412$). [Conclusions] After inadequate response to TNF or non-TNF biologic agents, patients on a non-TNF biological agent with MTX have significantly higher drug persistence rates.

P1-139

The comparison of treatment outcome using non TNF inhibitor with rheumatoid arthritis

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Conflict of interest: None

[Object] The number of patients using biological agents with rheumatoid arthritis (RA) is increasing. Tumor necrosis factor (TNF) inhibitors are recommended for use with methotrexate (MTX). Some patients for whom MTX or TNF inhibitors are contraindicated. The aim of this study was to compare the effects of Tocilizmab (TCZ) and Abatacept (ABT), both of which are non-TNF inhibitors. [Methods] We used the data of patients with RA who received TCZ or ABT at April, 2017 at Tottori University Hospital. [Results] Of the total 46 patients (8 male, 38 female; mean age, 68.3 years; mean treatment duration, 12.7 years). There were no between-group differences in swollen and tender joint counts. Nevertheless, erythrocyte sedimentation rates were lower in patients who received TCZ (12.6), compared to those who received ABT (48.6). The Clinical Disease Activity Index score was higher in patients who received TCZ (6.4), compared to that in patients who received ABT (3.4). There was no observed discontinuation due to adverse events and overall adverse events were did not significantly differ between the two groups. [Conclusions] Deep remission was more difficult, but the persistency rate was higher in patients who were treated with TCZ, compared to those treated with ABT.

P1-140

The clinical efficacy of Certolizumab Pegol (CZP) in multicenter research

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Conflict of interest: None

[Object] CZP, PEGylated anti-TNFα biologic antibody has shown high and rapidly efficacy in domestic clinical trial. but there is little examination of the CZP efficacy in the routine clinical practice. Object: We investigate efficacy of CZP in the RA conference participation institution and consider positioning of CZP in the routine clinical practice. [Methods] It was carried out and analyzed a retrospective survey about the case that used CZP for more than 24 weeks at October 2016. [Results] 23 cases (19 women) were evaluated. Average age 55.6 years, mean disease years 12.1 years, mean CZP use 2.94 years, all of cases used MTX, mean MTX 8.9mg/week, 52.2% of cases used PSL, mean PSL 2.82mg/day, Bio-naïve 43.5%, baseline DAS28-ESR 5.07±1.32, 2.96±1.20 at 52 weeks, 3.07±1.26 at 104 weeks. In 12 of 13 cases, reached moderate response (MR) at 12 weeks, remission and low disease activity were maintained in 1 year and 2 years. On the other hand, 3 of 10 cases in unreachable MR at 12 weeeks became MR at 24 weeks. A Bio-naive rate was 69.2% in the MR group, and 0% in unreachable MR. [Conclusions] A clinical efficacy of CZP exceeding a certain level was obtained in clinical practice, and it was shown that the treatment effectiveness at the 12 weeks will be the future effect prediction.

P1-141

The changes of RA patients between non-biologics era and biologics era in our hospital

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Conflict of interest: None

[Object] We compared the patients' characters and treatments between non-biologics era and biologics era (20 years passed changes) in our hospital. [Methods] Non-biologics group 30 patients and biologics group 30 patients consulted our hospital at 1997, 2015-2016 respectively. Disease duration and CRP, RF, swollen joints counts, tender joints counts, medications, and operations of two eras were compared with first visit and one years passed. Ages of non-bio and bio era groups are 60.7 yrs. and 62.3 yrs. [Results] Duration of diseases was 81 months and 47 months. CRP (mg/dl) changed from 6.35 to 3.61 in non-biologics era and changed from 4.17 to 0.79 in biologics era. The numbers of swollen joints were changed from 4.22 to 4.29 in non-bio era and were changed from 7.5 to 1.0 in bio era. MTX were used 23% in non-bio era and were 59% in bio era. NSAIDs were more used and many arthroplasties were performed in non-bio era. [Conclusion] The usage of biologics brought the decreases of CRP and swollen joints numbers in bio era. Early onset

(within one year) patients were consulted 13.6% (non-bio) and 70% (bio). Early treatments were performed in biologics era patients. These changes must be considered as social aspects changes.

P1-142

Decreasing methotrexate dose after remission in case of rheumatoid arthritis patients who had MTX plus BIO: a clinical course observation

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Conflict of interest: None

[Object] methotrexate (MTX) is an anchor drug in RA treatment. But the side effect of MTX, especially MTX-related lymphoproliferative disorder (MTX-LPD) has been addressed in RA. It is reported that the daily dose and cumulative dose of MTX are related to the development of lymphoma, so maybe it is important to decreasing MTX as low as possible. However, the timing to decrease of MTX is not known in present. In patients with rheumatoid arthritis (RA) that maintained remission by MTX plus Biologic DMARD (BIO) and got their consent, the clinical course after decreasing MTX was evaluated. [Methods] Subjects were 49 patients who had MTX plus BIO from Aug 2012 to Oct 2016. Baseline characteristics were mean age 55.1years, mean duration of illness 64.7months, mean use period of BIO 64.7months, and corticosteroid were not used. The course of DAS28-ESR, SDAI, CDAI and remission rates were analyzed. [Results] Mean DAS28-ESR, SDAI, CDAI were no significant rise at 52 weeks after decreasing MTX (1.70→1.82, 0.37→0.75, 0.30→0.69). Remission rates of DAS28-ESR, SDAI, CDAI were 87.8%,95.9%,95.9% at 52 weeks. [Conclusions] This study shows the possibility that decreasing methotrexate after remission in case of rheumatoid arthritis patients who had MTX plus BIO might be a useful option after REM.

P1-143

Therapeutic effects of certolizumab pegol in patients with rheumatoid arthritis: a retrospective study from a single center in Japan

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Conflict of interest: None

[Object] Certolizumab pegol (CZP) is a tumor necrosis factor-α (TNF-α)-blocking agent approved by Japanese Ministry of Health, Labour and Welfare for RA. Since CZP has characteristics which are different from the other TNF-α-blocking agents, CZP might be effective for RA refractory to not only conventional, oral DMARDs but also bDMARDs including the other three TNF-α-blocking agents. Analyses of therapeutic effects and safety of CZP in patients with RA with more sample numbers are still needed. [Methods] We evaluated clinical courses of ten patients with RA in our department treated with CZP retrospectively. [Results] Eight of ten patients completed 24 week administration of CZP and obtained improvements in disease activity of RA. Whereas administration of CZP improved disease activities in four of six patients who had been treated with other TNF-α-blocking agents, adverse effects were observed in the other two patients within 12 weeks from the introduction of CZP. [Conclusions] This study suggested that CZP would be useful even for patients RA refractory to other TNF-α-blocking agents. However, careful observation for early adverse effects is indispensable.

P1-144

The evaluation of patients with RA in Akita Orthopedic Group on Rheumatoid Arthritis registry 2017 who received adalimumab

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Conflict of interest: None

[Object] The purpose is investigating of rheumatoid arthritis patients who received adalimumab (ADA). [Methods] We evaluated 86 patients (mean age; 63.6years) who received ADA in the Akita Orthopedic Group on Rheumatoid Arthritis (AORA) registry 2017 (n=2238). [Results] The mean disease period was 172 months. The cases had Steinbrocker classification stages 1/2/3/4 (16/21/18/30 patients), classes 1/2/3/4 (33/38/14/1 patients). The cases of naïve were 74 cases, the mean DAS28CRP (4) was 3.87 (0.96-5.37) in the first ADA administration. The mean follow-up period was 172 weeks. The cumulative continuation rates were 83% (1year), 76% (2years), and 64% (3years) in the Kaplan-Meier analysis. Twenty-seven patients had failure of ADA administration, due to primary failure in 12 cases and secondary in 6. The 59 patients who could continue ADA therapy were mean DAS28CRP (4) was 2.0, and 49 patients (83%) had good response according to the criteria of the EULAR in the final examination. 58 patients (98.3%) received methotrexate (MTX; mean dosage 6.4 mg/week); and 18 cases with prednisolone (mean dosage 3.3mg/day). [Conclusions] The patients received ADA therapy had a high combination rate with MTX, high continuation rate, and good results.

P1-145

Outcome of Certolizumab pegol (CZP) for rheumatoid arthritis (RA) patients and investigate effective patients background

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Conflict of interest: None

[Object] We examine a treatment outcome of Certolizumab pegol (CZP) for rheumatoid arthritis (RA) patients, and investigate effective patients background. [Methods] Follow-up intended for 24 cases among RA patients treated using CZP in this hospital by September, 2017 in 52 weeks. We examied it between two groups of CZP continuation group and the non-continuation group. [Result] The patient was mainly female (79.2%), and the average age was 58.3 years old. The combined use of csDMARD and PSL was 5 patients (23%) and 8 patients (33%), respectively. There were 10 bio-naive patients and the average MTX dose was 5.9/w.52 cases of CZP continued in 14 cases (58%). 10 patients were discountinued because they were ineffective with 8 patients and 2 patients with adverse events. The average MTX dose in the CZP discountinuation group was 4.2mg/w and only 3 cases were used in combination with 8mg/w or more. Eleven cases (78.6%) of 14 cases with MTX of more than 6mg/w were continued. Three out of ten paients (30.0%) had CZP of less than 6mg/w continued to be administered. [Conclusions] The 52 weeks treatment continuation rate by CZP was 58%. It is expected that high efficacy and continuit can be expected because MTX dosage is 6mg/w or more and there is no use history of bDMARDs.

P1-146

A case of ankylosing spondylitis associated with Takayasu's arteritis

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Conflict of interest: None

A 75-year-old woman, who was treated for hypertension and tachyarrhythmia. The pain of the right sternoclavicular joint, lower back pain, polyarthralgia were developed from September, 2014. She became the introduction in the department of rheumatology in our hospital in January, 2015. She was given salazosulfapyridine (SASP) and methotrexate (MTX) as spondyloarthritis, and her joint symptom was improved. However, her symptom and inflammatory response gradually turned worse from February, 2017. Then, she were admitted to our hospitals for further examination and treatment in June, 2017. She was surffered from low back pain, and had limitation of motion of the lumbar spine, and had sacroiliitis in X-rays and Magnetic resonance imaging (MRI). She could not stretching up of her left arms, and have laterality of the bloodstream of both arms, and contrast-enhanced computed tomography (CT) showed circumferential thickening and narrowing of aorta or its primary branches. she was diagnosed as ankylosing spondylitis (AS) associated with Takayasu's arteritis (TA). She was treated with Infliximab in addition to SASP and MTX, and after that not only joint symptom and inflammatory response and also CT and MRI findings were gradually improved. We reported a rare case of AS associated with TA and reviewed the literatures.

P1-147

Mid-term effectiveness of Infliximab in patients with Ankylosing Spondylitis

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Conflict of interest: None

[Object] In this study, we report the clinical time course of patients with Ankylosing Spondylitis (AS) treated with Infliximab (IFX) in our institution. [Methods] Four patients with AS were assessed about demographics and baseline characteristics at start of IFX and BASDAI (Bath Ankylosing Spondylitis Disease Activity Index), BASFI (Bath Ankylosing Spondylitis Functional Index), ASDAS-CRP (Ankylosing Spondylitis Disease Activity Score) and retention rate at final follow up. [Results] All patients were male and the mean age was 39.5 years old. The mean disease duration of AS was 138.3 months. HLA-B27 was positive in one patient, negative in one patient and 2 patients were not investigated. Three of four patient used celecoxib 400mg daily and 3 of 4 patient used Methotrexate 10.7 mg weekly. All patients continued the therapy with IFX until final follow up and the mean duration was 34.3 months. BASDAI reduced from 7.47 at start IFX to 2.53 at final follow up. At the last visiting, the mean ASDAS-CRP was 1.42. All patients were less than moderate disease activity and 2 of 4 patient reached and maintained inactive disease. [Conclusions] Infliximab kept enough effectiveness and retention rate in the therapy of Ankylosing Spondylitis over a year.

P1-148

The Clinical characteristics and outcome of TNF inhibitors in patients with ankylosing spondylitis

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Conflict of interest: None

(Object) To evaluate the clinical features and outcome of TNF inhibitors in patients with ankylosing spondylitis (AS). (Methods) 9 AS patients (6 males and 3 females) were registered. The average age was 43.9 (range; 27 to 68) years old. The average duration was 12.6 years. Isotypes of HLA antigens, enthesitis, efficacy and safety of TNF inhibitors were evaluated. (Results) HLA-B27 was positive in 3 cases (33%). All cases had lumbago. Knee pain was detected in 33 %, the insertion pain of calcaneus tendon and joint stiffness was detected in 22 %. TNF inhibitors (adalimumab; 6, infliximab; 2, and infliximab after adalimumab; 1) were administered at the average age of 43.1. The disease duration was 11.6 years on average. About conventional synthetic DMARDs, salazosulfapyridine was used in 4 cases (44%) and methotrexate was not used any case. Bath Ankylosing Spondylitis-Disease Activity Index was evaluated in 7 cases and the average index improved from 7.34 to 4.23 at the minimum. Of 9 cases, the elevations of AST and ALT were detected in 4 cases. No other adverse event was detected during observation. (Conclusion) The duration from the onset of AS to the administration of TNF inhibitors are still long. Once TNF inhibitors are administered, good efficacy and safety were acquired.

P1-149

Diffuse idiopathic skeletal hyperostosis in patients with psoriatic arthritis -a report of two cases-

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Conflict of interest: None

[Object] Diffuse idiopathic skeletal hyperostosis (DISH) is a condition characterized by calcification and ossification of soft tissues, ligaments, and entheses leading to presence of flowing bony bridges in the anterolateral aspect of the thoracic spine and peripheral enthesopathy. It was reported that DISH was observed in 78 (8.3%) of 938 patients with PsA in 2013. Here, we report two cases of DISH obserbed in patients with PsA (according to Hadadd's criteria). [Results] Spine CT showed flowing mantles of ossification occurring in the anterior longitudinal ligament and to a lesser extent in the paravertebral connective tissue and the peripheral part of the annulus fibrosus. DISH is reported to be associated with known DISH-related factors including older age and high BMI, as well as the presence of radiographic damage to peripheral joints. Thus, the presence of DISH might be a marker of severe disease in PsA.

P1-150

Comparison of clinical and imaging features among arthritis preceding-, skin-lesion preceding-, simultaneous onset psoriatic arthritis, and psoriatic arthritis sine psoriasis

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Conflict of interest: None

[Object] PsA was once thought to be slow progressive. However, in recent reports, as with RA, joint destruction is progressive and irreversible. Therefore, early diagnosis and treatment should be required. Although skin lesions precede in many PsA cases (SP-PsA), arthritis may precede. In patients with early stage of arthritis preceding PsA (AP-PsA) there may be some difficulty in early diagnosis. We analyze the clinical features of AP-PsA comparing to SP-SpA and sine syndrome. [Methods] Clinical features were compared in 14 cases of AP-PsA satisfying CASPAR or Fournie criteria, 16 cases of SP-PsA, 16 cases of PsA sine psoriasis, and 22 cases of spondyloarthropathies (SpA) including AS. [Results] The mean age of arthritis was slightly younger (47.4 years old) in AP-PsA than in SP-SpA (50.1 y.o.) and sine syndrome (54 y.o.), and female ratios were 78.6%, 68.8% and 68.8%, respectively. Although there was no difference in ACPA positivity among three subtypes of PsA in 10%, both CRP and RF were lower in AP-PsA. [Conclusions] Differential diagnosis of arthritis preceding type PsA is challenging in distinguishing early RA, OA, erosive OA, SpA, myositis with peripheral arthritis. Early diagnosis before appearance of skin lesions is not always easy with current classification criteria.

P1-151

A case report of total hip arthroplasty in patient with psoriatic arthritis

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Conflict of interest: None

[Introduction] Total hip arthroplasty (THA) in a patient with psoriatic arthritis (PsA) is rare. Here we present a case report with some reviews.

[Case Presentation] A 60-year-old woman was diagnosed with psoriasis vulgaris in 2007. Although she received antiallergic drug and ointment at the clinic, skin condition did not improve, so that etretinate was started at department of dermatology in 2009. While skin disease improved with etretinate, she still had multiple tender joints including knees, elbows and interphalangeal joints in 2010. She came to department of rheumatology in 2011. It was difficult to treated with biologics due to economical problems, we first treated with SASP and PSL. Despite of the treatment, joint space narrowing of hip aggravated, so we converted to IFX from January 2016. In addition we started combined use of MTX from January 2017 but discontinued due to leukopenia in 3 months. As right hip joint destruction progressed regardless of the treatment, we planed THA. [Clinical Significance] While the main symptoms of PsA are psoriasis, peripheral arthritis, spinal lesions, enthesitis and dactylitis, joint destruction of large joints such as hip is rare. Hip lesion was reported to occur within 1 year after the onset of PsA and should be carefully observed.

P1-152

Newly-onset psoriatic arthritis following BCG immunotherapy

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Conflict of interest: None

[Background] Bacillus Calmette-Guerin (BCG), a live, attenuated strain of *Mycobacterium Bovis*, is widely used as an adjuvant therapy for non-muscle invasive bladder cancer. Arthritis is reported in 0.5 to 1% of cases after intravesical administration of BCG. The phenotype is usually reactive arthritis (ReA) or septic arthritis. We report a case of newly-onset psoriatic arthritis (PsA) following BCG immunotherapy. [Case] A 75-year-old man with bladder carcinoma started to suffer from fever and swelling of his hands and feet after fifth administration of intravesical BCG. Two weeks later, he was referred to our hospital. On admission, bilateral conjunctival hyperemia, dactylitis, and knee arthritis were noted. Although ReA was suspected at first, erythematous plaques with silver scale were documented on his scalp, extensor knees and gluteal cleft, which led to the diagnosis of psoriasis vulgaris by dermatologist. Our final diagnosis is PsA. [Discussions] The exact mechanism of BCG against cancer remains to be elucidated. Although the elaboration of Th1 response is believed to be the integral part, Th17 activation by BCG is also reported, which might be important mechanism in PsA development. [Conclusions] PsA should be a differential diagnosis of arthritis following BCG immunotherapy.

P1-153

Efficacy of Ixekizumab to refractory psoriatic arthritis accompanied by spondyloarthritis: Two case reports

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Conflict of interest: None

Psoriartic arthritis (PsA) manifests not only skin lesion but also peripheral arthritis and spondylitis, thus the disease is considered to be part of spondyloarthritis. Ixekizumab (IXE) is a humanized monoclonal antibody which selectively binds to the IL-17A relating to pathogenesis of PsA. We administrated IXE to two cases of refractory PsA to conventional therapy. **[Case No.1]** A man aged 46 was diagnosed with psoriasis in 27 years old. He presented sacroiliitis in 39 years old and had been treated with infliximab and cyclosporine, but these treatments showed failure. Furthermore, MRI showed an inflammation of atlantoaxial joint. Psoriasis area and severity index (PASI) score was 39.4 on admission and improved to 2.1 at 4 weeks after administration of IXE. In addition, the inflammation of atlantoaxial joint also improved. **[Case No.2]** A man aged 82 was diagnosed with psoriasis in 62 years old and had taken topical treatment for many years. Before 2 months ago of admission, he had been suffered from buttock pain. MRI showed sacroiliitis and ultrasound imaging demonstrated enthesitis of Achilles tendon. At 4 weeks after administration of IXE, PASI score declined from 6.7 to 2.1 and sacroiliitis also improved. **[Clinical significance]** IXE probably improves spondylitis of PsA.

P1-154

Analysis of 23 cases of Psoriatic Arthritis

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Conflict of interest: None

[Object] The progress of the treatment of Psoriatic Arthritis (PsA) is remarkable. [Methods] We retrospectively studied 23 patients in our division of internal medicine of Rheumatology, Nagoya Medical Center between January 2015 and October 2017. [Results] 23 patients were included (14 male, 9 female). The mean age at diagnosis of PsA was 52.4±13.7years (33~80). Onset of PsA developed at an average of 6.08±9.9 years (-1~37years) after the diagonosis of Psoriasis.10 Patients was treated with biological DMARDs (bDMARDS). 5 patients have continued bDMARDs at October 2017. [Conclusions] We often treated PsA with bDMARDs, and the persistency rate was 50%. We consider that we should positively treat fefractory case of PsA with bDMARDS.

P1-155

Clinical features and treatment of 88 patients with pustulotic arthro-osteitis

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Conflict of interest: None

[Object] To examine clinical features and treatment of pustulotic arthro-osteitis (PAO). [Methods] A multicenter, retrospective cross-sectional study was conducted on 88 PAO patients who were able to visit directly at 4 hospitals from January to June 2017. Evaluation items were clinical features, image findings, blood biochemical tests, and treatment methods. [Results & Conclusions] Average age at examination was 55.4 y.o., palmoplantar pustulosis / PAO onset age was 44.4 / 49.3 y.o. Tender of sternoclavicular joints have 33.0% of cases, shoulder joints 22.7% in order. The most frequent enthesitis was 21.4% in the Achilles tendon. The average of ASDAS-CRP was 1.4, but insufficient disease activity control (severe/very severe disease activity) remained in 25% of cases. The X-rey showed bone change in 81.8% of the sternum / sternoclavicular joints. MRI showed changes 76.9% in the sternum / sternoclavicular joints. Bone scintigraphy showed an accumulation image in the anterior chest 96.4%, the spine 23.6%, and the sacrum 30.9%. Serum CRP 0.35 ± 0.52 mg / dl, RF positive rate 9.4%, ACPA positive rate 5.1%. Therapeutic drug selection was selected for first-line drugs (NSAIDs, biotin, antibiotics), second-line drugs (Iguratimod sulfasalazine MTX).

P1-156

Femoral lesion associated with SAPHO syndrome successfully treated with TNF-α inhibitor

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Conflict of interest: None

A 61-year-old woman had endured shoulder and knee pain for eight years and low back pain for two years. She was referred to the outpatient rheumatology clinic at our hospital with palmoplantar rash and sternocla-

vicular joint swelling indicating resistance to NSAIDs. We diagnosed SAPHO syndrome based on palmoplantar pustulosis, polyarthritis, and sternoclavicular hyperostosis. Methotrexate was started, but left knee pain and swelling were aggravated. An X-ray revealed a 2.5-cm linear, radiolucent area in the left distal femur. We diagnosed this lesion as bone involvement of SAPHO syndrome based on MRI findings and negative microbiological results. We administered infliximab (IFX) to treat the lesion and found that her knee pain remarkably improved after a second infusion. Furthermore, the radiolucent area diminished after one year. The lesion did not recur for over four years after IFX therapy. SAPHO syndrome is a relatively rare disorder associated with skin lesions and bone involvement, often at the anterior chest wall, sacroiliac joint, and spine, but rarely in the long bones. This case report describes a femoral lesion associated SAPHO syndrome successfully treated with a TNF-α inhibitor.

P1-157

Study of involvememt of axial joint lesion in the SAPHO syndrome

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Conflict of interest: None

The osteoarticular lesion of the SAPHO syndrome is characterized by osteitis and hyperostosis. We experienced the case with multiple spinal lesions similar to axial spondarthritis (SpA), however chronic recurrent multiple osteomyelitis (CRMO) and the case with a sternal swelling and spinal multiple ostitis. Case 1: 45 y.o. female with both ankle joint arthritis and back pain without skin lesion, treated as axial SpA. MRI showed multiple bone marrow edema of the thracolumber vertebrae. The bone scintigraphy showed accumulation to the same vertebrae, left foot joint. The CT showed hyperostosis of the same vertebrae, osteosclerosis of sacrum and iliac. The distribution of hyperostosis and ostitis was atypical for SpA, therfore she was diagnosed SAPHO syndrome. Case 2: 49 y.o. male with sternum swelling associated with sternoclavicular, sacroilial and toes joint pain, without skin lesion visited. MRI showed the bone marrow edema of manubrium and body, and thoracic vertebra. He was diagnosed SAPHO syndrome. The SAPHO syndrome is related disease of SpA as involvememt of axial joint lesion presenting CRMO and hyperostosis. In the case to lack in skin lesion and/or a precordial lesion, the interview of back pain and various imaging study are important for making diagnosis of SAPHO syndrome.

P1-158

Analysis of clinical findings, laboratory data, imaging and treatment of SAPHO syndrome

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Conflict of interest: None

[Object] In this study, we aim to collect data on clinical symptoms, blood examinations, image findings of patients with SAPHO syndrome in our hospital and analyze their characteristics. [Methods] There were 25 patients with SAPHO syndrome who met the Chamot's classificasion criteria. Data on clinical symptoms, blood tests and image findings were collected. [Results] Among 25 patients, 22 were female. As skin symptoms, palmoplantar pustulosis (PPP) was found in 14 cases (56%), acne in 3 cases (12%), and nine cases have no skin symptoms (36%). As musculoskeletal symptoms, swelling and/or pain of the sternoclavicular joint was found in 21 cases (84%), low back pain in 22 cases (88%), peripheral arthritis in 8 cases (32%). AS image findings, sternocostoclavicular hayperostosis (SCCH) was found in 14 cases (56%), sacroiliitis in 7 cases (28%), osteitis in 13 cases (52%). Spinal ankylosis and syndesmophyte was observed in 17 cases (68%). In the group with PPP, the SCCH was greater (83% vs 55%), and sacroiliitis was greater (83% vs 22%) than in the group without PPP. There was no significant correlation between skin findings, imaging, and CRP or disease activity. [Conclusions] 36% of cases were no skin symptoms. In the group with PPP, SCCH and sacroiliitis was greater than without PPP.

P1-159

A retrospective study of 45 patients with spondyloarthritis

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Conflict of interest: None

[Objective] To evaluate the clinical characteristics of spondyloarthritis (SpA). [Method] We retrospectively analyzed the clinical characteristics of 45 patients with SpA in Oita Red Cross Hospital. [Results] We identified 45 patients with SpA (25 men, 20 women), including 16 AS, 7 PsA, 4 IBD-SpA, 5 ReA, 2 SAPHO syndrome and 11 uSpA. All patients fulfilled the ASAS classification criteria. The mean age at diagnosis (year-old) was 49.8±15.7 (AS:63.0, PsA:49.4, IBD-SpA:43.8, ReA:29.8, SAPHO:53.0, uSpA:41.5). The median time (months) from the onset to diagnosis was as follows; AS:36.8, PsA:34.3, IBD-SpA:30.8, ReA:1.3, SAPHO:15.0 and uSpA:34.3. Thirteen cases were tested for HLA-B27 and 2 were positive. Twenty-three cases (51.1%) were diagnosed with other diseases when the first symptoms appear, 11 of them were rheumatoid arthritis and 3 were fibromyalgia. In 17 of 23 cases, change of diagnosed were triggered by the substitution of primary doctor. NSAIDs was used in 34 (75.6%), GCs in 9 (20.0%), SASP in 18 (40.0%), MTX in 16 (35.6%) and TNF α inhibiter in 11 (24.4%). [Conclusion] It took prolonged period from onset to diagnosis in many patients. And half of them were made other diagnoses at onset. Hence, whenever we feel uncomfortable in diagnosis, need to review it.

P1-160

Clinical characteristics of spondyloarthritis in patients with psoriasis or inflammatory bowel disease

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Conflict of interest: None

[Object] Spodyloarthritis (SpA) is well known as musculoskeletal manifestations in patients with psoriasis (PsO) and inflammatory bowel disease (IBD). However, the difference of clinical features between SpA with PsO (PsA) and SpA with IBD (IBD-SpA) are poorly described. The purpose of this study is to compare the clinical features of PsA with IBD-SpA. [Methods] Overall, 192 patients with PsO and 37 patients with IBD were referred to our department to assess SpA from department of dermatology and gastroenterology. Diagnosis of PsA and IBD-SpA were performed using the CASPAR criteria and ASAS criteria, assisting with ultrasound. The patients with PsA and IBD-SpA were evaluated for DAS28-CRP, MMP-3, CRP, anti-cyclic citrullinated peptide antibody (ACPA), rheumatoid factor, biologics use, and proportion of peripheral and axial disease. [Results] Among referred patients 45 patients were diagnosed as PsA and 12 as IBD-SpA. The mean age was 58.3±14.8 years in PsA, 46.2±11.9 years in IBD-SpA (p=0.014). Axial SpA was observed in 4 (8.9%) in PsA, 4 (33.3%) in IBD-SpA (p=0.052). Biologics was using in 17 (37.8%) patients in PsA,9 (75%) patients in IBD-SpA. [Conclusions] The patient with IBD-SpA was younger than patient with PsA. The axial disease was more common in IBD-SpA.

P1-161

A study of the existence mode of enthesis lesion in spondyloarthritis by using ultrasoundsography

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Conflict of interest: None

[Object] The existence mode of spondyloarthritis (SpA) enthesis lesion was examined by using ultrasoundsonography because of the importance of enthesitis in SpA. [Method] Articular ultrasound examinations were made in 103 SpA patients (11 males, 92 females) with an average age of 61 ± 12. The tendon/ligament fibrillary pattern disappearance, bone erosion, bursitis, calcification and the inflammatory blood flow signal was examined regarding the bilateral 12 enthesis. [Results] The SpA patients had 0 site of enthesis lesions in 31%, 1 site in 14%,2 sites in 20%, 3 sites in 6%, 4 sites in 13%, 5 sites in 10%, 6 sites or more in 6%. Positivity of each enthesis lesion was 17% of elbow, 7% of tibia, 36% of proximal of patellar ligament, 8% of distal of patellar ligament, 52 of Achilles tendon, 5% of plantar aponeurosis. The patellar ligament proximal part showed the fibrillary pattern disappearance of 1 %, the calcification of 28% and 10% in the blood flow signal of 10%. The enthesis of the Achilles tendon showed the fibrillary pattern disappearance of 2 %, the calcification of 39%, bursitis of 4%, blood flow signal of 5%. [Conclusions] It was suggested that it is necessary to focus on the patellar ligament proximal part and the enthesis of the Achilles tendon for SpA.

P1-162

Long-term results of the silastic metacarpophalangeal joint arthroplasty in rheumatoid hand

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Conflict of interest: None

[Object] We evaluated short-term results of metacarpo-phalangeal joint (MCP) arthroplasty using flexible hinge silicone implant. [Methods] Sixteen RA patients (20 hands) were assessed for the range of motion, radiographic findings and satisfaction questionnaire. [Results] Range of motion of MCP joint increased from -32 degree in extension, 71 degree in flexion preoperatively to -7 degree in extension, 48 degree in flexion postoperatively. Radiographically, ulnar deviation was corrected from 18 degree preoperatively to 7 degree postoperatively. Subsidence of implant was seen in12 fingers and periprosthetic bone reaction was seen in 26 fingers. Destruction of silastic implant was shown in 6 fingers. One implant was required implant exchange due to worsened pain and increased stiffness. The subjective evaluations revealed overall satisfaction in range of motion, alignment, pain and cosmetic appearance. [Conclusions] At long-term follow up, improvement in range of motion and alignment and relief of pain result in improved hand function and patient's satisfaction.

P1-163

Anatomical study of the lateral femoral cutaneous nerve with special reference to direct anterior approach for hip

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Conflict of interest: None

[Object] To document the anatomical variation of the lateral femoral cutaneous nerve (LCFN) at the proximal aspect of the thigh and suggest how it can be protected during total hip arthroplasty via a direct anterior approach. [Methods] We obtained 49 thighs from formalin-preserved cadavers of 32 Japanese individuals. All nerve branches of the LFCN were carefully traced distally in the subcutaneous tissue of the proximal aspect of the thigh. The branching pattern and distribution at the proximal aspect of the thigh were described. [Results] The branching pattern of LFCN was highly varied. There were 37% of the dominant anterior type, characterized by a thicker anterior branch of LFCN, which coursed along the medial border of the tensor fascia lata (TFL) muscle with thinner branches. There were 63% of the posterior-fan type, characterized by posterior branches thicker than or equal to the anterior branch of the LFCN. The anterior branches of the LFCN were not injured in our skin incision, but in 39% of the posterior-fan type, the thick posterior branches were damaged. [Conclusions] LCFN injury is inevitable because it is difficult to protect the posterior and thin branches completely.

P1-164

Long-term clinical result of re-revision total hip arthroplasty with impaction allo-graft for infected THA

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Conflict of interest: None

Objective; We studied the clinical long-term result of re-revision THA with impaction allo-graft for infected revision THA. **Methods;** 70 years old woman with infected THA was replaced using constrained re-revision THA with impaction allo-bone graft. After a follow-up period of least 8 years, she was assessed about clinical condition before and after surgery, radiographic changes. **Results;** This patient was satisfied for results of constrained re-revision THA. Radiological loosening was none. **Conclusion;** A constrained re-revision THA with impaction allo-bone graft for infected THA provide good pain relief in the arthritic hip leading to high patient satisfaction and long-term survivorship.

P1-165

A case of spin out requiring multiple surgeries after the mobile type total knee arthroplasty

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Conflict of interest: None

(Introduction) Mobile type total knee arthroplasty (TKA) is a concept that reduces implant loosening and polyethylene wear by permitting rotational motion of the insert. However, if surgical techniques and implants select are not correct, specific complications of mobile TKA will occur. We report a case study that multiple surgeries were performed because of repeated spinout which is a specific complication of mobile type TKA. (Case) A 66-year-old woman. Right TKA was performed for osteoarthritis of the knee. Spin out occurred soon and the insert was exchanged. Ten years later, the patient visited our hospital complaining of swelling, pain and instability of the right knee. X rays showed insert spinout and post breakage. The insert was exchanged from 12.5 mm in thickness to 17 mm in thickness. One month after surgery, knee dislocation occurred with minimal external force. It was considered difficult to deal with mobile type TKA, and revision surgery was performed by hinge type TKA. (Discussion) In this case, it was thought that the insert spinout due to opening of the flexing gap and lateral collateral ligament failure. Even in cases where ligament failure due to inflammatory diseases such as rheumatoid arthritis is considered, it is necessary to carefully select the type of TKA.

P1-166

Six Eosinophilic Granulomatosis with Polyangiitis (EGPA) inpatients which have improved their activity of daily living (ADL) and quality of life (QOL) by rehabilitation

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Conflict of interest: None

[Object] There are diverse symptoms in EGPA. The neurological one commonly appears and often results in dysfunction irreversibly as a permanent damage. We report six EGPA inpatients rehabilitation in our department. [Methods] We make a comparative review of six EGPA inpatients rehabilitation (one is from remission induction) in our department from December 2015. [Results] The frequent complaint was numbness in the extremities. It was residual but predominantly controllable by some

drug such as Pregabalin. The drop foot and hand were frequent and led to depression of ADL or the functional impairment. Although they were permanent, all patients could come back to home or work with orthosis and self-help devices. [Conclusions] Within a frame of the International Classification of Functioning, disability and health (ICF), all patients achieved the improvement in life function regardless of difference about their background and hope. [Clinical significance] Through the practice of EGPA, unfortunately the experience of disorder is not uncommon in the mental and physical function as body structure. We think that comprehensive approach including background factor not only health condition with multi job categories can improve the quality of the activities and participation in a frame of the ICF.

P1-167

The change of upper limb function in rheumatoid patients over time

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Conflict of interest: None

[Object] The objective of this study was to examine the change of upper limb function in rheumatoid patients over time using the Simple Test for Evaluating Hand Function (STEF), and to study the factors influencing on the upper limb function. [Methods] 54 hands of 27 cases were tested. The average age was 60.6 years, and the average morbidity period was 77.6 months. All cases were classified to Steinbrocker's CLASS: 14 cases, CASES: 10 cases, CLASS3: 2 cases, CLASS4: 0 cases. From Larsen grade (LG), all hands were classified to LG0: 20 hands, LG1: 12 hamds, LG2: 8 hands, LG3: 3 hands, LG4: 10 hands, LG5: 1 hands. In each cases STEF was tested with bilateral hands and was retried after over two years. The STEFscore was compared between 1st and 2nd time. Das28, mHAQ, Hand grip power were evaluated, and the factors influenced STEFscore were considered. [Results] The average period form 1st time to 2nd time was 44.1 months There was no significante difference for STEFscore with bilateral hands between 1st and 2nd time DAS28 of 2nd time was significantly lower than 1st time, but no significant difference was seen for about mHAQ and grip power between 1st time and 2nd time. [Conclusions] The upper limb function of rheumatoid arthritis patients did not decline over time.

P1-168

Usefulness of Handicraft Activities in Patients with Rheumatoid Arthritis: Association with Disease Activity

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Conflict of interest: None

[Object] In our hospital, outpatients with rheumatoid arthritis (RA) are required to engage in handicraft activities, such as bead crafting, Japanese paper crafting, and pottery. We examined the effects of occupational therapy on the long-term course of RA patients engaged in handicraft activities. [Methods] Grip strength and disease activity (DAS28ESR and DAS28CRP) were measured at baseline and after 1 year of intervention in 24 female outpatients with RA (mean age, 71 ± 7 years; mean disease duration, 17 ± 7 years) treated at our hospital between 2016 and 2017. Occupational therapists intervened only when necessary, so as not to worsen a patient's arthritis symptoms. [Results] Grip strength measurements at baseline versus after 1 year were 161 ± 62 vs 166 ± 62 for the right hand and 156 ± 55 vs 155 ± 46 for the left hand, with improvement in right-hand performance. The left hand showed no prominent exacerbation. Additionally, DAS28ESR and DAS28CRP were 2.74 ± 0.6 vs 2.42 ± 0.5 and 1.96 ± 0.4 vs 1.86 ± 0.3, respectively. Both parameters showed improvement. [Conclusions] Handicraft activities were useful as occupational therapy and did not worsen symptoms in RA patients. RA patients with low disease activity and those in remission could engage in handicraft activities.

P1-169

Three cases with rheumatoid arthritis enabled to long-term manage foot self-care by self-help devices

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Conflict of interest: None

[Background] To keep foot hygiene is difficult for patients with rheumatoid arthritis (RA) because limited range of motion of upper and lower extremities. Here we report 3 patients with RA were able to management foot in the long term by self-help devices. [Case1] A 74-year-old woman. Her hands could not reach the feet or press a container for moisturizer. We offered self-help devices to apply moisturizer and press a container for the feet. [Case2] A 59-year-old woman. In 2013, a total hip arthroplasty was performed on the right. Her both hands could not reach the forefeet on the right. We offered a brush body towel with a loop, a long handle interdigital brush and a long puff for moisturizing the foot. [Case3] A 68-year-old woman. In 2015, multiple spinal compression fractures were treated using with a rigid corset. Spinal flexion was difficult for her due to the corset. We offered a long puff for moisturizing the feet and a long handle interdigital brush. [Results] They were able to perform appropriate foot self-care including skin moisturization and keep foot hygiene using self-help devices recently. [Discussion] They have been using self-help devices for a long term. Thus, self-help devices for foot self-care were made by an occupational therapist are useful for patients with RA.

P1-170

The predictive factor of Japanese knee osteoarthritis measure (JKOM) at 1 year after TKA of patients with rheumatoid arthritis

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Conflict of interest: None

[Object] It is important to clarify JKOM score prediction factors of 1 year after TKA in the pre- or earlier post- operation. The aim of this study is to clarify JKOM score prediction factors of 1 year after TKA of patients with RA. [Methods] Fifteen joints of 11 cases for which TKA were performed from Apr. 2014 to Sep. 2015 and were examined at pre-, 4 weeks after- and 1 year after-operation were included in this study. To clarify the predictive factors of JKOM score at 1 year after TKA, preoperative JKOM, JOA score of the knee, age and BMI, and the hip abductor and the knee extensor muscle strength, ROM of the knee and time of standing on one leg of the affected lower extremities, and timed up and go test at 4 weeks after TKA were used as independent variables and simple and multiple regression analysis were performed. [Results] The affected knee extensor strength at 4 weeks after TKA was chosen as the predictive factor of JKOM at 1 year after TKA (std β: -0.759, p: 0.011, R^2: 0.524). [Conclusions] The knee extensor muscle strength after TKA is more important for JKOM score at 1 year after TKA than preoperative knee joint function. It is expected that postoperative knee extensor muscular strength reinforcement contributes to improvement of the QOL one year later.

P1-171

A case report of total knee arthroplasty with schizophrenia and malignant rheumatoid arthritis

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Conflict of interest: None

[Background] Kohnodai Hospital merged with the National Center of Neurology and Psychiatry in 1987. I report a case of total knee arthroplasty (TKA) with malignant rheumatoid arthritis (MRA) and with schizophrenia. [Case] 44 year old, female. Past History: schizophrenia was developed in 1940. History of present illness: MRA was developed

in 2003 and gonalgie appeared, finally she could'nt walk. TKA was performed in September on the right knee in September 2013, and TKA on left knee was performed in December 2015. Range of motion (ROM) of right knee was flex 130 degree and extension -75 degree. ROM of left knee was flex 135 degree and extension -30 degree. Japan Orthopedic Association (JOA) Score were both 30 points. After operations, flexion contractures proceeded, so joint passive surgery was performed in 2015. After operation, rehabilitation was performed, and she could stand. She refused outpatient rehabilitation. In September 2017, ROM of right knee was extension -95 degree, flexion 115 degree, and ROM of left knee was extension -75 degree, flexion 115 degree. JOA score were both 30 points, and she could'nt stand. [Conclusions] I treat a patient of total knee arthroplasty with schizophrenia and malignant rheumatoid arthritis. Rehabilitation influenced ADL.

P1-172

Evaluation system of locomotive syndrome for patients with rheumatoid arthritis

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Conflict of interest: None

[Object] Sit-to-stand movement from a chair is a mechanically demanding component of activities of daily living. We used a novel method using a force plate placed beneath the feet to quantify sit-to-stand movement (sit-to-stand score) and investigated age-related changes in the sit-to-stand score as a method to evaluate reduction in performance. [Methods] The study enrolled 18 rheumatoid arthritis subjects (male/female ratio, 6/12; mean age, 61.1 years; range, 37-77 years) who were able to walk independently. The subjects were instructed to stand up as quickly as possible on a force plate, and the sit-to-stand (STS) score was calculated as the combination of the speed (S) and balance (B) indices. We compared the STS score with the timed up and go (TUG) test, a well-known clinical test used to evaluate an individual's mobility. [Results] There was a significant negative correlation between STS score and age (r = -0.490). STS score and S was significantly correlated with TUG time (STS score; r=-0.724, S; r=-0.704). [Conclusions] STS score decreased with age among rheumatoid arthritis subjects aged 37-77 years. STS score represents individual's mobility and can be used to identify the deterioration of motor performance.

P1-173

Two cases of antiphospholipid antibody syndrome nephropathy with elderly-onset primary anti-phospholipid syndrome

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Conflict of interest: None

[Objective] To investigate histological and clinical features of glomerular lesions in primary APS (PAPS). [Methods] Renal histology and clinical features were examined for two cases in which proteinuria was preceded and later diagnosed as PAPS. [Results] Both cases were females and older. They admitted hypertension in the past. One case had lacuna cerebral infarction. The period from proteinuria to APS diagnosis was 15 years and 3 years, both preceded by proteinuria, but the former suddenly increased proteinuria from 2 years ago. One had nephrotic syndrome. Each anti-cardiolipin antibody was positive. In the renal histology, double contour and subendothelial edema were observed in both, and thrombotic microangiopathy (TMA) lesions were present. Although immunostaining was negative in both cases, subendothelial depositions were observed by electron microscopic observation. [Conclusion] Although glomerular lesions of PAPS are rare, TMA lesions occurring in glomerular capillaries are considered. Two patients with elderly-onset APS nephropathy were characterized by a history of high blood pressure and precedence of proteinuria. It was thought that asymptomatic APS had been present for a long time, and it became older to develop proteinuria and APS nephropathy as nephrotic syndrome.

P1-174

A case of bilateral Achilles' tendon rupture in patient with SLE

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Conflict of interest: None

[Case report] A 65-year-old female diagnosed as SLE was treated with prednisolone for 20 years. She felt swelling and uncomfortable feeling in the left lower leg without any cause. She felt slight pain but could walk a little slower than usual. The diagnosis remains unknown. One month later she felt the same symptoms in the right lower leg Then the definitive diagnosis with bilateral Achilles' tendon rupture was made by physical signs and MRI findings. She underwent surgical repair. After complete wound healing, she practiced walking exercise for 8 weeks. Finally, she recovered independent gait and full ROM of her ankles and MRI showed complete tendon repair. [Discussion] Some reports described the idiopathic tendon rupture of patients with SLE, but rupture of the bilateral Achilles' tendon is very rare. It tends to get old if it was missed at the first examination. Because of fragility of the tendon tissue, tendon rupture in patients with SLE may occur by minor trauma. Because of vague complaint, correct diagnosis and proper treatment was delayed for a month. [Conclusions] In patients with SLE, Achilles' tendon rupture may occur without apparent cause, and it should be one of differential diagnosis for symptoms like swelling of lower leg or uncomfortable feeling.

P1-175

A primary antiphospholipid syndrome presenting with splenomegaly and clinical signs of SLE, coexisting with intracardiac myxoma-like mass

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Conflict of interest: None

A 72-year-old woman, who was diagnosed with primary antiphospholipid syndrome at 58-years old, referred for recurrent high grade fever. She had some symptoms of SLE (photosensitivity, pancytopenia, hypocomplementemia, pericarditis, and positive for anti dsDNA antibody). She also had splenomegaly with increased uptake of FDP-PET and high titer of sIL-2 receptor. A splenectomy was performed to rule out malignant lymphoma of spleen. Pathologically, the spleen showed many reactive lymph follicles with large germinal centers and cytotoxic T cell infiltrate in red pulps but no tumor formation. After splenectomy, her symptoms improved transiently, but she referred again for relapse of high grade fever, thrombocytopenia, and pericarditis. Serum sIL-2R and IL-6 level were elevated. Her echocardiography showed a left atrial mass suspicious of cardiac myxoma. Cardiac myxoma has been demonstrated to produce IL-6 and to be responsible for the chronic inflammation and immunologic abnormalities including autoimmune diseases. In this case, it is postulated that IL-6 produced by the myxoma might trigger an immune activation in spleen, leading to splenomegaly and SLE-like symptoms. Cardiac myxoma should be ruled out in patients with constitutional symptoms accompanied by immunologic abnormalities.

P1-176

Identical twins of antiphospholipid antibody syndrome complicated with systemic lupus erythematosus: one maintains good control of thrombosis while on warfarin, the other developed chronic thromboembolic pulmonary hypertension while on dabigatran

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Conflict of interest: None

Case 1 is a fatty 44-year-old female. She developed deep-vein thrombosis (DVT) 16 years ago, and started taking warfarin. She presented

thrombopenia and oral ulcers 6 years ago. Antiphospholipid antibody (aPL) and antinuclear antibody (ANA) were positive. She was diagnosed as aPL syndrome (APS) with systemic lupus erythematosus (SLE), and prednisolone (PSL) was added. She has never experienced DVT since the start of warfarin. Case 2 is an identical twin younger sister of Case 1, and also fatty. They have lived together since birth. She showed thrombopenia and serositis 5 years ago. ANA and 3 types of aPLs were positive. Days later, she developed DVT and pulmonary arterial thromboembolism, and was diagnosed as APS with SLE. She was successfully treated with urokinase, warfarin and PSL, and dabigatran was substituted for warfarin. She developed chronic thromboembolic pulmonary hypertension 3 years later. Recently, direct oral anticoagulants (DOACs) are widely used for thromboembolism, because they do not require monitoring of coagulation tests. However, there were several reports of APS patients developing recurrent thrombosis while being treated with DOACs. DOACs inhibit only a part of coagulation cascade, and may be inappropriate for high-risk APS patients.

P1-177

Drug lupus caused by mesalazine in a patient with ulcerative colitis: A case report

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Conflict of interest: None

Introduction: Certain drugs may trigger an autoimmune response. In some patients, clinical syndrome with features like systemic lupus erythematosus (SLE) may develop which is termed drug-induced lupus. Case report: The patient is a 61-year-old female who was diagnosed Ulcerative colitis (UC) 30 years previously. She was managed well with mesalazine, 5-aminosalicylic acid (5-ASA). She had joint pain in her both hands and knees for 3 months. She visited to our department from the clinic because of symptoms and elevation of liver function test (LFT). The laboratory date showed that Antinuclear antibody (ANA) was positive (1280 HO), WBC count was decreased (3500/μL), LFT was elevated (GOT 139IU/L, GPT 93 IU/L). She was diagnosed drug lupus caused by methylamine. Treatment was to quit mesalazine and to start prednisolone 40mg/end, hydroxychloroquine 200mg/d. During course of admission, the joint pain was disappear and LFT was decreased. She was quit prednisolone in 10 months later without recurrence. Conclusion: Drug-induced lupus in UC has been recognized. The coexistence of the UC and SLE is rare. In the other hand, treatment of UC, for example, 5-ASA and anti-TNF, can cause drug lupus. Treatment includes discontinuation of the offending drug and administration of corticosteroids.

P1-178

A case of systemic lupus erythematosus (SLE) with thrombotic microangiopathy (TMA)

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Conflict of interest: None

Case: 34-year-old pregnant woman was referred to our department, because proteinuria and occult blood in urine accompanying pregnancy were seen during treatment for SLE and lupus nephritis (LN) at another hospital. The dose of prednisolone (PSL) was increased. But nephrotic syndrome, thrombocytopenia, and hypocomplementemia were developed, and she was admitted to our hospital. After admission, PSL was increased to 1 mg/kg/day, and tacrolimus was also administered. No improvement in her symptoms was seen, so caesarean section was performed at gestational week 27. After surgery, steroid pulse therapy was used. Schistocytes were seen, and fresh frozen plasma supplementation was started for suspected TMA. Her condition was improved by enhancing the immunosuppression. Discussion: From 2012 to 2017, we treated 4 TMA in our department. The cause of it was exacerbation of SLE was the cause in 2 cases. The cause of one case was drug-induced and the other thrombocytopenic purpura (TTP). The drug-induced TMA patient was improved with the discontinuation of cyclosporin. Plasma exchange (PE) was performed in the other two patients one was SLE exacerbation and in the the other TTP patient. The reason that PE could be avoided in this case was thought to be that treatment to SLE performed early.

P1-179

Case of transverse myelitis and macrophage activation syndrome concomitant with central nervous system

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Conflict of interest: None

[Case] 32-year-old female [Main complaint] Fever, disturbance of consciousness [Current history] She exhibited arthralgia and purpura in April, 20XX. At general hospital, she was diagnosed with SLE in hair loss, joint pain, urine protein, pancytopenia, ANA, anti-dsDNA antibody and low complement, and kidney biopsy showed lupus nephritis (IV-S). High-dose steroid was administered, but confusion appeared, and head MRI revealed inflammatory lesions in vermis. we started IVCY, but fever, LDH elevation, ferritin elevation appeared. Since then, multiple organ dysfunction appeared, and she was refered to our hospital. [Post-hospitalization] Bone marrow examination revealed HPS. Steroid pulse therapy, CsA, VP-16 was started. Although LDH and ferritin decreased, septic shock happened. As administered antibiotics and G-CSF, disordered consciousness and lower limb weakness appeared, and transverse myelitis, Cerebral infarction was observed in MRI. I considered as central nerve lupus, reexecuting IVCY and steroid pulse therapy revealed the consciousness level and muscular strength improved. Rehabilitation transfer became. [Discussion] I experienced SLE with MAS, ATM, NPSLE concurrently during treatment. This case is educational and reports on literature considerations.

P1-180

A Case of CNS Lupus with Hyponatremia

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Conflict of interest: None

51-years-old women presented to our hospital with shortenss of breath and dyspnea. Antibiotics was not effective for her bronchitis. She had also polyarthritis, hair removal and soft vitiligo in the eyegrounds. Laboratory shows that antinuclear antibody and anti-ds DNA antibody and anti-SS-A antibody were positive. Therefore she was diagnosed with SLE and Sjogren Syndrome. After Predonisolone and MMF were administered, her respiratory symptoms were improved. When she took PSL 9mg/day, she was taken to our hospital for distubance of consciousness. After the treatment of the hyponatremia, Her consciousness did not improved, so we decided to treat for the CNS lupus. PSL 60mg/day and IVIG were effective to her symptoms.

P1-181

Self-injections of unfractionated heparin and hydroxychloroquine were effective against chronic stillbirth: A case report

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Conflict of interest: None

A 29-year-old female. The patient was being treated at the another hospital for childhood-onset systemic lupus erythematosus. Her first, second and third children were stillborn. When she was third pregnant, she was referred as a case of APS pregnancy based on thrombocytopenia, and she was lupus anticoagulant-positive and anticardiolipin antibody-positive. When she was fourth pregnant, she used subcutaneous injections of unfractionated heparin and low doses of aspirin, but she delivered a stillborn child. Placental pathology indicated an infarct and stillbirth due to APS. Eight weeks prior to her fifth pregnancy, she began a course of HCQ, and following confirmation of the gestational sac, she began a course of self-injected unfractionated heparin. She was admitted to the hospital during week 32 of the pregnancy and switched to continuous drip of unfractionated heparin. On day 4 of hospitalization, she delivered a healthy infant via emergency Caesarian section. We reported on a case in which HCQ administration led to improvement in neonatal survival in a pregnancy complicated by APS. This result suggests survival was improved by the anticoagulant action of HCQ. Pre-pregnancy administration of HCQ should be considered in cases of APS patients who desire children.

P1-182

Dramatic improvement of thrombocytopenia with positive anti-nuclear antibody after starting hydroxychloroquine: 2 Case reports

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Conflict of interest: None

[Introduction] Steroids are the first-line treatment for immune thrombocytopenia (ITP) but relapses during tapering steroids are not uncommon. [Case1] A 15-year-old man presented with hematuria. Thrombocytopenia with platelet count of 4000/μL was found and treated with prednisolone (PSL 120mg/d). Three months after discontinuation of PSL platelets dropped to 3000. Serological studies showed positive anti-nuclear antibody (ANA), anti-cardiolipin antibodies and low complement levels. We started PSL (60mg/day) and tacrolimus, and tapered PSL. When PSL was reduced to 8mg /day, the platelet count dropped to 21000. We added hydroxychloroquine (HCQ). The platelet counts at 1, 2, 3, and 4 months were 44000, 36000, 66000 and 132000 respectively and maintained above 100000 thereafter even with lowering PSL to 3mg/d. [Case2] A 28-year-old woman with a history of immune thrombocytopenia and positive ANA on PSL (4mg/day) started HCQ. The platelet counts before starting HCQ was 108000. The platelet counts at 1, 2, 3, and 4 months after starting HCQ were 172000, 207000, 261000, and 291000 respectively, and maintained above 200000 even with lowering PSL to 2mg/d. [Discussion] HCQ may be a good option for ITP with ANA regardless of whether patients meet criteria for classification of SLE or not.

P1-183

Thrombotic microangiopathy (TMA) after delivery; Unusual clinical course of Systemic lupus erythematosus (SLE)

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Conflict of interest: None

Case A 32 year old woman was admitted to the hospital because of anemia, thrombocytopenia and renal failure. She had been diagnosed as SLE 8 years before presentation. She got pregnant 1 year before admission and had been well before June 28, when she went into emergency hospitalization because of premature rupture, and she gave suction birth on June 30th. After that, she complained of lasting abdominal pain, and it became clear that there was placental remnant, so on the same day placental ablation surgery was performed. On the same day, Anemia and thrombocytopenia were observed, adding that there was crushed erythrocytes, elevated LDH, renal dysfunction. TMA was considered. It was found later that ADAMTS 13 activity, inhibitor were in normal range, and Shiga toxin in the feces was negative, a condition often seen in an atypical hemolytic uremic syndrome. We performed plasma exchange every day from July 4th, and started steroid pulse therapy, and mycophenolate mofetil was started. We then started to use Rituximab on July 21 against refractory TMA. After that, hemolytic anemia and thrombocytopenia were improved, and plasma exchange was discontinued. She was discharged on August 14. Conclusion This case teaches us a lesson that TMA can occur even after delivery.

P1-184

A case of central nervous lupus (npsle) with idiopathic intracranial hypertension

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Conflict of interest: None

One day, a 21-year-old woman was developed floaters. She has been diagnosed with papilledema. There was not the neurologic abnormal finding. MRI, MRA and CT showed no abnormality findings, while a CSF analysis revealed an extremely high opening pressure (300 mmH_2O) with normal CSF indices. She has presented with butterfly shaped erythema since 2 days ago, the laboratory findings showed lymphopenia and hypocomplementemia. Anti nuclear antibody, Anti DNA antibodies, anti Sm antibody and anti-cardiolipin antibodies were positive.A diagnosis of definitive SLE was promptly made according to SLICC classification in 2012. In addition, it was CSF IL-6 9.14pg/ml and judged it with NPSLE which corresponded to the headache of the ACR classification in 1997. We made start of therapy by steroid pulse therapy and 1mg/kg/day of prednisolone. She was normalized immediately with CSF IL-6 4.11pg/ml after 31 day. We use Mycophenolate mofetil together and push forward prednisolone gradual decrease. Currently there is no ophthalmology abnormalities and the serologic abnormality are improved, too, with normal CSF indices a half year later. Reported cases of NPSLE which presented only the papilledema due to the intracranial hypertension symptom without a focal sign to doubt cranial neuropathy is very rare, we report it.

P1-185

A concomitant case of systemic lupus erythematosus (SLE) and lymphomatoid granulomatosis (LYG)

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Conflict of interest: None

A 64-year-old was diagnosed as having SLE by positive antinuclear antibody, positive anti-double strand DNA antibody, positive antiphospholipid antibodies (aPLs), hypocomplementemia, lymphopenia, and a few-year history of Raynaud phenomenon through the pre-operation examination for her mitral valve regurgitation (MR) due to mitral valve prolapse. Simultaneously, she had multiple nodular lesions and small amount of pleural effusion in her bilateral lungs and the pathological diagnosis for her resected right lower lobe was lymphomatoid granulomatosis (LYG), grade I. **[**clinical significance**]** LYG is a type of lymphoproliferative disorders characterized by angiocentric and mixed infiltration of EBV-positive B cells and abundant reactive T cells, involving lungs and occurs most commonly in immunosuppressed patients but occasionally in patients with a variety of autoimmune diseases. In the present case, the onset of SLE with aPLs was not clear, however if it was a cause of her mitral valve degeneration, she was thought to be complicated by LYG during her course of SLE, probably related to the immune dysregulation by SLE itself because she had not received any immunosuppressive therapy. Therefore, we are reporting this case as we consider the concomitance of SLE and LYG.

P1-186

A case of refractory immune thrombocytopenic purpura (ITP) complicated by systemic lupus erythematosus (SLE) treated with rituximab (RTX) and hydroxychloroquine (HCQ)

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Conflict of interest: None

[Introduction] Although glucocorticoid (GC) is usually selected as the first-line therapy for ITP complicated by SLE. Recently, the efficacy of HCQ and RTX is reported for refractory ITP. [Case presentation] The patient was 68-year-old woman. She was diagnosed as Sjögren's syndrome before two years and under observation without any vital organ complication. She had anemia, slight fever and polyarthritis four month before this admission. She was admitted for examination of acute thrombocytopenia (6,000/μl). She was diagnosed as SLE, because polyarthritis, thrombocytopenia, hypocomplementemia and anti-nuclear antibody positive were observed. She was also diagnosed as ITP because drug induced thrombocytopenia and any other diseases were excluded, and bone marrow biopsies showed the increase in megakaryocytes. We administered GC mass therapy. However, her platelet count did not increase. Therefore, we started GC pulse therapy. Although her platelet count temporarily increased, she experienced a fever and re-exacerbation of thrombocytopenia. We diagnosed as GC-resistant refractory ITP, and introduced HCQ and RTX. The platelet count increased to normal range, and it became possible to taper GC promptly. [Conclusion] HCQ and RTX could be effective for refractory ITP complicated by SLE.

P1-187

A case of SLE-PAH (Systemic lupus erythematosus-pulmonary artery hypertension) exacerbated during immunosuppressive therapy and addition of pulmonary vasodilator was effecitve

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Conflict of interest: None

A 34-year-old woman, who has past medical history of idiopathic thrombocytosis and lupus erythematosus, takes 3mg of prednisolone (PSL) complains of fever and shortness of breath 3 month after her second delivery. Laboratory findings showed lymphocytopenia, thrombocytopenia, decrease of complement and haptoglobin and elevated anti-ds DNA antibody. Direct coombs and anti cardiolipin antibody was positive. ECG showed right heart strain, chest X-ray and CT scan showed dilatation of pulmonary artery, cardiac enlargement and ground-glass attenuation. UCG showed elevated tricuspid regurgitation pressure gradient (TRPG) 44.7mmHg and right heart catheter revealed elevated mean pulmonary artery pressure 26mmHg. Pulmonary ventilation-perfusion schintigraphy denied pulmonary embolism and we diagnosed pulmonary artery hypertentsion (PAH). We treated serositis, interstitial pneumonia and PAH with PSL (1mg/kg/day) and cyclophosphamide pulse and that was effective at first but she developed steroid psychosis and infection and we tapered PSL fast and TRPG elevated. We added pulmonary vasodilator and which provided improvement.

P1-188

Systemic lupus erythematosus with selective IgM deficiency

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Conflict of interest: None

Of selective immunoglobulin deficiencies, selective IgM deficiency (SIgMD) has an estimated frequency of 0.03%. SIgMD is associated with autoimmune diseases such as systemic lupus erythematosus (SLE). Here, we report a case of SLE with SIgMD. A 31-year-old woman was diagnosed with SLE at age 7 years due to malar rash, photosensitivity, persistent proteinuria, leukocytopenia, lymphocytopenia, hypocomplementemia, and positive anti-nuclear, anti-DNA, and anti-Smith antibodies. Renal biopsy showed lupus nephritis WHO Class IV. Serum IgM at SLE diagnosis was normal. High-dose methylprednisolone pulse therapy was started and IgM level decreased. We started plasmapheresis, azathioprine, mizoribine, and cyclophosphamide pulse therapy; SLE disease activity was controlled. IgM levels were undetectable at age 24 years, but IgG and IgA did not decrease. Peripheral blood lymphocyte count decreased to 300/μL; specifically, B-lymphocytes were 2.5%. No infections developed after the SIgMD. In this case, SIgMD was not seen at SLE diagnosis, but was noted after starting steroid and immunosuppressant therapy. The reason for SIgMD in this case is unclear. We suggest two possibilities: a drug side effect and the pathology of SLE, which itself involves decreased levels of IgM.

P1-189

Two cases of asymptomatic deep vein thrombosis identified by elevated D-dimer levels in systemic lupus erythematosus with antiphospholipid antibodies

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Conflict of interest: None

[Case 1] A 43-year-old woman was diagnosed with systemic lupus erythematosus (SLE) 15 years ago, and had been treated with corticosteroids. Not being diagnosed with antiphospholipid syndrome (APS), she was positive for lupus anticoagulant and anti-cardiolipin antibody (aCL), and she had taken aspirin. On preoperative examination for adenomyosis, D-dimer was elevated without any symptoms, and then lower limb ultrasonography showed thrombi, measured 15 cm in her bilateral fibular veins. [Case 2] A 66-year-old woman was diagnosed with SLE 15 years ago, and she had been treated with corticosteroids. Although she was positive for aCL, she wasn't diagnosed with APS. Because of the renal failure in lupus nephritis (Class-4), she was scheduled to undergo peritoneal dialysis. D-dimer was increased, and ultrasonography revealed multiple thrombi in her bilateral posterior tibial vein without symptoms. [Clinical significance] Although SLE patients with aPL have a higher risk of thrombosis, a monitoring method of asymptomatic thrombosis is not established. In our cases, elevated D-dimer levels revealed asymptomatic deep vein thrombosis, suggesting the importance of regular screening test for thrombosis in asymptomatic cases.

P1-190

Unusual presentation of Systemic Lupus Erythematosus: Case report

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Conflict of interest: None

Introduction Bullous systemic lupus erythematosus (BSLE) is a rare distinctive subepidermal blistering disorder that can occur in patients with SLE. Case Report A 17-year-old female was admitted with the appearance of blisters over the cheek and cardiac enlargement. Blood investigations revealed high ANA, anti-ds DNA antibody, and immunocomplex, and low levels of C3 and C4. The chest X-ray showed increased cardio-thoratic ratio and ECG showed sinus rhythm with negative T wave in V3-V6. The echocardiogram revealed slight dilation of the left ventricle with moderate impaired global systolic function, and mild circumferential pericardial effusion. Skin biopsy revealed the predominantly neutrophilic infiltrate with degeneration of basal cells and a deposition of IgA, IgM, and C3 at the dermoepidermal junction. The patient was diag-

nosed with BSLE. She was pulsed with metylprednisolone and started on oral micophenolate mofetil (MMF) along with hydroxychloroquine (HCQ). She responded well to the regimen with improvement in signs and symptoms. She was discharged with oral prednisolone, MMF and HCQ. Discussion Bullous lesions may be a risk for developing lupus nephritis resulted in worse prognosis. SLE should be entertained in the differential diagnosis of patients with bullous lesions.

P1-191

Ulcerative rectal involvement in systemic lupus erythematosus: three case reports

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Conflict of interest: None

[Object/Methods] We describe three cases of ulcerative rectal involvement related to systemic lupus erythematosus (SLE). [Results] Case 1: A 45-year-old woman, who had 27-year history of having prednisolone (PSL) therapy since her lupus nephritis (LN) onset, indicated the recurrence of rectal ulcer. The colostomy was previously performed because of rectal perforation ascribable to multiple rectal ulcers which occurred 18 years after LN onset. Intravenous cyclophosphamide (IVCY) together with steroid and mesalazine enema were required because increased PSL and addition of azathioprine were insufficient for the remission. Case 2: A 33-year-old man, who had treated with PSL for 8 years since his LN onset, developed rectal ulcer with arthralgia. He was treated with high dose PSL, tacrolimus (TAC), and mesalazine enema. Case 3: A 33-year-old woman, who initially indicated LN with skin involvements, had treated with PSL and TAC. Mycophenolate mofetil was administrated after ceasing TAC because neuropsychiatric SLE occurred 6 years later. She developed rectal ulcer, which was treated with IVCY, high dose PSL, and mesalazine enema, 7 years later. [Conclusions] The combination therapy was required in all patients despite refractory to PSL alone.

P1-192

A case of systemic lupus erythematosus with scleritis and urticaria presented diagnostic difficulties for hypocomplementemic urticarial vasculitis

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Conflict of interest: None

Hypocomplementemic urticarial vasculitis syndrome (HUVS) is an uncommon immune complex-mediated entity characterized by urticaria with persistent acquired hypocomplementemia. HUVS is associated with connective tissue diseases such as systemic lupus erythematosus (SLE) and Sjogren disease. HUVS is similar to SLE in various organ disorders so it's difficult to distinguish two diseases. A-55-year-old-man who got urticarial erythema visited a doctor at a nearby hospital. He took betamethasone 1mg/day for 5 days and used topical corticosteroid. In March, he visited our hospital. We found urticarial rush and scleritis in him. Laboratory tests showed that lymphocytes 936/μL, a high titer of antinuclear antibody (1:160, homogeneous, speckled), double-stranded DNA, anti-Ro/SS-A, and anti-Lo/SS-B are positive. C3 32.0 mg/dL, C4 4.1 mg/dL, CH50 12.3 mg/dL, immune complex (C1q binding) 22.8 μg/dL. Skin biopsy revealed the presence of immune deposits (C3, IgM) around capillary blood vessels. Urticarial rush and scleritis are more associated with HUVS than SLE. We report a case of SLE which is hard to distinguish from HUVS with a review of the literature.

P1-193

Efficacy of intravenous immunoglobulin therapy for hemophagocytic syndrome

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Conflict of interest: None

A case is a 48-years-old woman. She was diagnosed as SLE with anti-U1RNP antibody test positive, anti-nuclear antibody test positive, anti-DNA antibody test positive, malar rash, and leukocytopenia and Reynaud's phenomenon. On April, she had proteinuria of 1-2g/day without any trigger and started the treatment with 10mg of prednisolone, however her proteinuria did not improved. She was hospitalized on May to have kidney biopsy. Before the biopsy, she developed hemophagocytic syndrome (HPS) without any trigger. Stained bone marrow aspirate showed a macrophage with phagocytised cells inside the cytoplasm. On hospital day 17, she was treated with methylprednisolone pulse therapy and her symptoms improved. However after the medication of Co-trimoxazole, to prevent pneumocystis pneumonia, she developed HPS for the second time. We treated her with methylprednisolone pulse and also cyclosporine and plasma exchange. However, we had to quit it because the spike fever prolonged after the treatment. Then we chose intravenous immunoglobulin (IVIG) therapy for 5 days and her symptoms improved. Her proteinuria was also improved, so we did not execute kidney biopsy. This case indicated that administration of IVIG therapy shows great therapeutic effects for HPS, as previously reported.

P1-194

Systemic lupus erythematosus detected for the first time during pregnancy; a report of two cases

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Conflict of interest: None

(Introduction) It is important to control SLE activity immediately, because of exacerbation of SLE for pregnancy. The treatment for introducing-maintaining remission isn't established. (Case1) A 26-year-old woman was introduced for nephrotic syndrome. She had arthritis, proteinuria, lymphopenia, anti-ds-DNA antibody positive, anti nuclear antibody positive and decreased complement, and we diagnosised her SLE. She was treated for 0.8mg/kg mPSL, steroid pulse and TAC, and was improved, and delivered low birth weight infant at pregnancy 36weeks and 3 days. Then, she had renal biopsy, and diagnosised lupus nephritis 3 type (A), and her SLE activity hasn't been flare up. (Case2) A 29-year-old woman had pancytopenia, oral ulcer, proteinuria, anti-ds-DNA antibody positive, anti nuclear antibody positive and decreased complement, and was diagnosised SLE. She was treated for 1mg/kg PSL, TAC and HCQ. She is well at pregnancy 29weeks. (Discussion) New-onset SLE for pregnancy is poor outcome. SLE can be flare up in second trimester. High activity of SLE can cause maternal complications. if her renal function deterioration and fetal growth retardation are, we must think pregnancy termination. we treat SLE with PSL generally, high dose use can cause maternal complications. We able to treat these for TAC and HCQ with PSL.

P1-195

A case of systemic lupus erythematosus with thrombotic microangiopathy

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Conflict of interest: Yes

[Case] 66 years old, male [Clinical history] He was treated interstitial pneumonia since 2011 and had influenza A in January, 2017. Pericarditis due to virus infection was suspected with pericardial fluid effusion, psychiatric symptoms and stasis liver. Thrombotic microangiopathy (TMA) was diagnosed in acknowledgment of thrombocytopenia, hemolytic anemia (Coombs negative) and renal dysfunction. Because hypocomplementaemia, antinuclear antibody, double-strand DNA antibody positive and proteinuria were showed, the diagnostic criteria of the systemic lupus erythematosus (SLE) were completed. Renal biopsy was performed on the seventh day of illness and accepted kidney pathologic findings such as

enlargement of endothelial cells, wireloop and dualization of the glomerular basement membrane. We had a diagnosis of SLE with TMA and having performed plasmapheresis, then performed cyclophosphamide and steroid pulse therapy. He contracted a disease for cytomegalovirus pneumonia and was in a condition of the respiratory failure and was passed away subsequently on the 53rd day of illness. [Discussion] The onset on SLE with TMA is regarded as virus infection, but there are many questions. The frequency of SLE with TMA is rare with 0.5%. We report it based on some discussion from literatures.

P1-196

Massive renal infarction due to the antiphospholipid syndrome in a patient with idiopathic thrombocytopenic purpura

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Conflict of interest: None

We present a 40 year-old female patient who had had diagnosis of idiopathic thrombocytopenic purpura (ITP) for 14 years with antiphospholipid syndrome (APS). She still had low platelet counts despite the ITP therapy using steroid and eltrombopag, a thrombopoietin receptor agonist (TPO-RA). She was treated with increases of both steroid and eltrombopag for the last 1 months and visited our hospital because of abdominal pain. She was referred to our division because of renal dysfunction (Cr 3.1 mg/dL), and was admitted to our division for further diagnostic work-up. On the basis of rapidly progressive renal dysfunction without contrast defects of bilateral kidney on CT, biopsy of the left kidney was performed. A pathological examination of the biopsy specimen distinctly showed the interstitial and glomerular necrosis. According to the results, we diagnosed the patient with renal dysfunction caused by bilateral renal infarction. After the diagnosis, anticoagulation therapy was administered to improve renal hemodynamics. Her renal dysfunction was alleviated and she was discharged. We believe that recent increase of eltrombopag contributed to her renal infarction. The risks of thromboembolism must be carefully weighed in APS patients receiving TPO-RA therapy.

P1-197

Pre-eclampsia in a patient with SLE twice

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Conflict of interest: None

An 11 year-old female was diagnosed as systemic lupus erythematosus (SLE) based on her symptoms of fever, polyarthritis, malar rash, hemolytic anemia. She was treated with prednisolone (PSL) of 40mg/day. PSL was tapered but it was difficult to reduce PSL less than 15mg/day because of hypocomplementemia and rash. When the first pregnancy at 26 year-old, the SLEDAI score was 2 (positive anti-ds-DNA antibodies). At 22 weeks, she developed hypertension, proteinuria (10g/day), hypocomplementemia, which was regarded as SLE flare, and she was admitted. We used PSL 30 mg/day and antihypertensive agents. Her disease was marked worsening after admission and developed edema and oliguria. She delivered a baby by emergency caesarean section at 22 weeks. The child died the next day. The following day, her urine output increased. Her proteinuria decreased to 0.2 g/day (and cellular cast disappeared) on the 5th day. When the second pregnancy at 29 year-old, she was treated as PSL 12.5 mg/day. The SLEDAI score was 0. We used PSL 15 mg/day during pregnancy. She developed hypertension and she was admitted at 32 weeks, she delivered by caesarean section at 33 weeks. After delivery, her condition was improved with some antihypertensive agents. The child was discharged well.

P1-198

A case of severe SLE with positive conversion ANA in the course of Rheumatoid arthritis (RA)

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Conflict of interest: None

80-year-old female. She had Interstitial pneumonia (IP) and saw a doctor regularly. She came our hospital because of getting polyarticular pain in 201X-2. Anti CCP antibody was most positive, and her hand's bone was broken. So we diagnosed that she was RA. IP was thought to be due to RA. She didn't have other specific antibody and ANA (Homo/Speckled) was negative. We dispensed Tacrolimus and got a positive result about RA and IP. Although, She got fever and thrombopenia in April of 201X, after that came into being respiratory discomfort and a feeling of weakness of inferior limb. We looked see GGO on her lung by CT, blood return and hemosiderin phagocytosis of macrophage in BALF by bronchoscope. She got bladder and rectal disturbance and IL-6 was high in spinal fluid, so we thought she has transverse myelitis. Admission blood tests PLT:54000/μl, Lym:486/μl, and ANA (Homo/Speckled):40/80. She has facial erythema and hyperesthesia optica, so we diagnosed SLE. Medication was mPSL and PSL50mg/day, Cyclophosphamide 700mg/day, after that SLE improved. To be said SLE occur in combination with RA rarely. But it is usually mild case, Other reports don't say like our case. And ANA (Homo/Speckled) was change positive in this case, so I repot it added to the literature reports.

P1-199

Life-threatening acute back pain: A case of renal vein thrombosis and pulmonary embolism caused by class V lupus nephritis

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Conflict of interest: None

An 18-year-old woman presented with a 9-day history of back pain on the right side. Physical examination was unremarkable except for tenderness of liver and right costovertebral angle. Laboratory findings showed total protein of 4.9g/dL and albumin of 1.0g/dL. Urinalysis showed massive proteinuria (13.3g/gCre). Contrast-enhanced CT revealed massive thrombosis in the right renal vein and inferior vena cava, and bilateral pulmonary embolism. At first, we had some following differential diagnosis: massive proteinuria secondary to renal vein thrombosis caused by congenital or acquired hypercoagulable states; multiple thrombosis secondary to nephrotic syndrome; lupus nephritis concomitant with antiphospholipid-antibody syndrome. Her condition did not improved in spite of adequate anticoagulation therapy. Additional laboratory findings showed only positive for antinuclear antibody (1:1280; speckled pattern), and we suspect of lupus nephritis. We added prednisolone and immunosuppressive therapy, which led to full recovery. After 7 months of treatment, we successfully diagnosed with class V lupus nephritis by renal biopsy. The management of the patient with nephrotic syndrome concomitant with renal vein thrombosis is difficult, however, renal biopsy is mandatory for the diagnosis.

P1-200

A case of SLE/APS with myasthenia gravis who treated effectively by mycophenolate mofetil for diffuse alveolar hemorrhage recurrence

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Conflict of interest: None

[Case] A 39 years old man who was diagnosed myasthenia gravis in 2006. His symptom was improved by thymoma resection and prednisolone (PSL) administration. Thrombocytopenia, sustained proteinuria, arthritis, livedo reticularis and painless oral ulcer appeared in 2009. He was diagnosed SLE and APS by classification criteria. After increasing PSL, we gradually decreased PSL to 20 mg/day. Cerebral infarction and deep vein thrombosis were occurred in 2011 and warfarin was started. In April 2014, he was hospitalized by hemoptysis and the frosted glass shadow on chest XP. Diffuse alveolar hemorrhage (DAH) by SLE was diagnosed by BAL. The steroid pulse therapy was effective, but right after reducing PSL to 30 mg/day, DAH recurred. As he developed the glaucoma and was difficult to reduce PSL, we used cyclophosphamide (CPA) pulse therapy 500mg/ month (four times). But just after reducing to PSL20 mg/

day, DAH recurred in September 2015. We carried out a steroid pulse therapy and CPA pulse 750mg/month (two times). We decided to add 1,000 mg/day of mycophenolate mofetil (MMF) for increasing in proteinuria and DAH recurrence in December 2015. That was effective and we gradually reduced PSL. In October 2017, PSL17.5mg/day and MMF 2,000 mg/day are continued and there is no recurrence of DAH.

P1-201

A case of refractory lupus nephritis Class V, which incomplete remission type I was maintained by multi-target therapy

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Conflict of interest: None

[Background] The treatment of refractory lupus nephritis Class V is in the process of discussion. We experienced a case of Class V successfully treated by by multi-target therapy. [Case] A 35-year-old Japanese woman who was diagnosed as SLE nine years before, visited our division for the treatment of lupus nephritis. On admission, her urinary protein was 4.52g/gCr. [Course] We initiated multi-target therapy, and her urinary protein decreased to less than 1.0g/day. [Conclusion] Multi-target therapy was effective for our case.

P1-202

A case of difficult differential diagnosis of recurrence of lupus nephritis (LN) and pregnancy-induced hypertension (PIH) during pregnancy

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Conflict of interest: None

A 29-year-old woman was diagnosis with systemic lupus erythematosus (SLE) and LN at 20-year-old, and recently she received 0.5mg/day of betamethasone in remission. When she was 28-year-old, she was pregnant. Protein urea and hypertension appeared at 28 weeks of gestation, so we considered recurrence of LN or PIH. She was treated with 15mg/day of prednisolone (PSL), but protein urea was increased to 12 g/day and serum albumin level was decreased to 2.0 g/dl. Because of the elevation of anti-DNA antibody level and reduction of serum C3/C4/CH50, we considered the possibility of recurrence of LN. After the treatment with steroid pulse therapy (methyl-prednisolone 500mg/day for 3 days) and oral PSL (1mg/kg daily) at 30 weeks of gestation, protein urea was partially improved to 5~7 g/day. Because serum albumin level was decreased to 1.3 g/dl and pleural effusion and ascites appeared, she was performed an emergency cesarean procedure at 31 weeks of gestation. After the delivery, protein urea was drastically improved and disappeared at day 17. This is a case of difficult differential diagnosis of recurrence of LN and PIH during pregnancy. We report this case with literature considerations.

P1-203

A case of systemic lupus erythematosus presenting as aseptic meningitis with sensory loss in a sacral dermatome distribution and bladder and rectal disturbance

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Conflict of interest: None

Case: A 39 year-old woman was admitted to our hospital complaining of fever, headache, vomiting, sensory loss in a sacral dermatome distribution, and bladder and rectal disturbance. Cerebrospinal fluid (CSF) examination revealed the elevated protein and lymphocytes. Herpes simplex polymerase chain reaction were negative. Also cytology was negative. Anti-nuclear antibody (ANA) and anti-double-stranded DNA and *Anti-Sm antibodies* were positive. Lumbar MRI shows that the surface of conus medullaris was enhanced on T1-weighted images after gadolinium injection and her neurological symptoms were explained by lumbosacral radiculitis. She was diagnosed with SLE based on the diagnostic criteria proposed by SLICC. Also, aseptic meningitis was diagnosed in CSF study. Considering the clinical course, aseptic meningitis with lumbosacral radiculitis was due to SLE. After treatments with corticosteroid, intravenous cyclophosphamide, and mycophenolate mofetil, her symptoms gradually improved. Conclusion: We reported a 39 year-old with aseptic meningitis in SLE. In this case, lumbosacral radiculitis was accompanied by aseptic meningitis and this complication was not reported in the previous literature of SLE. With the immunosuppressant treatment, her neurological symptoms gradually improved.

P1-204

A case of systemic lupus erythematosus (SLE) developed with aseptic meningitis, retinal vasculitis

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Conflict of interest: None

A 33-year-old woman had a fever, polyarthritis. Laboratory examination showed lymphopenia, positive anti-nuclear antibody (speckled type), and positive anti-Sm antibody. SLE was suspected, but was followed without treatment. Two months later, she experienced fever, headache, visual disturbances, nausea, and anorexia. She was admitted to our hospital because of fever, nuchal stifness, bulbar conjunctiva hyperaemia, and sterile pustules. Head CT and MRI didn't reveal abnormal findings. Cerebrospinal fluid (CSF) examination showed that the level of protein, cell number (polymorphonuclear predominance), and IgG were high. Bacterial infection or herpes encephalitis was suspected. We administered ceftriaxone and acyclovir, but fever persisted. Ophthalmologic examination showed episcleritis, soft exudate, and retinal vasculitis. We diagnosed SLE retinopathy. HSV-1 and HSV-2 antibody in CFS neutralization test, cerebrospinal fluid bacteria culture, and blood culture were negative. We diagnosed aseptic meningitis concurrent with SLE and started to administer prednisolone 60mg/day. Fever, headache, and visual disturbances resolved. Ocular findings disappeared. Retinal vasculitis with central nervous system lupus is easy to progress, therefore it is important to diagnose and treat promptly.

P1-205

A case in which systemic lupus erythematosus that presented with polyarthritis accompanied by bladder cancer

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Conflict of interest: None

[Case] A 76 year-old man with polyarthralgia had been diagnosed with adult still's disease at another hospital at 2014, and received steroids, finally continued 5mg prednisolone (PSL). At 2016, he visited our hospital because of worsening of his symptom. Arthritis and tendosynovitis at many joints detected by ultrasound scan. There are additional positive findings of anti-nuclear antibody and anti-ds DNA antibody and hypocomplimentemia, he diagnosed as systemic lupus erythematosus (SLE) on the basis of classification criteria of SLICC. PSL30mg was effective, but arthritis was worse as tapering of PSL. In August 2017, he experienced an onset of gross hematuria and CT scan found bladder tumor. Transurethral resection or the bladder tumor was performed and manifested bladder cancer. Retrospectively, CT scan showed thickening of bladder wall slightly when he diagnosed SLE. [Discussion] Although SLE is most probable diagnosis on the basis of the labo data, if bladder cancer existed at the time, the possibility of paraneoplastic syndrome can't be denied. Carcinomatous polyarthritis is characterized by acute onset arthritis of symmetrical lower extremities of elderly people, so we should keep in mind possibility of malignancies when we examine elderly patients with such polyarthritis.

P1-206

The prognosis of dysphagia in dermatomyositis

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Conflict of interest: None

Objective: Dysphagia is a risk factor for mortality in dermatomyositis (DM) by causing aspiration pneumonia. Furthermore, dietary restrictions for aspiration prevention or treatment can diminish the patient's motivation to continue these treatments. This study aims to identify the clinical characteristics and responses to treatments for dysphagia in DM. Methods: We compared the 30 dysphagia-complicated patients with the 56 non-complicated patients in terms of age, sex, cancer complication, creatine kinase, duration between DM onset and first visit, autoantibodies, treatments and other factors. Result: The risk factors for dysphagia were found to be age (P<0.00001), sex (P=0.0007), anti-TIF1γ positivity (P=0.0001) and cancer complication. Survival rate correlated most closely with dysphagia recovery, with 94% of surviving patients (15/16) showing some dysphagia recovery (P=0.00003). Anti-TIF1γ negativity (P=0.051) and high initial PSL dose (44.4 mg/day vs 28.0 mg/day) (P=0.051) showed some contribution to dysphagia recovery. There was no relationship between combination therapies and recovery. Conclusion: Most of the surviving DM patients showed some dysphagia recovery, independent of treatment timing or type.

P1-207

Clinical pictures of anti-MDA5 antibody positive dermatomyositis patients in our department

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Conflict of interest: None

[Object] In order to understand its clinical features, we examined anti - MDA5 antibody positive dermatomyositis (DM) experienced at our hospital. [Methods] In this retrospective study, patients initially diagnosed as DM who hospitalized in our department from March 2013 were analyzed. [Result] 10 patients were positive for anti-MDA5 antibodies. All patients had interstitial pneumonia and were treated with aggressive immunosuppressive medications. 7 patients survived and 3 patients died of respiratory failure. The dead cases were significantly older than surviving cases. In the dead cases, ferritin levels appeared to be higher and serum albumin values tended to be lower than surviving cases before treatment. KL-6 levels tended to increase and serum albumin values tended to decrease during treatment. [Discussion] In anti-MDA5 antibody positive DM patients, age and serum albumin before treatment, as well as serum ferritin might be related to poor prognosis. Moreover, the increasing levels of KL-6 and the decreasing values of albumin during aggressive treatment could be associated with poor outcome.

P1-208

Elevated serum levels of soluble CD146 in patients with polymyositis/dermatomyositis

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Conflict of interest: None

[Object] CD146 is a transmembrane glycoprotein belong to Ig-superfamily constitutively expressed in endothelial cells. CD146 acts as adhesion molecule for the maintenance of cell monolayer and vascularization. The aim of this study is to determine the levels of soluble CD146 (sCD146) in the serum of patients with polymyositis (PM), dermatomyositis (DM) and clinically amyopathic DM (CADM) using sandwich ELISA, and to examine the association between the levels of sCD146 and the clinical features. [Methods] The specificity, quantity and sensitivity of the sandwich ELISA for CD146 were tested by recombinant CD146 protein. Levels of sCD146 were quantified in 88 serum samples from patients with PM/DM by ELISA and compared with those of 10 healthy control (HCs). [Results] Levels of sCD146 were significantly higher in patients with PM/DM/CADM than in the HCs (9.95ng/ml; p< 0.01), and patients with PM was significantly highest among PM/DM/CADM. Slight correlation was observed between sCD146 and Creatine Kinase; however, no correlation with other clinical features and myositis-specific autoantibodies was observed. [Conclusions] We identified the high levels of sCD146 in PM/DM/CADM, especially higher in PM. CD146 could be involved in pathophysiology of myositis.

P1-209

The relation between autoantibodies and clinical symptoms in inflammatory myopathy

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Conflict of interest: None

[Objective] Myositis specific antibody (MSA) and Myositis associated antibody (MAA) are often detected in inflammatory myopathies (IIMs), and it yields useful information for treatment. However, the clinical significance of multiple MSA/MAA and anti-Ro52 have not been sufficiently studied. In our study, the purpose was to clarify the clinical significance of multiple MSA/MAA and anti-Ro52. [Methods] 58 patients with IIMs in our facility were analyzed for MSA/MAA by ELISA and Line blot. We extracted multiple MSA/MAA (+) and anti-Ro52 (+) patients and examined the relation between MSA/MAA and clinical symptoms. [Results] 53/58 patients were positive for MSA/MAA, followed by Ro52 (n=27), PL7 (n=12), Jo1 (n=8), PM-Scl75 (n=7), Ku (n=6), SRP (n=4), EJ (n=4), TIF1γ (n=4), MDA5 (n=4), Mi2 (n=3), PL12 (n=1), PM-Scl100 (n=1), 5 cases were MSA/MAA (-). In patients with IIMs, anti-ARS or anti-Ro52 (+) patients complicated interstitial lung disease (ILD) and had a high titer of KL-6 at onset (P <0.05). In addition, multiple MSA/MAA (+) patients complicated rapidly progressive ILD and used a plurality of immunosuppressive agents (P <0.05). [Conclusions] We suggested that anti-Ro52 (+) and multiple MSA/MAA (+) may be useful for predicting the complication and clinical course of ILD.

P1-210

Swallowing ability outcomes of cancer associated myositis with dysphagia; A retrospective multicenter study

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Conflict of interest: None

[Object] To analyze swallowing ability outcomes of cancer associated myositis with dysphagia. [Methods] We retrospectively analyzed 13 cancer associated myositis with dysphagia and compared with either patients with improving swallowing ability or not. [Results] Nine patients improved their swallowing ability and 4 patients did not. Patients with improving swallowing ability received interventional procedure compared to patients without improving swallowing ability (P=0.007). However, other clinical characteristics and treatment were similar. On the other hand, 9 patients were advanced cancer stage (Stage>=3) and 4 patients

were early cancer stage (Stage<=2). Clinical characteristics and treatment were similar. Swallowing ability outcomes were higher than patients with early cancer stage. [Conclusions] Most of the cancer associated myositis patients with dysphagia may improve their swallowing abilities in spite of advanced cancer stage.

P1-211

Clinical characteristics and survival rate of cancer associated myositis: A retrospective multicenter study of 241 Japanese patients with Dermatomyositis and Polymyositis

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Conflict of interest: None

[Object] To analyze survival rate of dermatomyositis and polymyositis patients with malignancy. [Methods] We retrospectively studied 241 patients with dermatomyositis and polymyositis and compared with either with or without malignancy. [Results] Out of 241 patients with myositis in our database, malignancy was found in 30 patients. Myositis patients with malignancy were significantly older, higher prevalence of DM, dysphagia, anti-TIF1-γ antibody, lower MMT, and lower prevalence of interstitial pneumonia than patients without malignancy. Kaplan Meier method revealed that survival rate of myositis with malignancy were significant lower than myositis without malignancy. [Conclusions] Survival rate myositis with malignancy was significantly lower than myositis witout maligancy.

P1-212

Clinical characteristics and prognosis of polymyositis and dermatomyositis associated with malignancy: a 25-year retrospective study

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Conflict of interest: None

[Object] This study investigated factors predictive of malignancy and prognosis in patients with polymyositis (PM) or dermatomyositis (DM). [Methods] We conducted a retrospective study of PM and DM patients who were inpatients at our hospital between January 1992 and September 2016. [Results] Among 134 patients, 29 had cancer diagnosed between 2 years prior and 3 years following identification of PM or DM. Univariate analysis showed that male sex ($p = 0.003$), older age ($p<0.001$), past history of diabetes mellitus ($p<0.001$), dysphagia ($p = 0.01$) and absence of interstitial lung disease ($p = 0.01$), arthralgia ($p = 0.005$) and the Raynaud phenomenon ($p = 0.02$) were associated with increased malignancy. Multivariate analysis showed that independent factors included male sex (OR = 3.65, $p = 0.03$), older age (OR = 1.05, $p = 0.02$), past history of diabetes mellitus (OR = 10.4, $p = 0.005$) and absence of interstitial lung disease (OR = 0.25, $p = 0.03$). Survival was significantly lower in patients with malignancy than in patients without malignancy ($p<0.001$). [Conclusions] This study is the first to associate a past history of diabetes with malignancy; 28.6% of PM or DM patients with malignancy had diabetes mellitus whereas 7.3 percent of cancer patients had diabetes mellitus.

P1-213

Myocardial fatty acid metabolism and perfusion mismatch in scintigraphy predicts worse prognosis in clinically amyopathic dermatomyositis with interstitial lung disease

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Conflict of interest: None

Objectives: To evaluate clinical utility of myocardial fatty acid metabolism and perfusion mismatch in clinically amyopathic dermatomyositis (CADM) patients with interstitial lung disease (ILD). **Methods:** All patients who performed cardiac scintigraphy using ^{99m}Tl and ^{123}I-BMIPP were retrospectively evaluated. Patients who fulfilled Sontheimer's criteria for CADM were selected. We subtracted %uptake of metaboism (^{123}I-BMIPP) from that of perfusion (^{99m}Tl) on each 17 myocardial segments standardized by American Heart Association. An independent prognostic factor for poor outcome which was defined as death or receiving home oxygen therapy was determined. **Results:** We investigated 10 patients with CADM and there were 3 patients with poor outcome. All the CADM patients manifested with ILD and %VC, Aa-DO2, and serum ferritin were not significantly different between patients with good outcome and those with bad ($p=0.83$, $p=0.57$, $p=0.11$). A significantly higher level of mismatch score was detected in patients with poor outcome in CADM group ($p=0.02$) and it was selected as an independent prognostic factor for poor outcome by multivariate analysis (OR 2.3, 95%CI 1.0-3.3, $p=0.05$). **Conclusions:** High mismatch score in cardiac scintigraphy may predict poor outcome in CADM.

P1-214

Difference of interstitial lung lesions of anti-MDA5 antibody and anti-ARS antibody positive dermatomyositis in our department

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Conflict of interest: None

[Object] Anti-MDA 5 antibody and anti-ARS antibody are characteristic autoantibodies of polymyositis (PM) / dermatomyositis (DM) complicated interstitial lung disease. The purpose of this study is to clarify the difference of HRCT score at the initial stage in anti-MDA5 antibody DM and anti-ARS antibody DM. [Methods] Comparative study of the initial chest HRCT image findings of anti-MDA5 antibody and anti-ARS antibody positive DM patients diagnosed in our department from January 2015 to October 2017 was conducted. CT findings were graded on a one to six scale corresponding to consecutive pathologic phases. An overall score was obtained by quantifying the extent of each abnormality in three lung zones in each lung. [Results] There were 5 cases of anti - MDA 5 antibody DM, 8 cases of anti - ARS antibody DM. In lung function, %VC was 68.5% in anti-ARS antibody DM, 102.0% in anti-MDA5 antibody DM ($p = 0.002$). %DLCO was 67.9% and 82.9% each other ($p = 0.03$). The HRCT score was significantly higher the anti-MDS 5 antibody DM than the anti-ARS antibody DM ($p = 0.006$). [Conclusions] The HRCT score was significantly higher in the anti - ARS antibody DM, suggesting the possibility that fibrosis appeared earlier than in the anti - MDA 5 antibody DM.

P1-215

Clinical significance of magnetic resonance imaging of muscles in patients with polymyositis and dermatomyositis

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Conflict of interest: None

[Object] Muscle biopsy and electromyogram are important, but invasive examinations for diagnosis of polymyositis/dermatomyositis (PM/DM). Clinical significance of magnetic resonance imaging (MRI) of lower limb muscles was investigated in PM/DM patients. [Methods] 25 PM/DM patients who received MRI of lower limbs as well as muscle biopsy were subjected for the study. MRI was evaluated by short-T1 inversion recovery (STIR) and/or gadolinium contrast-enhanced T1-weighted imaging methods. [Results] MRI of lower limbs showed abnormalities in all 25 patients (100%). Muscle biopsy was positive for 20 patients (80%), and MRI of lower limbs was also positive for those 20 patients. In PM

patients, muscle biopsy was positive in all four patients, however, MRI of lower limbs was positive in two patients (50%). In five patients with serum creatine kinase (CK) level less than 300 IU/L, muscle biopsy was negative in all cases, whereas MRI of lower limbs was positive in all cases. [Conclusions] These findings suggest that MRI of lower limb muscles is useful for diagnosis of PM/DM, especially in patients with low CK levels. Careful interpretation of MRI results should be necessary in PM patients.

P1-216

Diagnostic clinical utility of myositis specific autoantibodies in idiopathic inflammatory myopathy

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Conflict of interest: None

[Object] Previous researches considering diagnostic accuracy of myositis specific autoantibodies (MSAs) in idiopathic inflammatory myopathy (IIM) are scarce. This research investigated diagnostic performance of MSAs in IIM suspected patients at rheumatic disease department. [Method] New patients with muscle weakness, CK elevation or dermatomyositis-like eruptions from November 2016 until August 2017 were included. Anti-ARS antibody, anti-Mi-2 antibody, anti-TIF-1γ antibody, anti-MDA5 antibody were measured by commercially available ELISA kits. As reference standard, muscle biopsy was positive when muscle pathology expert considered biopsy consistent with IIMs, skin biopsy was positive when interface dermatitis was present. In patients without tissue biopsy, muscle and skin biopsy were considered positive when these patients sign and symptoms improved under other diagnosis except for IIMs. [Result] 33 patients were included in analysis. In 10 MSAs positive patients, tissue biopsy were positive in all patients. In 23 MSAs negative patients, tissue biopsy was positive in 1 patient and negative in 22 patients. Positive likelihood ratio was ∞ and negative likelihood ratio was 0.09 (95% C.I. 0.086~0.097). [Conclusion] MSAs were useful in diagnosis of IIMs at rheumatic disease department.

P1-217

The plasma level of D-dimer as reflecting blood coagulation disorders may be one of useful biomarkers in interstitial lung disease associated with polymyositis / dermatomyositis

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Conflict of interest: None

[Object] The purpose of this study was to investigate biomarkers that reflect the activity of interstitial lung disease (ILD) associated with polymyositis (PM) / dermatomyositis (DM). [Methods] This is a retrospective observational study. Thirty-two participants who were diagnosed as having PM/DM-ILD in our hospital from April 2012 to September 2017 were enrolled. The participants complicated with deep venous thrombosis and malignancies affecting the blood coagulation test were excluded. Diagnosis of ILD was evaluated by chest high-resolution CT. We reviewed the laboratory findings and analyzed the correlation between KL-6 and D-dimer (DD), LDH, CRP. In addition, we analyzed the changes of these biomarkers before and after treatment with immune suppressants (IS). [Results] There was a positive correlation in the levels of between serum KL-6 and plasma DD, significantly (R= 0.45, p= 0.015). There was no correlation in the levels of between KL-6 and LDH and CRP. After treatment with IS, the levels of DD significantly decreased compared to the levels of KL-6 in patients with PM/DM-ILD. [Conclusions] The present study demonstrated that it is possible that DD is one of useful biomarkers for reflecting the activity of PM/DM-ILD.

P1-218

Comparison of Prognosis in Interstitial Lung Disease Between Polymyositis/ Dermatomyositis Patients with Anti-Jo-1 Antibody and Anti-EJ Antibody

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Conflict of interest: None

[Object] Although anti-aminoacyl-tRNA synthetase (ARS) autoantibodies were found in polymyositis/dermatomyositis, its close association with interstitial lung disease (ILD) has been elucidated. The aim of this study is to examine the differences in prognosis of ILD between anti-EJ and anti- Jo-1 positive anti-ARS syndrome. [Methods] Thirty-nine anti-ARS syndrome patients who had ILD with anti-Jo-1 or anti-EJ at Tokai University Hospital between 2011 and 2017 were selected. Autoantibodies were identified by immunoprecipitation assays and all clinical data were collected retrospectively. ILD is diagnosed based on findings of computed tomography. Cumulative survival rates are calculated using the Kaplan-Meier method and the differences in groups are compared with the log-rank test. [Results] Of the 39 patients, 16 (41%) were positive for anti-EJ and 23 (59%) were positive for anti-Jo-1. Induction rates of home oxygen therapy and recurrence rates of ILD during follow up period tended to be higher in anti-EJ antibody group in comparison with anti-Jo-1 antibody group (18.8% vs. 4.4%: P=0.14, 37.5% vs 21.7%: P=0.28, respectively). [Conclusions] These results suggest that anti-ARS syndrome patients with anti-EJ antibody had worse prognosis for ILD compared to those with anti-Jo-1 antibody.

P1-219

Nailfold capilloscopic changes appear to be a useful parameter to predict disease activities and clinical outcomes of patients with interstitial pneumonia complicated with dermatomyositis

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Conflict of interest: None

[Objectives] We investigated the relation between nailfold capillaroscopic changes and parameters for disease activities or clinical outcomes of patients with interstitial pneumonia (IP) in dermatomyositis (DM) [Methods] 25 DM-IP patients were evaluated by nailfold capillaroscopy (NFC). A semiquantitative rating scale to score NFC parameters was adopted. [Results] The patients complicated with rapidly progressive IP (RPIP) were 13 and slowly progressive IP (SPIP) were 12. The anti-ARS antibody-positive (ARS+) cases were 15 and the anti-MDA5 antibody-positive (MDA5+) cases were 5. Both of the scores of giant capillaries and disorganization of the capillary array were higher in the RPIP cases than the SPIP cases. The scores of hemorrhages and the disorganization of the capillary array were higher in MDA5+ cases than ARS+ cases, and tortuous capillaries were more frequently detected in ARS+ cases. LDH, CRP, KL-6, total GGO score, and total fibrosis score were related with the score of hemorrhages, and LDH, Ferritin, $AaDO_2$ were related with the score for disorganization of the microvascular array. [Conclusions] The patients with high scores of hemorrhages and disorganization of the microvascular array have high disease activities and appears to be related to poor prognosis.

P1-220

Clinical and Immunological Characteristics of Patients with Anti-KS Antibody

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Conflict of interest: None

[Object] Although anti-aminoacyl-tRNA synthetase (ARS) autoantibodies were found in polymyositis/dermatomyositis (PM/DM) at first, its close association with interstitial lung disease (ILD) has been elucidated nowadays. The aim of this study is to clarify the clinical and immunological features in patients with anti-KS antibody. [Methods] PM/DM or ILD patients who visited Tokai University Hospital between 2010 and 2017 were screened. Autoantibodies were identified by immunoprecipitation assays and all clinical data were collected retrospectively. ILD is diagnosed based on findings of computed tomography. Clinical and immunological features of anti-KS positive patients were assessed. [Results] Five patients with anti-KS positive patients were detected. Final diagnoses were ILD, rheumatoid arthritis (RA), Sjögren's syndrome (SjS), RA/SjS overlap and clinically amyopathic dermatomyositis each. Although the diagnoses of 5 patients were various, all 5 patients had no muscle weakness and serum CK elevation whereas all had ILD. Interestingly, 4 of 5 patients (80%) had xerostomia and positivity of anti-SSA antibody. [Conclusions] These results suggest that anti-KS antibody is closely associated with ILD as well as sicca syndrome.

P1-221

Disease activity and prognosis analysis using serum cyto/chemokines in interstitial pneumonia with anti-MDA5-antibody positive DM patients

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Conflict of interest: None

[Object] We evaluated the initial serum cyto/chemokines levels of anti-MDA5-antibody positive dermatomyositis (DM) with interstitial pneumonia (IP) patients and examined the relation with disease activity and prognosis. [Methods] Sixteen DM-IP patients (including 14 clinically amyopathic dermatomyositis) were included. [Results] The median age was 59.5 years and female were 12 patients. Fourteen patients were rapid progressive IP (RPIP) and 2 patients were slow progressive IP (SPIP). Nine patients died of IP. The serum TNF-α levels were significantly higher in the RPIP cases than in the SPIP cases (P=0.032). In the death group, initial serum LDH, ferritin, and $AaDO_2$ levels were significantly higher (P=0.030, 0.0026, 0.030), and IL-6 and IP-10 levels tended to high. In the survivor group, serum IL-2 levels at 2 weeks, and CCL2 and TNF-α levels at 4 weeks after treatment initiation decreased compared with initial. The disease activity indexes of IP weren't correlated with cyto/chemokines. [Conclusions] In anti-MDA5-antibody positive DM-IP patients, IL-2, IL-6, IP-10, CCL2, and TNF-α levels were likely correlated with the disease activity and the prognosis.

P1-222

Clinical features of patients with anti-Ku Antibody

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Conflict of interest: None

[Objectives] Anti-Ku Ab was reported first as a Ab found in Scleroderma/myositis overlapping syndrome. In the USA, the antibody was reported to be found in SLE. The aim of this study was to clarify the clinical features of patients with a-Ku Ab. [Methods] a-Ku Ab was measured in collected serum samples from CTD and CTD suspected patients using Euroline Myositis profile3 kit. [Results] a-Ku Ab was examined in serum samples from 947 cases. a-Ku Ab was positive in 32 patients (3.3%). The patients with a-Ku Ab were 7 male and 25 females with an average age of 50.6±19.9 years. Underlying diseases were 5 SLE, 4DM, 4 PM, 4 primary Sjogren syndrome, 1 MCTD and 1 APS. Four patients with an overlapping syndrome (SLE+ myositis) were positive for the Ab and required immune-suppressants because of poor response to glucocorticoid. No definite scleroderma case was found. There were patients of idiopathic interstitial pneumonia (IP) positive for a-Ku Ab. In patients with a-Ku Ab, IP was found in 14 cases. Muscle symptoms and Raynaud Phenomena and sclerodactlia were observed in 8, 3 and 2 cases, respectively. [Conclusion] Anti-Ku Ab was found in SLE/myositis and their overlapping syndrome with IP in addition to myositis/scleroderma overlapping syndrome.

P1-223

Clinical features of interstitial pneumonia associated with anti-MDA-5 antibody positive dermatomyositis in our hospital

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Conflict of interest: None

[Object] To examine our MDA-5 positive DM-ILD cases, using prognostic factors reported in previous studies. [Methods] We reviewed retrospectively the clinical characteristics, treatment, outcome of 6 cases seen in our department from February 2013 to October 2017. [Results] There were 3 cases of rapid progressive, 1 case of "slowly, then rapidly" progressive, and 2 cases of slowly progressive ILD. All patients were initially treated with a combination therapy with steroid and immunosuppressants (IVCY + Tacrolimus/Cyclosporine). Two cases survived, but 4 died of respiratory failure. The average duration from the beginning of treatment to death was 27.5 days. The age was younger in the survived cases, and the maximum value of LDH, the ferritin value and the IgG value at the first visit tended to be higher in the dead cases. At hospitalization, in all cases, keratotic erythema mainly with Gottron's sign was observed. In the chest CT, infiltrative shadow of the lower lung was observed in the 1 cases of death and the 1 case of survival, the remaining 4 cases were ground glass opacity. [Conclusions] All patients surviving in our department were slowly progressive, and age, LDH, serum ferritin level and IgG values may be the markers of worse prognosis.

P1-224

Clinical characteristics associated with pneumatosis cystoides intestinalis in patients with polymyositis and dermatomyositis

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Conflict of interest: None

Objectives: Pneumatosis cystoides intestinalis (PCI) is characterized by multiple gas cysts in gastrointestinal wall. We describe the clinical characteristics associated with PCI in patients with polymyositis (PM) and dermatomyositis (DM). **Methods:** In order to investigate the clinical findings related to PCI in patients with PM/DM, we reviewed the clinical records of 117 patients with PM/DM who had treated in our hospital. **Result:** PCI was demonstrated in 6 patients (one man and 5 women). Of them, one patient with PM and 5 with DM were included. Interstitial pneumonia was initially indicated together with diarrhea or constipation in 5 patients on admission. Although PCI was not shown as the initial involvement in PM/DM, it developed after initiating treatment or adding administration for the relapse. All patients were treated with high dose prednisolone (PSL) as well as immunosuppressant. Average dose of PSL was 36.6±12.1 mg daily at the onset of PCI, which improved with conservative treatment in all patients. **Conclusion:** It was suggested that the development of PCI is associated with high disease activity of PM/DM as well as high dose PSL administration. In the course of PM/DM, PCI assessment and care are required in order to prevent intestinal impairment.

P1-225

Three cases of dermatomyositis with anti-MDA5 antibody positive interstitial lung disease successfully treated by azathioprine combination therapy

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Conflict of interest: None

[Case 1] A 39-year-old female presented with fever, rash, arthralgia, and myalgia. She was diagnosed with ADM, and received PSL 60mg/day. Eruption tended to deteriorate during tapering of steroids, and concomitant use of calcineurin inhibitor was ineffective. Because she was found to possess anti-MDA5 antibody, we further added AZA, which improved her eruption. [Case 2] A 50-year-old man presented with wrist pain, fever, muscle symptoms, skin ulcers, and interstitial pneumonia, leading to the diagnosis of DM with anti-MDA5 antibody. Combination therapy (PSL+TAC+IVCY) was performed, but IVCY was discontinued due to fatigue. Since ferritin tended to increase, we used AZA for the purpose of steroid sparing. [Case 3] A 15-year-old female presented fever, polyarthralgia, eruption, and interstitial pneumonia. She was diagnosed with anti-MDA5 antibody positive JDM. AZA combination therapy with PSL and CyA exhibited improving effect for refractory skin ulcers. [Clinical Significance] With regard to anti-MDA5 antibody positive DM, the indication for multi-drug combination therapy including IVCY, and the optimal treatment period of IVCY are still unknown. In the present three cases, the effect of AZA combination therapy was suggested. AZA may be an alternative to IVCY in mild cases.

P1-226

Clinical result in elderly patients aged 75 over with ANCA associated vasculitis treated with rituximab

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Conflict of interest: None

[Object] To evaluate the efficacy and infection rate of Rituximab (RTX) in patients aged 75 over with ANCA assosiated vasculitis (AAV) in our hospital. [Methods] We investigated the medical records of 5 patients aged 75 over with AAV had admitted to our hospital from June 2015 until November 2017. [Methods] We investigated the medical records of 5 patients admitted to our hospital from June 2015 until November 2017. [Results] 5 patients (4 MPA and 1 GPA) were treated with RTX. 4 patients were treated as the first remission induction and 1 as the maintenance. Observation mean period was 11.8 months. The mean PSL dose was 23mg. MPO-ANCA titer was 35.6U/ml (mean; range 4.4-97.9U/ml). BVAS score was 5-17. Serum IgG was 1568mg/dl (median). RTX of 375mg/m^2/week was administered from 1 to 4 times. After the administration of RTX, MPO-ANCA titer was low and BVAS score was improved in all patients. The adverse events within 6 months were as follows, pneumocystis jiroveci pneumonia 2, bacterial pneumonia 1, pulmonary aspergillosis and infection of the urinary tract 1. Immunoglobulin was administered to two patients. No fatal cases were observed. [Conclusions] Although infection rate was higher within 6 month of RTX, RTX could be effective in elderly patients aged 75 over with ANCA associated vasculitis.

P1-227

Risk factors associated with relapse of ANCA-associated vasculitis

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Conflict of interest: None

[Object] We examined potentially novel factors predicting relapse in ANCA-associated vasculitis. [Methods] The 62 study patients (46 MPA, 16 GPA; n=38 females) had been treated at our center from 1998 to 2017 and had an available medical history. [Results] The median age of onset [interquartile range] was 76 [68-82] years. The relapse rate was 37% (MPA 28%, GPA 63%) and was significantly higher in the GPA group (p=0.03). The median time to relapse was 18 [11-30.5] months. Although pulmonary and cardiac lesions reportedly increase the relapse rate, significant differences in relapse could not be attributed to either one. In an assessment of medical histories, differences in diabetes, dyslipidemia, coronary artery disease, or cerebral infarction were not significantly different in patients with and without relapse. However, a history of hypertension (HT) was significantly less common in the relapse group (p=0.003). Sex, age, and variables with a P value <0.05 in the bivariate analysis were used as input and corrected in a multiple logistic regression analysis. The results showed that a history of HT was significant in predicting relapse (OR: 0.19; 95% CI 0.05-0.70, P = 0.01). [Conclusions] In addition to known factors, a history of HT at onset may predict MPA and GPA relapse.

P1-228

Re-hospitalization for ANCA-associated vasculitis of the elderly

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Conflict of interest: None

[Object] In this study, we determined the factors related to re-hospitalization of elderly ANCA-associated vasculitis people. [Methods] 66 ANCA-associated vasculitis patients who diagnoses at Showa university hospital department of Rheumatology were targeted. They were hospitarized among Junuary 2006 and November 2016. The main outcome is re-hospitarization which was unexpected. The type of vasculitis, damaged organ, age, underlying disease, BMI, nutritional status, steroid pulse, the maximum dose of steroids, the use of immunosupressunt, and infection durling first hospitarization were considered as risk factors. [Results] 66 patients with anca-associated vasculitis were examined. Of the 66 people, 49 MPA, 16 GPA, 9 EGPA, age 78.0 ± 7, female 72.7%. and 25.8% have died within the range that can be confirmed. The prevalence of the unscheduled hospitalization within one year was 31.8% (21 of 66 patients). Infections were the most common reasons for hospitalization. The factor of the unscheduled hospitalization within one year was renal involvement (OR 3.8, 95%CI, 1.06-15.7). [Conclusions] The prevalence of the unscheduled hospitalization within one year was 31.8%. The type of damaged organs may reflect to the unscheduled hospitalization within one year.

P1-229

A case of drug-induced ANCA associated vasculitis with multiple abdominal aneurysms

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Conflict of interest: None

[Case] A 57-year-old woman was diagnosed with hyperthyroidism and was started on thiamazole in January. She presented with fever and abdominal pain and was admitted to our hospital in March. She had purpura at the legs and a skin biopsy was performed. We suspected drug-induced vasculitis. She was started to PSL at a dose of 60mg/day after cessation of thiamazole and her symptoms improved. Histopathological analysis of the biopsied tissues showed infiltration of neutrophils and lymphocytes around arterioles. C-ANCA by FA technique was positive. After her PSL had been tapered gradually to 35mg/day, she presented with abdominal pain in April. CT showed multiple aneurysms of the abdominal arteries. She was treated with mPSL pulse therapy followed by PSL at a dose of 60mg/day, and aneurysms disappeared gradually. She presented with fever and consciousness disturbance on July. We suspected exacerbation of vasculitis or infection, and started to mPSL pulse therapy and antibiotics. But her condition getting worse, and she died. We performed an autopsy. [Conclusions] Most cases of drug-induced ANCA associated vasculitis related to thiamazole showed positivity of MPO-

ANCA. But this case showed positivity of C-ANCA by FA technique. We reported this case because of its rarity.

P1-230

Single Center, Retrospective Analysis of Rituximab (RTX) Treatment for Microscopic Polyangiitis (MPA) and Granulomatosis with Polyangiitis (GPA): A Real World Practice Data

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Conflict of interest: None

Objectives: To determine the real-world practice of RTX treatment for MPA and GPA. **Methods:** Twenty nine patients with GPA/MPA, who had started RTX for remission induction or relapse, were retrospectively analyzed. The median age at RTX induction was 77.0 yo (range: 57-85), and 28 were positive for MPO-ANCA. They were followed up regularly by 24 months for the efficacy and safety, PSL tapering, and remission maintenance. **Results:** For the initial RTX cycle, only 1 infusion in 9, 2 in 13, 3 in 2, and 4 in 5. After RTX, 19 could be observed at month 3, 18 at month 6, 6 at month 12, and 1 at month 24. At month 6, 77.8% (14/18) reached BVAS=0, and PSL was 4.5mg/day (median, range 4-5) at RTX start, and at month 3, 6, 12, 18, and 24, PSL levels were 40mg/d, 4.5mg/d, 1.5mg/d, 1mg/d, and 0mg/d, respectively. Only 1 relapsed at month 12. The reasons for RTX discontinuation, 9 by month 3 (6 AEs, 1 death, and 2 for other hospitals), 1 for other hospital between 3-6 months, 5 within 6-12 months (2 AEs, 1 for other hospital etc.). AEs included 11 CMV activation, 2 sepsis, 2 herpes zosters, 1 bacterial pneumonia, 1 PCP, etc. **Conclusions:** Low dose of RTX were used as initial therapy and relapse for Japanese patients, but were still effective. Monitoring of opportunistic infections was needed.

P1-231

Gene expression analysis of peripheral blood immune cells in ANCA-associated vasculitis (AAV)

Haruyuki Yanaoka[1,2], Yasuo Nagafuchi[1], Yusuke Takeshima[1], Mineto Ota[1], Harumi Shirai[1], Yusuke Sugimori[1], Mai Okubo[1], Satomi Kobayashi[1], Tomohisa Okamura[1], Yukiko Iwasaki[1], Hirofumi Shoda[1], Shuji Sumitomo[1], Yuta Kochi[3], Kazuhiko Yamamoto[3], Keishi Fujio[1]
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Conflict of interest: None

[Object] The goal of this study was to determine pathologically meaningful immune cell subsets and genes in AAV using RNA-sequencing data analysis. [Methods] Thirteen patients with AAV (GPA or MPA) and 9 HCs were included in the study. Nineteen immune cell subsets from peripheral blood were sorted by FACS, and RNA-sequencing was used to measure mRNA expression. We compared the gene expression data between AAV and HCs, and performed pathway analysis using IPA when there was a large amount of differentially expressed genes (DEGs). [Results] Mean age of AAV was 63.6±13.2 y.o. (vs. 60.2±14.2), and female percentage was 84.6% (vs. 55.6%). BVAS was 2.6±2.6 with 4.5mg/d PSL in average. Th17, Tfh and CD16- monocyte had more than 1,000 DEGs, and pathway analysis was done for these. The top pathway enriched among the upregulated mRNAs in Th17 and Tfh was oxidative phosphorylation pathway (p-value<$1.0*10^{-23}$ and <$1.0*10^{-12}$). The most activated pathways were sirtuin signal pathway in Th17 (z-score 3.5, p-value<$1.0*10^{-9}$), leukocyte extravasation pathway in Tfh (z-score 3.5, p-value<$1.0*10^{-6}$), and iNOS signal pathway in CD16- monocyte (z-score 2.3, p-value<$1.0*10^{-6}$). [Conclusions] The study implies that several pathways related to cell metabolism are involved in the pathogenesis of AAV.

P1-232

Treatment outcome of the ANCA-related vasculitis with Rituximab in our hospital

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Conflict of interest: None

[Object] Cyclophosphamide (CY) is recommended for standard treatment of the induction of remission therapy with ANCA-related vasculitis (AAV) guidelines 2017. Similarly, in Rituximab (RTX), use is accepted by a case judged AAV induction of remission to be appropriate. About use experience of RTX for AAV in our hospital, we compared it with CY, retrospectively. [Methods] We divided 25 AAV patients that induction of remission therapy was performed from 2013 through 2017 11 RTX group,14 CY group and investigated it on the basis of medical records. [Results] Average age were 73.6 years in the RTX group and 68.9 years old in the CY group. It included 17 microscopic polyangitis (MPA), 6 granulomatosis with polyangiitis (GPA), 2 eosinophilic granulomatosis with polyangitis (EGPA). One of 11 cases (9%) recurred in the RTX group. On the other hand, nine of 14 cases (64%) in the CY group. (P=0.035) It accepted significant difference by the Log Rank analysis about relapse. [Conclusions] In this study, as for the RTX group, the possibility that it was the induction of remission that was effective for intractable AAV which recurred by CY therapy was suggested. It will be necessary to increase cases, and to investigate results in a long-term thing observing for the remission maintenance in RTX.

P1-233

Trigeminal neuralgia in otitis media with ANCA-associated vasculitis (OMAAV): three case reports

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Conflict of interest: Yes

We describe 3 cases of OMAAV with trigeminal neuralgia. **Case 1**: A 75-year-old woman demonstrated complete hearing loss. She also had left facial nerve palsy and trigeminal neuralgia, which were promptly improved after the treatment with methylprednisolone (mPSL) pulse therapy and following high dose prednisolone (PSL). Partial remission of hearing loss was achieved after additional administration of intravenous cyclophosphamide. **Case 2:** A 29-year-old woman, who had otalgia, bilateral facial nerve palsy and trigeminal neuralgia, was orally treated with high dose PSL after mPSL pulse therapy. She promptly achieved complete remission. **Case 3:** A 77-year-old woman with otalgia, deafness, bilateral facial nerve, right trigeminal neuralgia, and headache demonstrated hypertrophic pachymeningitis (HP). High dose PSL was orally administered after mPSL pulse therapy. Trigeminal neuralgia and headache promptly disappeared. The radiographic finding of HP also improved. All patients demonstrated trigeminal neuralgia; meanwhile, favorable outcome of it was obviously demonstrated. The trigeminal nerve anatomically exist near the internal ear, suggesting the pathogenesis of trigeminal neuralgia may be associated with inflammatory dissemination from otitis media as well as direct influence of vasculitis.

P1-234

Myalgia on lower legs as the initial symptom in ANCA-associated vasculitis

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Conflict of interest: None

We report 5 patients having myalgia on their lower legs as the initial symptom of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). Mean age of them (one man and 4 women) was

69.6±6.4. Four patients were diagnosed as microscopic polyangiitis and granulomatosis with polyangiitis corresponded to the diagnosis of one patient. All patients indicated myalgia as well as elevated levels of C-reactive protein (CRP) within normal range of serum creatine kinase. MPO-ANCA positivity was shown in 3 patients, and PR3-ANCA positivity in one patient. Another patient indicated both MPO- and PR3-ANCA positivity. Three patients had interstitial pneumonia, and 3 had renal involvement. Muscle MRI demonstrated high intensity signal on a lower leg in all patients. Muscle MRI demonstrated high intensity signal on a lower leg in all patients. Muscle biopsy was performed in 4 patients, resulting in the pathological findings of vasculitis. All patients were treated with high dose prednisolone (PSL); however, intravenous cyclophosphamide was additionally required in one patient because of refractory to PSL alone. All patients achieved a remission. The proven vasculitis in muscle biopsy based on the muscle MRI finding was useful for the diagnosis of AAV even in early phase of disease.

P1-235

Predictors for remission, relapse and mortality in patients with ANCA associated vasculitis patients: A multi-center study of 154 patients

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Conflict of interest: None

[Object] We investigated factors associated with remission, relapse and mortality of patients with AAV in a multi-center cohort study. [Methods] A total of 154 consecutive patients with AAV diagnosed in 13 centers were recruited since 2012. The predictive values of variables associated with remission, relapse and mortality were analyzed. [Results] 21 cases of EGPA, 40 GPA, 75 MPA and 17 unclassified AAV were recruited. The average ages were 57, 67, 71 and 73 years old respectively. During follow-up of a median duration 676 days (range 9-2200 days), 112 out of 154 cases got remission (73%), 28 out of 112 cases relapsed (25%) and 21 out of 154 cases died (13.6%). Independent predictors of remission were the existence of lower respiratory tract infections ($p<0.005$), the absence of heart disease and higher eGFR ($p<0.05$). An independent predictor of relapse was the existence of PR3-ANCA ($p<0.05$). Independent predictors of mortality were higher age, lower eGFR ($p<0.005$), the underachievement of remission in 6 months ($p<0.01$), pulmonary UIP pattern and PR3-ANCA ($p<0.05$). [Conclusions] Prognoses of AAV patients were dependent on the varieties of factors. It is essential to plan the careful treatment strategy based on their backgrounds for the goal of speedy remission induction.

P1-236

Examination of 5 cases administerd immunoglobulin high dose therapy (IVIG) for multiple mononeuritis in ANCA associated vasculitis

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Conflict of interest: None

[Object] We examined the effect of the IVIG on multiple mononeuritis complicated with ANCA associated vasculitis in this hospital. [Methods] Sex ratio is men one case, women four cases, the age of the cases is 36-67 years old. The period from the onset time to start of therapy is two weeks-nine months, and the period from start of therapy to IVIG induction is two weeks-six months. As for the disease, Eosinophilic Granulomatosis with Polyangiitis is four cases, Granulomatosis with Polyangitis is one case. We cure all cases in PSL and various immunosuppressant [azathioprine (n=3), tacrolimus (n=1), rituximab (n=1)]. Dosage interval of IVIG is an average of 30 weeks. As for the number of dose, once is three cases, four times is two cases. [Results] As for the case which we gave IVIG four times, we showed clear improvement of neurologic symptoms at the second time. In all cases, serious side effect was not found, we do not detect the exacerbation of neurologic symptoms. It is said that to administer IVIG repeatedly to multiple mononeuritis complicated with ANCA associated vasculitis improve neurologic symptoms. [Conclusions] IVIG is effective in ANCA associated vasculitis. We add discussion from literatures and consider the effect of IVIG on multiple mononeuritis of ANCA associated vasculitis.

P1-237

Efficacy and safety of Rituximab induction therapy for ANCA associated vasculitis (AAV)

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Conflict of interest: None

[Objective] To investigate the Efficacy and safety of Rituximab induction therapy for Anca associated vasculitis. [Methods] AAV patients who were started initial treatment with RTX in our hospital from Jun 2013 to July 2017 were enrolled. We retrospectively analyzed clinical background, treatment, relapse rate, incidence rate of infection. [Results] A total of 10 patients (GPA 8, MPA2) were enrolled. Mean age was 75 years. Organ symptoms were below; Cutaneous 2, Mucous membranes/eyes 3, ENT 6, Nose/paranasal sinus 3, IP 3, DAH 1, RPGN 8 (mean Creatinine:1.87 mg/dl), Peripheral nerves 3. Remission induction therapy; average PSL 0.94 mg/kg, Steroid pulse 3, IVCY 4 (average total dose 0.64g), IVIG 1 and plasma exchange 2. Immunosuppressant for maintenance; AZP 7 cases and MMF 1. One case was got maintenance dialysis. Average PSL dose at the time of achieve remission was 0.42mg/kg. Two cases had relapse with RPGN, and both achieved re-remission fortunately. During this study period, the rate of patients with opportunistic infections (CMV, several Fungi) was over 60%. [Conclusion] Aged Patients with AAV and with RPGN tended to be administered with RTX for induction remission therapy in our hospital. They were good prognosis, but the rate of opportunistic infection was higher than predicted.

P1-238

A case of otitis media with ANCA-associated vasculitis and intestinal hemorrhage that was difficult to differentiate from giant cell arteritis

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Conflict of interest: None

[Case] A 61-year-old man was admitted to our hospital because of bloody bowel discharge with abdominal pain, binaural hearing loss, double vision, fever, and headache. His laboratory data were as follows: WBC, 15,000/μl; CRP, 20.2 mg/dl; MPO-ANCA, 10.1 U/ml; and PR3-

ANCA, 13.2 U/ml. Otitis media (OM) and mixed hearing loss in both ears were observed, which were thought to be OM with ANCA-associated vasculitis (AAV). Colonic endoscopy revealed a nonspecific colitis almost throughout the large intestine, and inflammatory mucosa and small intravascular fibrin thrombus were observed in the mucosal tissue image. In contrast, magnetic resonance imaging and ultrasonography revealed the wall thickening of the bilateral carotid artery. On the basis of these findings, giant cell arteritis (GCA) was also suspected. Soon after the administration of prednisolone (PSL) (60 mg/day), all abnormalities except the left-ear deafness recovered. In the superficial temporal artery (STA) biopsy that was performed 5 days after PSL administration, no abnormality was found in the STA. However, inflammatory findings were observed in the surrounding small vessels. [Clinical Significance] In the case of vasculitis of the head and neck region, AAV is sometimes difficult to differentiate from GCA.

P1-239

A case of neck pain as an initial symptom in ANCA-associated vasculitis

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Conflict of interest: None

A 79-year-old woman developed a two week history of neck pain, sensory disorders and dysuria. She was admitted to our hospital because of worsening of neck pain and abrupt full quadriplegia. MRI revealed dura matter thickening and cervical spinal cord compression between C3 and C6 level, and decompression-removal surgery was performed. The exfoliated tissue looked not hemorrhagic or tumorous but scar-like. Although quadriplegia gradually improved after surgery, she showed sustained fever and elevated CRP levels. The pathological findings of exfoliated tissue were inflammatory cell infiltration including neutrophils and proliferation of collagen fibers, suggesting hypertrophic pachymeningitis (HP). Hematuria and acute renal failure with various urinary cast occurred, and the serum level of MPO-ANCA was elevated at 239 RU/mL. We diagnosed her as HP and rapidly progressive glomerulonephritis due to ANCA-associated vasculitis (AAV). Intravenous methylprednisolone (500 mg) and cyclophosphamide (500 mg) were initiated and followed by oral prednisolone (40 mg). Renal failure quickly improved and dural thickening resolved in one month. Spinal cord lesions are rare in HP. This is the first case of AAV with neck pain as an initial symptom due to HP in Japan.

P1-240

A case of secondary membranous nephropathy with ANCA associated vasculitis

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Conflict of interest: None

[Object] We report a case of secondary membranous nephropathy (MN) with ANCA associated vasculitis (AAV). Case 1; a 82-year-old man with hypertension developed acute kidney injury, proteinuria, and hematuria with RBC cast 1 year ago. p-ANCA was 71 IU/ml, High dose methylprednisolone and Cyclophosphamide was initiated for AAV as induction therapy. Azathioprine for maintenance therapy was stopped due to hepatotoxicity, He developed flare when he was on prednisolone 10 mg/day, so underwent the renal biopsy. The specimen shows 20 % of all glomeruli with segmental sclerosis and fibrous crescents. Other glomeruli doesn't show any other findings that consist with AAV. Electron microscopic analysis didn't revealed apparent subepithelial and mesangial electron dense depositions (EDD), thickening of glomerular basement membrane (GBM). The scar of EDD which have little distances from GBM is found to be the possibility of secondary MN. His proteinuria gradually subsided with rituximab for AAV. [Clinical significance] Secondary MN based on AAV might be caused by MPO-MPO-ANCA immune-complex granular deposition along GBM. Immune-complex and pauci-immune mechanism might alter the pathogenic action of MPO. Refractory proteinuria due to AAV should be considered the possibility of secondary MN.

P1-241

A case of anti-neutrophil cytoplasmic antibody-associated vasculitis with periaortitis diagnosed by pathology

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Conflict of interest: None

An 81-years old man with high fever and general malaise. Abdominal CT levealed wall and periaortic soft tissue thickening of the right iliac artery. He admitted to cardiovascular surgery on suspicion of infectious aneurysm. Antibiotics is ineffective, and the blood culture was negative. The renal function gradually got worse. Eleventh day after hospitalization, graft replacement of iliac artery was done. Granulomatous fibrinoid necrotizing vasculitis of vasa vasorum was pointed out in the operation specimen. Furthermore blood examination showed positivity for MPO-ANCA. He was made a diagnosis of ANCA-associated vasculitis (AAV) complicated periaortitis, and was enrolled rheumatology. Owing to 60mg/day of prednisolone, inflammatory symptoms were disappeared, and renal function and urinalysis improved. AAV is rarely complicated with periaortitis. But it's unclear whether the small vessel vasculitis happened to aortic vasa vasorum or complication of large vessel vasculitis, because biopsy on the lesion is difficult. This time, We experienced a case of AAV diagnosed with an aortic pathology. This is regarded as valuable case, so we report it and summarize the literature.

P1-242

4 cases of otitis media ANCA associated vasculitis

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Conflict of interest: None

[Background] Recently, it has been reported that the otitis media complicated ANCA associated vasculitis (AAV) was treated as the otitis media ANCA associated vasculitis (OMAAV). It has been suggested that hearing prognosis is depended on time of initiation of therapy, and earlier diagnosis for OMAAV is needed. We report 4 cases of OMAAV and those clinical feature and course of treatment with bibliographic consideration. [Case 1] 73 year old woman. The patient initially presented with fever, arthritis, and a feeling of fullness in the ear. Therapy with PSL25mg was started and therapy produced a complete response. [Case 2] 63 year old woman. The patient initially presented with fever, cough, headache, and a feeling of fullness in the ear. Patients achieved a complete response after pulse steroid therapy. [Case 3] 60 year old woman. The patient initially presented with otorrhea. Findings led to a diagnosis of otitis media with effusion. Therapy with PSL20mg was started and therapy produced a response. [Case 4] 79 year old woman. The patient initially presented with hearing loss. The patient was found to have acute exacerbation, and referred to our hospital for further examination. Therapy with PSL25mg and AZA50mg was started but therapy didn't produce a complete response.

P1-243

A case report of difficult diagnosis in the patient with ANCA-associated vasculitis

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Conflict of interest: None

[Case] A 82-year-old female had lumbago and high fever. She was admitted to hospital for urinary tract infection. It was improved by antibiotics. There was still lumbago and both meralgia, and so she could't walk. There was lumbar spinal canal stenosis on MRI without surgical indication by an orthopedist. There was high fever once again, and both

meralgia. It was considered a possibility of polymyalgia rheumatica. She took prednisolon 20mg/day, and the symptom was improved. High fever was seen once again and both buttock pain was worse. The dose is elevated to 30mg/day and the symptom was improved. PR3-ANCA was positive. She was diagnosed with multiple mononeuropathy of both lower limbs on nerve conduction studies by a neurologist. She was diagnosed with ANCA-associated vasculitis from clinical course. [Clinical Significance] The infection preceded and so urinary findings improved by antibiotics. High fever was seen once again and inflammatory findings continued. Because of the elderly, high fever and both meralgia, there was a possiblity of polymyalgia rheumatica. It was difficult to diagnose. It was needed to consider a possibility of C-ANCA-associated vasculitis as the cause of elderly fever of unknown origin and both meralgia by C-ANCA positive and multiple mononeuropathy.

P1-244

ANCA-Associated Vasculitis Complicated with Malignant Lymphoma

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Conflict of interest: None

A 53-year-old woman was accepted fever from October 2016. Antibiotics did not reduce a fever for a month. Because of a high titer of PR3-ANCA, ANCA-associated vasculitis was suspected. Although she was followed without therapy, proteinuria and granular cast appeared in the urine. Therefore, renal biopsy is performed in January 2017. As a result, there was no crescent formation, however, tubulointerstitial inflammatory cell and a pauci-immune type was found. Therefore, she was diagnosed with ANCA-Associated vasculitis and treated using pulse therapy of intravenous cyclophosphamide and prednisolone. Because of treatment-resistant, rituximab and various immunosuppressive drugs as additional treatment were used. However, these therapy did not induce a strong inflammatory response. Thereafter, pancytopenia appeared and soluble interleukin-2 receptor titer was increased. There was a large atypical lymphoid cell by bone marrow aspiration, started chemotherapy on the suspicion of a malignant lymphoma. The last diagnosis becomes diffuse B cells-related lymphoma and it follows good progress.

P1-245

A case of pustular psoriasis needed to distinguish ANCA-related vasculitis

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Conflict of interest: None

[Patient] a 71-year-old man [Chief complaint] fever, lower limb weakness [Present illness] The patient developed papules with pustules in both legs at age 61. He was diagnosed with pyoderma gangrenosum (PG) by skin biopsy. He also developed scleritis 6 months before the first consultation. Steroid therapy was initiated and scleritis was improved. He presented with 2 weeks of fever and lower limbs weakness. The fever and inflammatory reactions were refractory to antibiotic therapy. His blood exam revealed positive ANCA and ANCA-related vasculitis was suspected. At the time of admission, he showed scales with pustules in the limbs, hip and trunk. Skin biopsy specimens showed parakeratosis, microabscess formation in the dermis and lymphocyte infiltration around the blood vessel in the papillary layer. In conjunction with general symptoms and systemic eruptions, we diagnosed him with Pustular psoriasis (PP). He was successfully treated with etretinate, secukinumab and GMA. [Discussion] Review of the skin biopsy specimen at 61 years old revealed that it is not typical for PG, but rather compatible with psoriasis vulgaris (PV). Administration of steroids might have induced transition from PV to PP. We discuss the implications of ANCA for the pathological mechanism of PV and PP.

P1-246

A case report: Cogan's syndrome with lower limbs vascular disorder and histopathological findings of vasculitis in skin biopsy

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Conflict of interest: None

Cogan's syndrome (CS), a rare disease, occurs primary in young adults, and typically presents with intestinal keratitis and Meniere's disease like episode developing within several months of each other's. Although histopathological examination of corneal tissue and cochlea showed lymphocytic and plasma cell infiltration, to our knowledge, no repot have described similar findings in the skin biopsy. We report a case of Cogan's syndrome, and histlogical findings of vasculitis in skin biopsy. A 65-year-old female has lower legs pain, right ear hearing loss with dizziness, and scleritis. We found erythema, nodules and cyanosis on her legs. Histopathological examination of skin biopsy of her lower extremity erythema showed plasma cells and lymphocytes infiltration in the arterial wall of subcutaneous fat tissue. We diagnosed CS, and started corticosteroid therapy for her. But we could not preserve her lower limbs ischemia progressed, expanded the intravascular balloon but eventually the left lower knee and the right leg cleft cutted. We added methotrexate and Tocilizumab, but these treatments were ineffective and were canceled. Next, we initiated combination therapy with cyclophosphamide and cyclosporine, and could bring her into introduction of remission.

P1-247

A case of atypical Cogan syndrome with large vessel vasculitis: successful treatment with Infliximab

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Conflict of interest: None

[Case] A 57 year old woman was treated as rheumatoid arthritis, but her arthralgia gradually worsened and C-reactive protein elevated. She was hospitalized because of abdominal pain, diarrhea and headache with marked inflammatory reaction. Antibacterial agents were ineffective. She had vertigo and ocular pain during the course. She was diagnosed as atypical Cogan syndrome at the basis of the following: (1) Eye symptoms (central retinal vein occlusion, necrotizing scleritis, keratitis), (2) Vessel wall thickening of the aorta and major branches with FDG uptake on PET/CT, (3) Necrotizing medium-sized vasculitis and panniculitis from skin biopsy. She partially improved after methylprednisolone pulse therapy, but vertigo remained. After Infliximub therapy, further improvement of vertigo was obtained. [Discussion] Cogan syndrome is a rare systemic vasculitis that causes non-syphilitic interstitial keratitis and vestibular auditory symptoms similar to Meniere's syndrome. Identifying affected blood vessels is important for the diagnosis of systemic vasculitis. Efficacy of Infliximab in the treatment of Cogan syndrome has been reported, and early infliximab treatment was effective for steroid-resistant vertigo in this case. We report detail of this case with review of the literature.

P1-248

The Successful Treatment of Infliximab in A Patient with Adult-onset Kawasaki Disease who were showing an Inadequate Response to Intravenous Immunoglobulin

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Conflict of interest: None

Kawasaki disease (KD) is an acute febrile illness that predominantly affects children less than 5 years of age. KD is characterized by systemic

inflammation in all the medium-sized arteries. High-dose intravenous immunoglobulin (IVIG) and acetylsalicylic acid (ASA) are standard treatment for KD. Recently, some reports demonstrated that the efficacy of infliximab (IFX) for patients with refractory KD. Adult-onset KD (AKD) is rare. There are only about 100 case reports published for the medical literature. Here we present a case of AKD with treatment of IFX. A previously healthy 24-year-old man presented with fever, diarrhea and erythema of his lower limbs. He was admitted to the local hospital. Blood test showed the elevation of AST/ALT/LDH/CRP. Intravenous antibiotics were administered without any improvement. On day 4, the patient was transferred to our hospital, and had conjunctivitis and right lower abdominal pain. On day 11, membranous desquamation of the fingertips occurred. Subsequently, echocardiogram revealed the coronary artery aneurysms. Then, he was diagnosed as AKD. On day 18-19, the patient was administered high-dose IVIG and ASA. However, his fever persisted. On day 21, he was administered treatment of IFX. Then, his symptoms had recovered.

P1-249

Muscle biopsy proved rheumatoid vasculitis

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Conflict of interest: None

[Case] An 85-year-old woman with rheumatoid arthritis (RA) was admitted to our hospital for evaluation for refractory polyarthritis, fever and peripheral dysesthesia. She had a three-year history of RA and had been in her moderate disease activity under adalimumab treatment. She needed to have oral prednisolone (PSL) at least 5 mg per day to relieve her symptoms. On admission, a high-grade fever and scleritis in her eyes were observed. There was no target organ damage such as interstitial pneumonia, nephropathy or skin ulcer. Laboratory data showed positivity of immune complex (C1q 8.3 μg/ml), low complement (C3 60 mg/dl, C4 4 mg/dl), CRP 30.14 mg/dl and RF 1,186 IU/ml. MPO-ANCA and PR3-ANCA were negative and CPK was within normal range. A test for peripheral nerve conduction velocities was normal. The biopsy of the vastus lateralis muscles revealed lymphocyte infiltration in the wall of small arteries, and then she was diagnosed as rheumatoid vasculitis (RV). 40 mg PSL per day was administrated and her symptoms were resolved. [Conclusions] A muscle biopsy was useful to diagnose vasculitis in small arteries and it should be considered among patients suspected RV.

P1-250

Autopsy findings of severe polyarteritis nodosa treated with tocilizumab and rituximab

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Conflict of interest: None

A 62-year-old male was suffering from fever, tonsil swelling and laryngeal edema two years ago. These were improved by glucocorticoid (GC) treatment, GC was continued because autoimmune diseases were suspected. Along with GC tapering, he had erythema nodosum, scleritis, and right testicular swelling, and then he was referred to our hospital. His clinical course suggested the diagnosis of polyarteritis nodosa (PN) although pathological examinations could not be performed. Because immunosuppressants such as cyclophosphamide, methotrexate, and tacrolimus failed to achieve remission, the dosage of GC could not be tapered. Therefore, we selected rituximab (RTX) treatment to refractory PN, but skin nodules on his extremities appeared four months after RTX therapy. Skin biopsy revealed vasculitis in panniculus. We judged RTX as ineffective, and next started tocilizumab (TCZ). Two days after TCZ therapy, he complained of dyspnea and was diagnosed with legionella pneumonia. Despite the intensive care, respiratory failure was not improved and he died on 38th day after admission. Autopsy showed intra-bronchus, alveolar hemorrhage and medium vessel vasculitis in almost all organs. PN is known to be more severe than other vasculitis, and the autopsy in our case also confirmed the issue.

P1-251

A case of primary central nervous system vasculitis who presented with ataxia and cognitive disorder and diagnosed by MRI

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Conflict of interest: None

A man in his 70s was admitted with a 1-month history of throbbing headache. Because the erythrocyte sedimentation rate was elevated, the most likely diagnosis was giant cell arteritis. 5 days after the admission, he suddenly developed ataxia and cognitive disorder. A temporal artery biopsy and ultrasound showed negative findings. MRI of the brain showed hyperintense signals on FLAIR sequence within multiple brain sulci. CSF analysis showed 133 μL white blood cells and protein concentration of 79 mg/dL. Neck MRI with gadolinium demonstrated wall enhancement of vertebral arteries. Cerebral angiography showed stenosis in basilar artery. He was diagnosed primary central nervous system vasculitis and treated with high dose intravenous methylprednisolone followed by oral predonisone 60 mg/day, and intravenous injections of cyclophosphamide. The MRI features was the key element in making the diagnosis. Early diagnosis and initiation of therapy are necessary to avoid irreversible CNS events.

P1-252

Two cases of IgA AS

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Conflict of interest: None

[Case 1] A 74-year -old man. He showed urin occult blood and proteinuria 26 year ago, and it was diagnosed as IgA nephropathy by kidney biopsy. Further he has been showedn polyarthralgia for 17 years, then diagnoed with seronegative rheumatoid arthritis, but he complained severe low back paein three years before, and showed bamboo spine and sacroiliac arthritis in XP findings, and was diagnosed with AS. [Case 2] A 80-year-old man was admitted to our hospital becaused of purpura in upper and lower lims. He also shown joint pains in his Knees, hand, and ankles, and was diagnosed with IgA vasculitis. He was treated with hugh dosages of glucocorticoids, initially he showed improvement in both purpura and polyarthralgia, but exacerbation was showen in both symptoms along with tapering og GC. Further he was found the and bamboo spine in his XP findings, and was diagnosed. [Results and Discussion] Although complications of IgA nephropathy and AS are frequently shown, the coplication of IgA vasculitis is rarely found in AS. We experienced both types of cases, and considered the relationship between IgA nephropathy and IgA vasculitis in AS.

P1-253

A case of solitary arteritis complicated in Crohn's disease

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Conflict of interest: None

A 15-year-old female was admitted to our hospital because of left femoral pain in May X. She had been diagnosed with Crohn's disease. in January X and had been prescibed Budesonide 9 mg and Mesalazine 1500 mg. but the disease activity had been still high. From around February of the same year without particular incentive, left femoral pain appeared and walking became impossible, and that, iInflammatory response also had a tendency to exacerbate and she visited the our department in

May X. Both Contrast CT and MRI showed the inflammation of left femoral artery. Solitary arteritis was diagnosed and Prednisolone (PSL) 50 mg was started as a treatment for both Crohn's disease and solitary arteritis, improvement of left femoral pain and inflammation were promptly obtained. PSL gradually decreased in the following course, Azathioprine 25 mg and Infliximab 5 mg / kg were added and the current PSL has been reduced to 7.5 mg, but the disease activity of both Crohn's disease and solitary arteritis remains calm. In inflammatory bowel disease, vasculitis may be complicated (Semin Arthritis Rheum. 2016, 45, 475-482). If there are inflammatory findings that can not be explained only by the course of inflammatory bowel disease, the presence of vasculitis must be considered.

P1-254

A case of thrombotic microangiopathy merged with adult onset Still's disease

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Conflict of interest: None

Thrombotic microangiopathy (TMA) is a rapidly progressive and fatal diseases that described as the association of microangiopathic hemolytic anemia, thrombocytopenia, and an organ injury, especially in the kidney. This case report describes a case of patient with adult onset Still's disease merged with TMA. Case: A 50 year-old male presented with high fever, polyarthralgia, lymphadenopathy and eruption. His blood examination showed hyper-ferritinaemia (4,928 ng/mL) and inflammation (CRP 2.08 mg/dL). He has been treated as adult onset Still's disease (AOSD) with 1mg/kg/day of prednisolone. After 9 days, his thrombocyte has decreased. He was diagnosed as having TMA merged with AOSD on grounds of his thrombocytopenia, renal dysfunction, anemia and confirmation of schizocytes at peripheral blood. He has not gotten better after treatment with steroid pulse and intravenous cyclophosphamide therapy. After rituximab and plasma exchange with hemodialysis on his therapy, the patient's condition has taken a turn for the better. And now, the state of his condition has been unnecessary of dialysis, and taking 10 mg/day of prednisolone.

P1-255

Case of livedo vasculopathy treated as rheumatoid arthritis

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Conflict of interest: None

<Case> A 48-year-old Japanese male presented with a 2-year history of lower leg edema and 1-year history of pain and numbness on legs. At first, he visited orthopedi csurgery and was examined. Laboratory findings follow as; RF (-), ANA (-), anti-CCP antibody (-), P-ANCA (-), C-ANCA (-), CRP 4.93mg/dl, ESR 56mm/h. No apparent synovitis or arthritis with MRI. Since rheumatoid arthritis or RS3PE syndrome were suspected, he was treated with prednisolone 10mg, MTX and tacrolimus, but his pain was not changed. He was referred for our department to assess the his leg pain. On dermatological examination, livedo reticularis and atrophie branche lesions spread on the legs, especially on the ankles and feet. Histopathological examination revealed intraluminal thrombosis and segmental hyalinization of dermal vessels. Based on these findings, he was diagnosed as livedo vasculopathy, and colchicine administration was added. Then, CRP almost became negative, numbness and pain improved. <Clinical Significance> Livedo vasculopathy is not well known outside of dermatology, and often diagnosis is difficult without skin biopsy. It was considered that colchicine administration was useful for liveo vasculopathy in our case. We also examined the usefulness of colchicine in the treatment of vasculitis.

P1-256

Relapsing Polychondritis with Uveitis which was Refractory to Tumor Necrosis Factor-Alpha Antagonist

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Conflict of interest: None

Relapsing polychondritis (RPC) is an immune-mediated condition associated with inflammation in cartilaginous structures and other tissues throughout the body, particularly the ears, nose, eyes, joints, and respiratory tract. Here we report a patient with RPC with uveitis which was refractory to adalimumab (ADA) but had a good response to tocilizumab (TCZ). A 44-year-old man with diabetes presented with congestion, pain, photophobia and blurred vision in his right eye. He also developed swellings at his root of nose and auricles. By using McAdam's Criteria, he was diagnosed as RPC. Furthermore, anti-type II collagen antibody was positive. He was refractory to glucocorticoid monotherapy (1mg/kg, prednisolone equivalent), so ADA was added. But it was not effective for uveitis and switched to TCZ. TCZ markedly improved his ocular symptoms. It was suggested that TCZ might be effective to RPC, particularly to anti-type II collagen antibody positive patients.

P1-257

A case of rheumatoid arthritis who developed IgA vasculitis during Abatacept therapy

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Conflict of interest: None

[Background] There are some reports describing the development of autoimmune diseases during the treatment with Abatacept. [Case Presentation] Fifty-nine years old woman was admitted to our hospital because of sustained proteinuria. She had been treated for RA for 15 years. Abatacept was initiated 3 years ago. Three months before admission to our hospital, purpura appeared on her lower legs and thighs. Skin biopsy revealed IgA vasculitis and administration of 20 mg/day of prednisolone improved purpura. However, proteinuria increased from (±) to (2+) and she was admitted to our hospital. Clinical data were as follows: urinary protein/Cr, 3.41 g/gCr; urinary RBC, 8 cells/hpf; serum Cr, 0.56 mg/dL. Renal biopsy revealed mesangial proliferative glomerulonephritis with cellular crescent formation. Immunofluorescent staining showed IgA and C3 depositions. The diagnosis of purpura nephritis was made. Abatacept was discontinued and methylprednisolone pulse therapy was initiated. Urinary protein became less than 0.5 g/gCr within a month and hematuria also disappeared. [Discussion and Conclusion] Our case would be the second case of IgA vasculitis during the treatment of Abatacept. Further accumulation of patients is needed to clarify whether this is accidental or not.

P1-258

A case of Goodpasture syndrome with secondary thrombotic microangiopathy

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Conflict of interest: None

<Case> A 73-year-old woman was admitted due to oliguria and general malaise. Her blood examination revealed hemolytic anemia with thrombocytopenia, showing a large number of schistocytes, and severe renal dysfunction (sCr 21mg/dL). In addition, the titer of anti-glomerular basement membrane (GBM) antibody was highly elevated and a disintegrin and metalloprotease with a thrombospondin type-1 motif, member 13 (ADAMTS13) activity was decreased without anti-ADAMTS13 antibody. Shiga toxin-producing E.coli wasn't detected in her fecal culture. The second day of the admission, she had hemoptysis and her chest ra-

diograph revealed bilateral pulmonary consolidation. Thus, she was diagnosed with Goodpasture syndrome with secondary thrombotic microangiopathy (TMA). After starting plasma exchange and steroid therapy, alveolar hemorrhage and bicytopenia were resolved, but renal dysfunction persisted and a periodic hemodialysis was continued. <Conclusion> We experienced a case of Goodpasture syndrome with secondary TMA. Previous reports indicated that endothelial cell damages associated with anti-GBM antibody might induce organ injuries, contributing to TMA. In this case report, we discuss more about its clinical management and pathophysiology.

P1-259

A case of IgA vasculitis complicated with gastric cancer

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Conflict of interest: None

A 79 year-old man presented with a 2-week duration of watery diarrhea. He was referral to our hospital due to 3 days abdominal pain. A physical exam revealed epigastric tenderness and lower extremity palpable purpura. Laboratory data was WBC 14700 /μL, CRP 5.79 mg/dL, Cre 2.3 mg/dL, urinary RBC >100/HPH, protein 11.4 g/gCr. Abdominal CT revealed duodenal wall edema. Possible diagnosis of IgA vasculitis (IgAV) complicated with duodenitis and nephritis prompted to administration of PSL 50 mg/day on 3rd day. On 5th day, gastrointestinal endoscopy revealed an erosion in the stomach and duodenum and irregular ulcerative lesions in the anglar region. Skin biopsy revealed leukocytoclastic vasculitis. Conversely, stomach ulceration revealed moderately differentiated adenocarcinoma. Despite immunosuppressive therapy, renal function deteriorated (Cre 5.8 mg/dl), and hemodialysis was initiated On 27th day. On 48th day, he was discharged after PSL was tapered up to 30mg/day. The gastric cancer was conservatively followed up because of his disagreement with surgical therapy. We report a rare case of IgAV complicated with gastric cancer. Although the relationship between IgAV and cancer remain unknown, thorough malignancy screening may be necessary especially for any old patients with IgAV.

P1-260

A case of IgA vasculitis complicated with alveolar hemorrhage

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Conflict of interest: None

[Case] Sixty-four-year-old male had suffered from fever and dyspnea for one month. He saw a local doctor. Fine crackles were auscultated in the back. Urinalysis showed urine protein 3+, urine occult blood 3+. WBC was 13200 /μl, CRP 10.72 mg/dl. Chest X-ray showed reticular opacity. He was diagnosed as pneumonia with some urinary abnormalities and was referred to our hospital. Chest computed tomography revealed interstitial pneumonia. Serum creatinine was 1.23 mg/dl, IgA 347 mg/dl and MPO-ANCA, PR3-ANCA and antinuclear antibody were negative. IgA vasculitis was suspected from urinary findings. He was hospitalized and received mPSL 500 mg for 3 days and PSL 60 mg/day. His dyspnea and urinary abnormalities were promptly relieved and he was diagnosed as IgA vasculitis by renal biopsy. On the 13th day, he developed a pneumothorax. He was operated to treat the pneumothorax on the 26th day because it was not healed conservatively. From the specimen of his lung, the cause of his pneumothorax was pathologically shown to be alveolar hemorrhage. [Clinical meaning] IgA vasculitis is a frequent disease. However, complications of alveolar hemorrhages are very rare and lethal, so we should know the possibility of alveolar hemorrhage with IgA vasculitis.

P1-261

A case of polyarteritis nodosa-like vasculitis associated with myelodysplastic syndrome

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Conflict of interest: None

A 73-year-old male had high fever and malaise. He was diagnosed with combined pulmonary fibrosis and emphysema at previous hospital. Although he was treated with 30mg/day of prednisolone, the symptoms were not improved. When he visited our hospital, he had systemic erythema, high count of eosinophils and platelets, and an elevation of LDH and soluble IL-2 receptor. Bone marrow biopsy showed hyperplastic bone marrow (especially eosinophilic myelocytes were increased), but it did not confirm the diagnosis. He was temporarily diagnosed as eosinophilic leukemia by the slightly increased blast cells, then he was treated with 100mg/day of imatinib and 50mg/day of prednisolone. During his course of treatment, he complained acute abdominal pain and nausea. Contrast CT showed extensive ischemic lesions in the intraperitoneal and retroperitoneal organs, then he died 3 hours after onset of stomach symptoms. His autopsy revealed superior mesenteric artery thrombosis and widely ranged intestinal necrosis. Pathological specimen confirmed the diagnosis as polyarteritis nodosa.A chromosomal abnormality related to myelodysplastic syndrome (MDS) was detected in peripheral blood analysis, that suggested a cancer-associated vasculitis based on MDS.

P1-262

Autoantibody production in the salivary glands of Sjogren's syndrome

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Conflict of interest: None

[Object] Sjögren's syndrome is an autoimmune disease characterized by lymphocyte invasion of exocrine glands. This study aims to estimate the relationship between infiltrating B cells and pathophysiology by examining the reactivity of invading B cells in salivary glands. [Methods] Labial gland biopsy specimen was minced and treated by collagenase to make single cells, and $CD19^{+}CD38^{+}$ cells were sorted. Single cell cDNA library was prepared using C1 system or FACS. Variable regions of H and L chain were cloned into expression vector, and expressed as monoclonal antibodies. Finally, we examined their reactivity to self antigens. [Results] A total of over 240 antibodies were prepared from 9 specimens, that included 11 anti-SSA antibodies and 8 anti-SSB antibodies. All 5 serum SSA positive samples and 2 out of 3 serum SSB positive samples contained anti-SSA/B antibodies respectively, and its ratio was 8.0 and 8.5% respectively. The usage of VH of anti-SSA/B antibodies were biased into V3-23 and V3-30. [Conclusions] The lymphocytes invading salivary gland contained SSA/B reactive B cells, and the autoantibody profiles in the serum and localized lesions were related. This result was suggested that autoantibodies are produced in the lesion and are involved in pathophysiology.

P1-263

Mast cells are involved in the pathogenesis of Sjogren syndrome by inducing tissue fibrosis

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Conflict of interest: None

[Object] We examined whether mast cells play a critical role in the pathogenesis of Sjogren syndrome. [Methods] Labial salivary gland samples were collected from 13 individuals with primary Sjogren syndrome and 5 with sicca syndrome. We used immunohistochemistry to identify and quantify tryptase-positive mast cells and vimentin-positive fibroblasts. Fibrous tissue was identified by using EVG stain. Human mast cell line 1 (HMC-1) cells were co-cultured with pulmonary fibroblasts. Cytokine expression in these cells was evaluated by RT-qPCR. [Results] The number of mast cells in labial salivary glands and lung tissues of patients with Sjogren syndrome was significantly increased. There was a significant negative correlation between the Saxon test results and the number of mast cells. The mast cells were usually present in close prox-

imity to EVG-stained fibrous tissue and vimentin-positive fibroblasts. In mast cell-fibroblast co-cultures, IL-6, TGF, and VEGF expression was significantly increased compared to in mast cell or fibroblast monoculture. [Conclusions] An amplification loop between mast cells and fibroblasts enhances production of the pro-fibrotic factor, TGF-β, and angiogenic factor, VEGF, which may contribute to tissue fibrosis in sialadenitis and interstitial lung disease.

P1-264

A retrospective analysis of relationship between ESSDAI and treatment in patients with primary Sjögren's syndrome

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Conflict of interest: None

[Object] To clarify the change in disease activity by ESSDAI before and after treatment in patients with primary Sjögren's syndrome (pSS). [Methods] We analyzed 1) baseline clinical background and ESSDAI,2) treatment, and 3) change in ESSDAI after 6 months, in patients with pSS diagnosed by 1999 Japanese criteria, who were admitted to our hospital between Jan 2015 and Aug 2017, retrospectively. [Results] 1) 23 patients (19 females/4 males) were included. The mean age was 56.3±10.3 years old. 9 patients were glandular form (GF) and 14 were extra-glandular form (EGF). The mean ESSDAI was 6.8±5.9 in all patients. ESSDAI was significantly higher in EGF (10.4±4.7) than in GF (1.3±1.9) ($P<0.05$). 14 patients (61%) had moderate or high activity defined by ESSDAI≧5. 2) 5 (22%) (GF1/EGF4) out of these 23 patients received corticosteroid (CS). 1 (4%) (GF1) patient received immunosuppressant (IS). 2 (9%) (EGF2) patients received both CS and IS. 3) ESSDAI improved in CS group (12.0±6.3 to 8.6±3.1), deteriorated in an IS treated case who converted from GF to EGF during therapy (1 to 10), and unchanged in CS with IS group (12.0±2.8 to 11.0±1.4) and no CS/IS treated group (4.8±4.7 to 4.8±4.6). [Conclusions] 35% of patients with pSS received CS and/or IS, and ESSDAI improved in CS treated cases.

P1-265

Utility consideration of salivary gland ultrasonography for Sjogren's syndrome ~utility of Share wave measurement (SWM)~

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Conflict of interest: None

(Objective) Previously we announced that there is a correlation between parotid gland US and salivary secretion, ESSDAI in SS patients. The presently proposed parotid gland classification is qualitative therefore we need the criteria that can be objectively quantified and evaluated. The aim of this study is to evaluate SWM in SS patients. (Methods) All SWM were performed at Convex Probe and a dedicated ultrasound scanner (HI VISION Avius, Hitachi Medical, Tokyo, Japan). The echostructure of each parotid grand was graded on a scale of 0-4, as Nagasaki classification. (Results) This study subjects were 42 female patients. The age of the patient was 33~86 years old (mean 61.0±12.7). The saliva secretion in the gum test is 0.5-19.2ml (mean 7.9±5.9). Grade0/1/2/3/4 in a parotid echo view was 6/12/5/13/6 respectively. The average saliva secretion amount according to US Grade, fell step by step mostly with 11.7/11.7/9.3/4.5/2.1 respectively and admitted clear negative correlation by Grade0/1/2/3/4 ($r=-0.6138$). Positive correlation was also admitted between ESSDAI ($r=0.6409$) and IgG ($r=0.3762$) with US Grade. (Conclusion) SMW could be expected as a substitute for the pathological evaluation of the parotid gland in SS patients.

P1-266

Assessment of submandibular glands using ultrasound elastography in Sjögren's syndrome

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Conflict of interest: None

Object: The submandibular gland ultrasonography (SGUS) is valuable for assessing salivary gland involvement in Sjögren's syndrome (SS) patients. Recently, Ultrasound elastography (USE) has been reported to be a new tool to evaluate tissue stiffness and diagnosis of tumor. The aim of this study was to examine the usefulness of SGUS using US staging and PD grading score in combination with USE in SS. Methods: Fifty-eight SS patients were studied. The submandibular glands (SG) were evaluated by US staging and PD grading score, and shear wave velocity (Vs) and elasticity (E) by USE. Results: The Vs and E were not correlated to the amount of whole saliva and the size of SG by SGUS. However, Vs and E were significantly decreased as US staging score (stage1 vs 3: 1.91 vs 1.62m/s, $p<0.05$, 11.3 vs 8.21kpa, $p<0.05$) and PD grading score (grade0 vs 2: 1.90 vs 1.61m/s, $p<0.05$, 11.1 vs 8.13kpa, $p<0.05$) increased. Conclusions: The present study demonstrated that the tissue elasticity increased in the SG due to inflammation and high viscosity at the early stage of the disease, and the tissue elasticity decreased as the structural change in the SG advanced. The USE may be a useful tool for elucidation of early stage histopathological changes of SG in SS when salivary gland functions are not impaired.

P1-267

Anti-citrullinated protein antibody and anti-carbamylated protein antibody in Sjogren's syndrome patients

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Conflict of interest: None

INTRODUCTION Anti-carbamylated protein antibody (aCaPAb) reacts against homocitrulline an amino acid harbouring additional CH2 residue on citrulline scaffold. aCaPAb is detectable in 45.2% of Japanese RA patients, and has been reported to be detectable in 27% of patients with primary Sjogren's syndrome (SS), and their titer correlates with disease severity. We here evaluated ACPA and aCaPAb in 302 patients with primary and secondary SS. METHODS The patients with primary and secondary SS syndrome, n=98 and n=204, respectively, were studied. The age was 65±13 years old, female ratio 92%, WBC 5598±4700/mm^3, CRP 2.2±mg/dL, and ESR 36±28mmHg. Ratio of positive patients for RF was 58.3%, anti-nuclear Ab 62.4%, anti-SS-A Ab 74.0%, anti-SS-B Ab 34.3%, and ACPA 31.2%. Saxon test of the patients was 1.2±1.1g/2min. Arthritis and extra-articular manifestations were studied. RESULTS ACPA was positive in 66 (7.6 %) and 192 (42.2%) of patients with primary and secondary SS patients, respectively. Among secondary SS patients, RA occupied 85, SSc 44, MCTD 25, SLE 16, PBC 12, PM 4, Hashimoto disease 4, autoimmune hepatitis 3, RS3PE syndrome 2, polymyalgia rheumatic 2, Raynaud's syndrome 2, Bechet syndrome 1, systemic vasculitis 1, sarcoidosis 1, crescent nephritis 1 and psoriasis 1.

P1-268

Successful treatment of sensory ataxic neuropathy (SAN) / ganglionopathy with Sjoegren Syndrome (SjS) by the tocilizumab therapy: a case report

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Conflict of interest: None

(Object) Peripheral sensory neuropathy may develop as an initial symptome in SjS. Sensory ataxic neuropathy (SAN) is frequent, progressive in peripheral neuropathy and refractory to steroids treatments. This neuropathy makes patients fall into walk-disability in a short time. Effective treatments for SAN have been unknow. (Case) A 48-year-old man. Mother died of SLE. In the morning of August.8,2016, the numbness of limbs developed suddenly and perception torpor gradually progressed. Electrophysiological findings revealed reduced sensory nerve action potentials and prolonged latencies in median and sural nerves. The motor nerve conduction velocity was normal. The neurological symptoms were worsening on a weekly basis. Touch sensation, thermal nociseptions, proprioception and vibratory sensation were profound loss and Romberg Sign was positive at the end of September. On laboratory examinations, Anti-SSA ab, Anti-SSB ab were positive. The minor salivary gland biopsy was Greenspan grade2. TCZ (8mg/kg every 4weeks) was started from 3 October. The toe proprioception, vibration sense and ataxic gait were improved 48 weeks later. (Conclusions) TCZ treatment was started at the time of 8 weeks following the disease onset. The neurological symptoms disappeared after 48 weeks. TCZ may be effective for SAN in SjS.

P1-269

Successful treatment of protein-losing gastroenteropathy with mizoribine monotherapy in a patient with Sjögren syndrome

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Conflict of interest: None

[Case] 80s, female. She had visited a medical clinic for type 2 diabetes and hypertension. On 18th April, she was pointed out the lower leg edema and the increase in urine protein. She was admitted to our hospital. Although urinary protein disappeared with low-sodium diet, thirsty feeling became stronger, hypoalbuminemia was exacerbated. Protein leakage from the stomach was confirmed by scintigraphy, and we diagnosed her as protein-losing gastroenteropathy (PLGE). Additionally, we diagnosed her as Sjögren syndrome (SS) because of anti-SS-A antibody and anti-SS-B antibody positive and characteristic sialography findings. Mizoribine (MZR) monotherapy improved dry mouth, and after 2 weeks, she was discharged from our hospital with recovery of hypoalbuminemia. [Clinical significance] Immunostaining of C3 and C1q in the stomach biopsy tissue showed interstitial capillary wall positive. Therefore, we thought that complement activation by the classical pathway occurred, complement was deposited on the wall of the capillary vessel, and the vascular permeability increased to progress to PLGE. MZR monotherapy is considered clinically significant in that it can be successful without causing deterioration of blood glucose level unlike steroid therapy in diabetes mellitus cases.

P1-270

Analysis of suppressive ability and its mechanisms of RORgt antagonist for spontaneous sialadenitis RORgt transgenic mice

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Conflict of interest: None

[Object] We previously reported that T cells specific RORγt transgenic mice (RORγtTg) developed spontaneous sialadenitis like Sjögren's syndrome (SS) in which reduced regulatory T cells (Treg) and RORγt-overexpressed $CD4^+$T cells contributed to the pathogenesis. The purpose of this study was to clarify suppressive ability and its mechanisms of RORγt antagonist (A213) for sialadenitis in RORγtTg. [Methods] 6 weeks (W) aged RORγtTg orally received A213 or PBS every three days for 2W. We analyzed 1) saliva volume, 2) histopathology of salivary glands, 3) expression of IL-17A and IFNγ, and population of Treg ($CD25^+Foxp3^+/CD4^+$) in splenocytes. [Results] 1) The ratio of saliva volume at 2W to that at baseline was significantly increased in A213-group (1.4±0.1) compared with PBS-group (0.9±0.1) ($P<0.05$). 2) The focus score of sialadenitis at 2W was significantly lower in A213-group (0.2±0.2) than in PBS-group (2.3±0.6) ($P<0.05$). 3) In splenocytes at 2W, the mRNA expression of IL-17A was significantly decreased in A213-group ($P<0.05$), that of IFNγ was comparable, and the population of Treg tended to be increased in A213-group (41.7±3.8%) compared with PBS group (33.1±5.2%). [Conclusions] A213 could suppress the sialadenitis in RORγtTg via inhibition of IL-17 production and increase of Treg.

P1-271

Clinical features and outcomes of pulmonary involvements in patients with primary Sjögren's syndrome

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Conflict of interest: None

[Object] To clarify clinical features and outcomes of pulmonary involvements in primary Sjögren's syndrome (pSS). [Methods] We retrospectively examined 1) prevalence of pulmonary involvements and background, 2) image findings, 3) autoantibodies, 4) pulmonary function tests, 5) ESSDAI, 6) treatments, and 7) response to treatments in 43 pSS cases at our hospital from Jan 2015 to Sep 2017. [Results] 1) 15 of 43 cases (34.9%) had pulmonary involvements (11 females/4 males). Mean age was 64.7±6.5 years old. 2) 12 cases had interstitial diseases, 2 had cystic lesions, and one had bronchial lesions. 3) Anti-SS-A/SS-B antibody was detected in 80.0% (12/15) / 53.8% (7/13), respectively. 4) 10 of 15 cases (66.7%) had abnormal pulmonary function. 5) ESSDAI before treatment was 12.3±4.8. 6) 8 of 15 cases (53.3%) were treated by initiation or increase of corticosteroid (CS). These cases had significantly lower %VC, higher KL-6, LDH and CRP, and higher frequency of exacerbation in images than those who did not require CS ($p<0.05$). 7) 5 of 8 cases improved, 2 did not change, and one exacerbated in image findings after CS treatments. [Conclusions] Interstitial diseases were most common pulmonary involvements of pSS. Low %VC, high KL-6, LDH, CRP, and exacerbation of images related to indication of CS.

P1-272

NR4A2 overexpression in CD4+ T cells plays a critical role in enhanced Th17 differentiation in the pathogenesis of Sjögren's syndrome

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Conflict of interest: None

[Objective] To clarify a role of NR4A2 in $CD4^+$ T cells in the pathogenesis of Sjögren's syndrome (SS). [Methods] 1) Following DNA microarray in labial salivary glands (LSGs) of SS, IgG4-related disease (IgG4-RD) and healthy controls (HC), validation analysis by qPCR was performed. 2) Immunofluorescence staining (IF) of the protein in LSGs of SS and IgG4-RD was performed. 3) Functional analysis of the gene was performed using peripheral $CD4^+$ T cells of SS patients. 4) NR4A2 in $CD4^+$ T cells in lymphoid tissue of RORγt transgenic mice (Tg), exhibiting sialadenitis, was analyzed. [Results] 1) NR4A2 up-regulation in LSGs of SS was validated compared with IgG4-RD. 2) IF of LSGs revealed higher NR4A2 in $IL\text{-}17^+CD4^+$ T cells in SS than in IgG4-RD. 3) Peripheral $CD4^+$ T cells showed significantly increased NR4A2 mRNA and polarization into Th17 cells in SS compared with HC. Nuclear NR4A2 in Th17-polarized $CD4^+$ T cells was significantly higher in SS than in HC. Importazole, inhibiting nuclear transport of NR4A2, suppressed Th17 polarization and IL-21 mRNA expression in $CD4^+$ T cells under Th17-polarizing conditions. 4) NR4A2 mRNA in $CD4^+$ T cells in spleen and thymus was higher in a RORγt Tg than in a wild-type mouse.

[Conclusion] NR4A2 contributes to enhanced Th17 polarization in the pathogenesis of SS.

P1-273

Analysis of suppressive ability and its mechanisms of rice seeds expressing altered peptide ligands against M3 muscarinic acetylcholine receptor (M3R) induced sialadenitis

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Conflict of interest: None

[Object] We previously reported that Rag1$^{-/-}$ mice inoculated with splenocytes from M3R knockout mice immunized with M3R peptides mixture developed sialadenitis like Sjögren's syndrome (M3R induced sialadenitis; MIS). We also found that administration of altered peptide ligands (APLs) of N-terminal 1 (N1) and 1st loop (1st) which were T cell epitopes of MIS suppressed MIS. In this study, we aimed to evaluate the suppressive ability and its mechanisms of rice seeds expressing APLs against MIS. [Methods] 1) Rice seeds expressing M3R peptides, APLs, and fluorescent substance (FS) were generated. 2) Rice seeds expressing FS were orally administrated to mice. After 24 h, fluorescence in the ileum, mesenteric lymph node (MLN), and spleen were observed by the fluorescence microscope. 3) Rice seeds expressing N1, 1st, and APLs were orally administrated to MIS, and the suppressive ability was analyzed. [Results] 1) M3R peptides, its APLs, and FS were expressed in the protein body of rice seeds. 2) Fluorescence was detected in the ileum, MLN, spleen, and splenic CD11c^{+}cells. 3) We are now analyzing the histological findings of MIS treated by rice seeds. [Conclusions] After oral administration, FS expressed in rice seeds could be transported into MLN and spleen, and then entrapped by CD11c^{+}cells.

P1-274

A case of autoimmune neutropenia associated with Sjogren syndrome

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Conflict of interest: None

55 -year old woman was admitted to our hospital with dry cough of 2 months duration and cervical lymphadenopathy of 1 month duration. She was seen by a nearby otolaryngologist who prescribed antibiotics, but these symptoms and neutropenia were not improved, then she consulted with our hospital. Laboratory findings; WBC 1990/μl (lymph 62.5 %, mono 16.0 %, Eos 1.5 %, Baso 10.0 %) Hb 9.8 g/dl PLT 47.8×104 /μl CRP 10.1 mg/dl IgG 4813 mg/dl IgA 670 mg/dl IgM 108 mg/dl CH50 56.0 U/ml RF 62 U/ml FANA x1280 (sp) anti-dsDNA ab 0.6 IU/ml anti-Sm ab (-) anti-SS-A ab > 240.0 U/ml anti-SS-B ab > 320.0 U/ml Saxon test 1.55g Schirmer test; positive Fluorescein eye stain test; positive Minor salivary gland specimen revealed focal lymphocyttic infiltration. Anti-neutrophil antibody was positive. We diagnosed as autoimmune neutropenia associated with Sjogren syndrome. The neutrophil count decreased to 25/μl, but neutropenia was resistant to antibiotics and G-CSF. Treatment with oral prednisolone (PSL) 30mg daily increased neutrophil count slowly. The neutrophil count was improved to 6864 on day 51 after the start of PSL. This case is noteworthy because agranulocytosis associated Sjogren syndrome was rare. We report and consider this case with reference to literature.

P1-275

A case with acute autoimmune autonomic neuropathy complicated with Sjögren's syndrome

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Conflict of interest: None

[Case] A 60-year-old female was admitted to our hospital because of recurrent syncope. She had a fever, sore throat, and headache, 5 days before. Sympathetic skin response test (SSR) showed no response. She showed syncope and noradrenaline rising rate was insufficient while head up tilt test (HUT). MIBG myocardial scintigraphy revealed sympathetic neuropathy. Both anti-SS-A and anti-SS-B antibodies were positive. Saxon and Schirmer test were positive. Salivary gland scintigraphy revealed low uptake of ^{99m}Tc. CSF examination revealed albuminocytologic dissociation. From these findings, she was diagnosed to have autoimmune autonomic neuropathy (AAN) complicated with Sjögren's syndrome. Treatment was started with 50mg/day of PSL. She no longer showed syncope and SSR and HUT findings improved after the treatment. Three months after, PSL dose was decreased to 5mg/day and she remained remission. [Discussion] AAN often progresses chronically in Sjögren's syndrome, while the course was acute in our case. There have been reported that acute AAN is often associated with preceding viral infection and it was consistent with our case. [Conclusion] We should consider autoimmune mechanism when we see autonomic neuropathy in a patient with Sjögren's syndrome or preceding viral infection.

P1-276

An autopsy case of primary Sjögren's syndrome complicated with severe obstructive sleep apnea syndrome and interstitial pneumonia with pleuroparenchymal fibroelastosis and usual interstitial pneumonia pattern

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Conflict of interest: None

A case of 75-year-old male. Developed a cough in June 201X, and in July first visited. He was diagnosed with primary Sjögren's syndrome (SjS) with interstitial pneumonia (IP). IP was exacerbated in October. The treatment with oral prednisolone (PSL) 20 mg / day was started, and tapering dosage of PSL. In December, complicated by right pneumothorax, thoracoscopic right lung bulla resection and right pulmonary lobectomy were performed. In March 201X+1, he was complicated by left pneumothorax. Dyspnea on exertion worsened, he was hospitalized on April 4 for introducing home oxygen therapy. At the time of exercise, the respiratory condition was stable with SpO2 95% by inhalation of oxygen 0.5 L / min. Complaining with insomnia, headache and nocturia, he was diagnosed with severe obstructive sleep apnea syndrome (OSAS) and introduced continuous positive airway pressure therapy. He developed pneumonia at the beginning of June and died on June 24th due to exacerbation of chronic respiratory failure. With informed consent, we performed pathologic dissection. The specimen of the lung showed PPFE (pleuroparenchymal fibroelastosis) with UIP (usual interstitial pneumonia) pattern. Although OSAS and PPFE are known to be complicated with primary SjS. We report with bibliographic consideration.

P1-277

A case of Sjögren's syndrome complicated with protein-losing gastroenteropathy

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Conflict of interest: None

[Case] 48-year-old man was diagnosed with protein-losing gastroenteropathy of unknown origin 3 weeks before in another hospital. He was diagnosed with cerebral infarction in left middle cerebral artery lesion with right side hemiplegia and dysarthria by his previous doctor, but transferred to our hospital because of right side pleural effusion, edema at the extremities, and prominent hypoalbuminemia. On admission, he was diagnosed with Sjögren's syndrome because of positive results of anti-SS-A antibody, gum test, and salivary scintigraphy. Colonoscopy revealed that his mucosa was moderately inflamed, but there were no specific findings of inflammatory bowel disease. The pathological findings of mucosa were non-specific inflammation with lymphocyte infiltration.

Amyloid deposit and dilatation of lymphatics were not found. He made complete recovery from hypoalbuminemia, pleural effusion, and edema after administration of prednisolone (30mg/day) and mizoribine (150mg/day). [Discussion] Protein-losing gastroenteropathy is rare in a patient with Sjögren's syndrome. Twenty four cases were reported in the world, including 19 Japanese cases. Moderate to high-dose corticosteroids were effective in most cases, and immunosuppressants or biologics were administered in steroid-resistant cases.

P1-278

A case of juvenile Sjögren's syndrome which showed only febrile symptoms

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Conflict of interest: None

[Case] A 26 year old women without history of significant diseases visited a near doctor because of sudden fever up to 40°C. She was diagnosed as having bronchitis and pneumonia. The therapy with antipyretic and antibiotic drugs didn't improve fever and CRP. She was referred to general department in our hospital. When she visited our hospital, there is no obvious focus of infection by physical findings. She was hospitalized after the observation as a virus infection which showed no improvement. Further investigations revealed no evidence of infection and neoplasmas. Although she didn't have eruption and arthralgia, investigations was done in regard to connective tissue diseases, which showed only anti-SS-A/Ro antibody. She was referred to our department and diagnosed as having Sjögren's syndrome after the histological examination of her lip. She doesn't have any sicca symptoms, though. Because she refused corticosteroids, colchicine 1mg/day was used for 2 weeks, which showed little improvement. Finally she was referred to us again and corticosteroids 15mg/day was prescribed as the treatment of Sjögren's syndrome. Several days later her high fever and CRP improved completely. [Conclusions] We report this rare case with some literature review, as juvenile Sjögren's syndrome with only febrile symptoms.

P1-279

A case of Sjogren's syndrome (SS) diagnosed after multiple drug hypersensitivity

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Conflict of interest: None

A 43-year old woman with atopic dermatitis was admitted for methicillin-resistant Staphylococcus Aureus (MRSA) cellulitis along the left elbow. We used vancomycin therapy, as culture of pus revealed MRSA. She developed immedeate hypersensitivity. This was stopped and she recovered. Her anti-infection therapy was switched to teicoplanin. On the 6th day of treatment, patient developed generalized maculopapular rash, accompanied by fever (39°C). The treatment was interrupted with suspicion of drug reaction. Prednisolone (PSL) 50mg/day was administered. However, no marked improvement was obtained. Her anti-infection therapy was switched to daptomycin. She immediately developed signs consistent with anaphylaxis. This was treated acutely with hemodynamic resuscitation and steroids. After a daily dose of 1g of mPSL for three days, the patient was given at PSL 80mg/day. She recovered from fever and rash. She was diagnosed with SS based on the presence of both dry mouth and eyes with seropositive anti-SS-A antibody. It is important to consider a diagnosis of SS when patients present multiple drug hypersensitivity.

P1-280

Sjögren syndrome with bilateral carpal canal syndrome : a case report

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Conflict of interest: None

[Introduction] Carpal canal syndrome is an uncommon findings in patients with Sjögren syndrome. We report a rare Sjögren syndrome case with a bilateral carpal canal syndrome. [Case] A 72-year-old female was diagnosed with Sjögren syndrome by the thirst and the Raynaud phenomenon in 2013. She had good clinical coarse by the symptomatic treatment. In August 2015, she began to be aware of left-hand numbness, and felt same numbness in right-hand in October. On physical examination, there was atrophy of birateral taileds thenar musculus, and birateral Phalen's maneuver and the Tinel's sign were positive, I suspected the bilateral carpal tunnel syndrome (CTS). I diagnosed it as the bilateral CTS by the nerve conduction velocity and magnetic resonance image. I suspected the secondary CTS by Sjogren syndrome. When the treatment was started in the prednisolone 0.5mg/kg/day (22.5mg/day), the symptom improved promptly. Prednisolone has been tapered to 2.5mg/day, and the symptom is stable. We consider the participation of some autoimmunities, such as an amyloidosis, because of the bilateral CTS and the complete response of the steroid.

P1-281

A case of autoimmune neutropenia associated with Sjogren's syndrome in which tacrolimus was effective

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Conflict of interest: None

The case is 40 years old woman. In December 20XX she came to our department because of general malaise, fever, and leukopenia. Blood test findings showed agranulocytosis. She was diagnosed with febrile neutropenia and received antibiotic treatment. Autoantibodies were positive of anti-SS-A and anti-SS-B antibody. She was diagnosed with Sjogren's syndrome because of ophthalmic test and lip biopsy. There was, Bone marrow showed no dysplasia, myeloid progenitor cell hyperplasia, and maturity disorders of granulocytes. Anti-neutrophil antibody reactive with HNA-1a antigen was positive. She was diagnosed with autoimmune neutropenia. After starting treatment with prednisolone 30mg/day, improvement of neutrophil count were poor. She also ingested tacrolimus in addition. After that the number of neutrophils improved. [Discussion] In the case of neutropenia associated with autoimmune disease, it was considered that measurement of anti-neutrophil antibody was useful considering the combination of AIN.

P1-282

Guidance of medical care of juvenile dermatomyositis. Part II: Management

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Conflict of interest: None

[Object] The aim of our study is to develop guidance of treatment for

Japanese patients with juvenile dermatomyositis (JDM). [Methods] On the basis of literatures reviewed by the group members, algorithm of the treatment for JDM was produced by consensus-based method under the support of the Japanese Health and Labor Sciences Research Grant. [Results] All patients with newly diagnosed or relapsed JDM should be examined for ILD by both high-resolution chest CT scan and serum KL-6 levels. We recommend steroid pulse therapy in combination with intravenous cyclophosphamide (IVCY), calcineurin inhibitors or both as the induction therapy for patients with ILD. Steroid pulse therapy in combination with IVCY is recommended for severe cases without ILD. In mild or moderate cases, a high dose corticosteroid, preferably steroid-pulse therapy, with weekly MTX is recommended. In steroid-resistant or steroid-dependent cases, change of DMARDs or addition of intravenous immunoglobulin or other immunosuppressive drugs may be considered. Withdrawing of MTX or DMARDs is considered, if the disease has been well-controlled at least 1 year after cessation of corticosteroid. [Conclusions] We developed a guidance in which management of ILD is separated from other severe cases.

P1-283

Guidance of medical care of juvenile dermatomyositis. Part I: Diagnosis

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Conflict of interest: None

[Introduction] The development of Japanese own guidance for Juvenile dermatomyositis (JDM) is necessary, because several demographic and ethnic differences of clinical characteristics have been uncovered. [Methods] The guidance of medical care of JDMs was written under the support of the Japanese Health and Labor Science Research Grant. Because of the rare diseases and few high level of evidence papers, this guidance were based on not only evidence from published literatures but also consensus among 12 members of JDM research group. [Results] Diagnosis is based on the criteria for the diagnosis of JDM by Japanese grant-in-aid program for chronic diseases in childhood. In this criteria, muscle MRI and some myositis specific antibodies are included and electromyography (EMG), findings of arthritis and blood examinations associated with inflammation are excluded. However, EMG is an important tool to detect myositis, we devoted one chapter to EMG. We also covered typical skin lesions, histological findings and tools to assess muscle strength. Chest CT and serum markers such as KL-6 should be done at the diagnosis of JDM, because ILD was found in a relatively high population and rapidly progressive-ILD is a major cause of death in japanese JDM patients.

P1-284

A pediatric case of Anti-Ku antibody-positive immune-mediated necrotizing myopathy preceded by infantile interstitial pneumonia and arthritis

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Conflict of interest: None

We present a child case of immune-mediated necrotizing myopathy preceded by interstitial pneumonia and arthritis. Five-month-old girl referred to our hospital because of dyspnea. She was diagnosed with idiopathic interstitial pneumonia, and treated with corticosteroids. It was initially effective, however, relapse was repeated as tapering of corticosteroids. She achieved partial remission after addition of hydroxychloroquine and azathioprine. At 5 years of age, she developed poly-arthritis and diagnosed with anti-cyclic citrullinated peptide antibody (ACPA) positive juvenile idiopathic arthritis. She was treated with corticosteroids and tacrolimus, instead of hydroxychloroquine and azathioprine. At the age of 6, serum myogenic enzyme elevated. Muscle biopsy was performed and she was diagnosed as having immune-mediated necrotizing myopathy. She was treated with methylprednisolone pulse therapy, intravenous immunoglobulin, and intravenous cyclophosphamide, but showed no response. Immune-mediated necrotizing myopathy tend to be refractory to conventional therapy such as corticosteroids and immunosuppressant.

P1-285

Comprehensive analysis of arthritis and enthesitis found by whole-body msculoskeletal ultrasonography in juvenile idiopathic arthritis

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Conflict of interest: None

[Object] To evaluate usefulness of Whole-body musculoskeletal ultrasonography (MSUS) with power Doppler (PD) JIA. [Methods] Joints and entheseal sites findings on MSUS of JIA cases with whole-body MSUS administered in our hospital from August 2012 to May 2017 were invetigated. [Results] Eighty-one cases were investigated. We evaluated clinical findings in 3402 joints and 3736 entheseal sites and MSUS findings in 3348 joints and 3116 entheseal sites. Arthritis: clinical manifestations were found in 414/3402 joints, and abnormal MSUS findings were found in 428/3348 joints (224 joints had abnormal PD signal). Subclinical arthritis was revealed in 187/3348 joints. The Kappa coefficient was 0.81 between 175 joints MRI and MSUS findings. Enthesitis: clinical manifestations were found in 65/3736 sites, 52/3116 sites had abnormal MSUS findings. Classification: 7 cases of oligoarthritis or polyarthritis (RF negative) were classified as enthesitis rerated arthritis by opinion including MSUS findings. [Conclusions] MSUS findings were dissociated from clinical findings, and consistency with MRI was good. Whole-body MSUS is useful to evaluate lesions accurately in juvenile idiopathic arthritis.

P1-286

Deciding second DMARDs other than methotrexate for juvenile idiopathic arthritis: a single center retrospective study

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Conflict of interest: None

Methotrexate (MTX) is often used as the first choice DMARDs for juvenile idiopathic arthritis (JIA). However, some patients are not controlled by MTX or become unable to continue by side effects, and we need to use other DMARDs but there are no guidelines for the choice of 2nd DMARDs. [Object] Review what kind of 2nd DMARDs are used for articular JIA patients in our center, and examine the characteristics of drug selection and the treatment efficacy. [Methods] Polyarticular or oligoarticular JIA (pJIA, oJIA) patients, who were under treatment in our center as of October 2017, who discontinued MTX or used 2nd DMARDs because of insufficient control by MTX were extracted from medical records retrospectively. [Results] The subject was 18 cases (5 males, 13 females; pJIA 14, oJIA 4). MTX was discontinued in 7 cases. 12 cases used biologic agents: tocilizumab 8, adalimumab 7, etanercept 5, infliximab 1, and abatacept 1. DMARDs other than MTX: tacrolimus (TAC) 8, iguratimod (IGU) 7, salazosulfapyridine (SASP) 5, bucillamine 2, and cyclosporine 1. TAC was often used to MTX discontinued cases;

IGU and SASP were used as addition to MTX. [Conclusion] TAC, IGU and SASP were often used other than MTX in our center. A recommendation of 2nd DMARDs for JIA is expected to be made by further research.

P1-287

Dynamics of the markers of disease activity for the diagnosis of macrophage activation syndrome complicating systemic juvenile idiopathic arthritis

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Conflict of interest: None

[Object] To identify which markers of disease activity are most valuable for the early diagnosis of macrophage activation syndrome (MAS) complicating systemic juvenile idiopathic arthritis (sJIA). [Methods] Twenty three MAS patients were enrolled. We serially measured the number of WBC and platelets, fibrinogen (FIB), FDP, FDP-D dimer (DD), AST, LDH, TG and ferritin levels from acute phase of sJIA to the diagnosis of MAS. We evaluated the change in values between the value at the preMAS visit in acute phase of sJIA and those at onset of MAS or full-blown MAS diagnosis. The change in values was calculated as the value at acute phase was set to 1.0. [Results] The change in values of each laboratory tests at onset of MAS and full-blown MAS was as follows: WBC (0.95, 1.03), platelets (0.87, 0.50), FIB (0.83, 0.74), FDP (3.13, 26.6), DD (3.95, 22.8), AST (1.78, 11.0), LDH (1.42, 3.53), TG (1.00, 1.19), ferritin (7.20, 18.3). The change in FIB and LDH was significant between acute phase of sJIA and onset of MAS. The change in platelets, FIB and LDH was significant between onset of MAS and full-blown MAS. [Conclusions] The change in FIB and LDH might be useful for early diagnosis of MAS. The change in platelets, FIB and LDH might be useful for monitoring the disease progression of MAS.

P1-288

G-CSF as a marker for disease activity in systemic juvenile idiopathic arthritis

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Conflict of interest: None

[Object] G-CSF plays an important role in the pathogenesis of various arthritis. However, the role of G-CSF in systemic juvenile idiopathic arthritis (s-JIA) remains obscure. The aim of this study is to investigate the role of G-CSF in the pathogenesis of s-JIA and clinical usefulness of its serum level as a marker of disease activity. [Methods] Forty eight patients with s-JIA including 8 complicating macrophage activation syndrome (MAS), 4 with EB virus-related hemophagocytic lympohistiocytosis (EBV-HLH), 23 with polyarticular JIA, 21 with oligoarticular JIA, and 8 healthy control (HC) were enrolled. Serum G-CSF levels were quantified by ELISA. The results were compared to clinical features of s-JIA. [Results] Serum G-CSF levels were significantly elevated in active s-JIA including MAS, EBV-HLH compared to HC, whereas those in other subtypes of JIA were not elevated. Serum G-CSF levels in active phase of s-JIA were significantly elevated compare to those in inactive phase, whereas increase in MAS was not significant. Serum G-CSF levels were significantly correlated with WBC counts, serum CRP and IL-6 levels in s-JIA patients. [Conclusions] Serum G-CSF levels can be a marker for disease activity in s-JIA. G-CSF might play a role cooperatively with IL-6 in the pathogenesis of s-JIA.

P1-289

Macrophage activation syndrome compricated with systemic juvenile idiopathic arthritic may be a risk factor of PRES, case reports

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Conflict of interest: None

Case 1: An 8-year-old boy had a diagnosis of systemic juvenile idiopathic arthritic (sJIA). Methyl prednisolone pulse (MPT) and prednisolone (PSL) was initiated, after which symptoms were improved. He was introduced tocilizumab (TCZ), and tapered corticosteroid. After 3rd TCZ, he developed macrophage activation syndrome (MAS). He was treated with MPT, symptoms and serum IL-18, IL-6 and sTNFR/1ratio were improved. After MPT he had calculus impaction in urine tract, and developed hypertention. After that, he had seizure, and MRI met posterior reversible encephalopathy syndrome (PRES). Case 2: A 7-year-old girl had a diagnosis of sJIA. MPT and PSL was initiated, and after which symptoms were transiently improved. She was introduced TCZ, and tapered corticosteroid. After 2nd TCZ, she developed MAS. She was treated with dexamethasone palmitate (Lipo-DEX) and cyclosporine A (CyA), symptoms and serum IL-18, IL-6 and sTNFR2/1ratio were improved. 7days after CyA initiation, she had thunder seizure, and MRI met PRES and reversible cerebral vasoconstriction syndrome. [Conclusion] In hemophagocytic lymphohistiocytosis syndrome, high disease activity may be a risk factor of PRES. Althogh disease activity was improved, these two patients developed PRES, which showed MAS may be a risk factor of PRES.

P1-290

Clinical examination of enthesitis-related arthritis in our hospital

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Conflict of interest: None

[Object] To evaluate the clinical symptom and treatment of ERA in our hospital. [Methods] We assessed the clinical symptom, laboratory data, and treatment of nine ERA patients who were diagnosed in our hospital since June 1984 until October 2017 retrospectively. [Results] Eight patients were male, and median age was 11 (3-15 age). The median time to diagnosis was 5 months (1-43 months). Seven patients were diagnosed ERA, seronegative polyarticular JIA and spondyloarthritis (SpA) were one patient respectively. HLA-B27 was observed in 4 patients. None of patients had rheumatoid factor, anti CCP antibody, antinuclear antibody. The median ESR before treatment was 30 (7-114) mm, and MMP-3 was 60.3 (29.9-149.3) ng/mL. Treatment was started with prednisolone (PSL) only in 1 patient, methotrexato (MTX) and salazosulfapyridine (SASP) in 1 patient, PSL and MTX in 5 patients, MTX and adalimumab (ADA) in 2 patinets. Three patients, 2 ERA and 1 seronegative polyarticular JIA, who had HLA-B27 were added ADA on their therapy, and diagnosed SpA subsequently. At last visit, 3 patients were treated with MTX and ADA, 2 patients were ADA only, 3 patients were MTX only, 1 patient was MTX and SASP and PSL. [Conclusions] We should observe ERA patients with HLA-B27 carefully, because of possibility to progress SpA.

P1-291

Asymmetrical oligoarthritis with enthesitis associated with acute mumps virus infection

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Conflict of interest: None

Mumps virus is the causative agent of parotitis. A previous study reported cases of epididymo-orchitis, CNS infection, and arthritis associated with this agent. Here, we report another case of arthritis presentation associated with mumps infection. The patient was a 13-year-old boy who developed asymmetrical oligoarthritis with enthesitis, with serologic evidence of acute mumps virus infection. His fever and joint lesions gradually resolved following treatment with NSAIDs. He achieved full clinical recovery and remains well. This case illustrates the protean cutaneous manifestations of mumps virus infection.

P1-292

Hydroxychloroquine for pediatric systemic lupus erythematosus

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Conflict of interest: None

There are only few reports of hydroxychloroquine (HCQ) treatment to Japanese pediatric systemic lupus erythematosus (SLE). Here we report 4 cases of childhood-onset SLE to which HCQ was safely used. Case 1 and 2 is a 12 year-old girl and boy, respectively. Both of them were difficult to decrease PSL dosage during maintenance therapy with mycophenolate mofetil (MMF) and prednisolone (PSL), because of low complement levels in case 1 and high anti-double-stranded DNA antibody (anti-dsDNA ab) level in case 2. In case 1, HCQ was started, and in case 2, rituximab (RTX) was used first with no improvement, and HCQ was started. Case 3 is a 12 year-old boy. He had a flare and even after intravenous methylprednisolone followed by PSL and MMF his anti-dsDNA ab did not decrease. We added HCQ and RTX. Case 4 is a 15 year-old girl. She was administered HCQ, tacrolimus, and PSL but her anti-dsDNA ab began to elevate with the decrease of PSL dosage and MMF was added. All 4 cases had no adverse events by HCQ. However, when we use HCQ to children, we need cautions to prevent retinopathy, a serious complication of the prolonged use of HCQ. Further investigation is needed to examine the proper duration, when to start HCQ administration considering about pregnancy, and the presence of side effects.

P1-293

A Case of Crohn Disease with Splenic Abscess

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Conflict of interest: None

Crohn disease is complicated by extraintestinal lesions in skin, eyes, and other organs, and rarely intraperitoneal abscess. Abscesses with Crohn disease is usually aseptic, but may be complicated by a septic abscess. A 2-year-old girl was referred to our hospital with persisted fever and an ulcer of the lower leg. She showed the painful edematous erythema, intraoral aphtha, stomachache, and persisted fecal occult blood. The symptoms improved with prednisolone, but they are worsened with tapering medication. By gastrointestinal endoscopic examination, we diagnosed Chrohn disease because of colonic longitudinal ulcers. To search for parenteral lesions, CT was performed and found a cystic lesion in the spleen. Antibiotic and antifungal drugs were invalid for the treatment of the cyst, but infliximab was effective. For the abscess in Crohn disease, it is important to consider whether it is septic or not.

P1-294

Survey of the concerns about the transitional care for adult patients with juvenile onset rheumatic diseases for adult rheumatologists

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Conflict of interest: Yes

[Object] To examine the concerns about the transitional care for patients with juvenile onset rheumatic diseases which the adult rheumatologists feel, and identify their requests for the clinical practice to accept smoothly the transition patients. [Methods] A questionnaire-based survey was conducted among adult rheumatologists working in 45 hospitals participated in NinJa (National Database of Rheumatic Diseases in Japan) and 36 hospitals which had already cooperated with the facilities belonging to PRAJ (pediatric rheumatology association of Japan). [Results] Forty-six doctors in 38 facilities responded to this survey. Twenty-four facilities had already cooperated with the pediatric departments, almost of which were in the same facilities. There were differences in average medical examination time between transition patients from the pediatric department (11.2 mins) and adult onset patients (8.9 mins). Many problems including "lack of independence of the patients", "too much parental involvement" and "ignorance about differences from adult patients" were clarified. [Conclusions] Based on the valuable comments received, we will prepare a transitional clinical guide that fully takes into account the needs and desires of adult rheumatologists.

P1-295

From childhood to adulthood; clarifying the problems of transfer from pediatric to adult rheumatologists

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Conflict of interest: None

[Objective] To clarify the problems of pediatric rheumatology transition. [Patients and method] We retrospectively investigated transitional status of 133 patients who are 18 and over in past 10 years. [Results] Ninety four out of 133 patients (71%) transitioned completely. Each disease was as follows; JIA 35/54 (65%), JAS 2/5 (40%), JDM 2/3 (67%), SLE 27/36 (75%), SjS 9/13 (69%), auto inflammatory syndrome (AIS) 0/13 (0%), others 7/9 (78%). The number of patients transitioned completely increased from 2015 by means of doctors' transitional encouragement. Incidence of complete transition to adult rheumatologists was low in patients with low compliance and/or with complications compared with patients without ($p<0.001$). No AIS patients attained transition even if they have no complication or good adherence. [Discussion] Many adolescent/young adults patients with rheumatic diseases transferred to adult care owing to cooperation with adult rheumatologists in this study. However, the complications (e.g. chromosomal abnormality or fibromyalgia, etc.) and rare disease such as AIS hamper smooth transition. [Conclusion] Frequent, efficient and stepwise communication during the transitional process with adult rheumatologists is needed to accomplish the successful transition of pediatric rheumatology.

P1-296

A case of adult onset still's disease (AOSD) resembling retropharyngeal abscess, which markedly elevated plasma presepsin and serum procalcitonin

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Conflict of interest: None

A 38-year-old female was admitted to our hospital because of a sore throat and fever. Initially, we suspected sepsis on the basis of laboratory studies, which showed high WBC (10,200/μl), CRP (27mg/dl), and markedly elevated presepsin and procalcitonin (2750pg/ml, 3.15ng/ml respectively). Furthermore, computed tomography findings revealed a retropharyngeal low densitiy area with enhancement. She was diagnosed as retropharyngeal abscess and treated with antibiotics, but the fever and pharyngitis persisted, and no bacterial growth was detected in throat and blood culture. The subsequent course was marked by a transient rash, arthritis of ankles and knees. After an extensive workup, the patient was diagnosed with AOSD based on Yamaguchi criteria. Her serum ferritin levels were markedly elevated (9,907ng/ml). The patient was treated with high doses of corticosteroids and cyclosporine, which rapidly allowed resolution of the clinical signs and correction of laboratory parameters. Our case shows the limitation in the use of presepsin and procalcitonin for the diagnosis of prolonged fever, evaluated these concentrations cannot serve as marker of bacterial infection. Presepsin and procalcitonin levels may reflect macrophage activation associated with AOSD.

P1-297

Tocilizumab therapy for Adult-onset Still's disease (AOSD); six-case reports

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Conflict of interest: None

[Object] An observation study for feasible planning on tocilizumab (TCZ) plus prednisolone (PSL) therapy for AOSD. [Patients] We treated 8 AOSD patients (Pts) in 2016-17. Except 2 Pts aged over 75, 6 Pts received TCZ therapy and were entered into the study. [Results] A mean age of 6 Pts (3 females, 3males) was 51 (41-73) years. Initially, all Pts received PSL monotherapy at maximal dose 80 mg/day or pulse steroid. In 4 Pts with intractable AOSD, TCZ was started before serum CRP reached negative. 5 Pts showed slowly progressive thrombocytopenia and after starting TCZ session, which returned to normal counts by the 4th session of weekly or biweekly TCZ. Thereafter, we reduced PSL dose rapidly under monitoring serum ferritin levels. We gave up TCZ in 1 Pt because of infection and switched to PSL monotherapy then added adalimumab/ADA. During maintenance therapy for remitted 6 Pts, AOSD flared in 1 Pt on TCZ monotherapy, and 2 Pts on low-dose PSL plus TCZ or ADA therapy suffered sporadic skin rash and arthralgias, whose serum IL-18 showed 10-40 ng/ml with normal ferritin levels. [Conclusions] Thrombocytopenia was common and transient during early course of TCZ therapy for our AOSD cases, and smoldering AOSD cases showed elevated IL-18 and normal ferritin levels.

P1-298

A case of adult-onset Still's disease (AOSD) in an elderly patient with relapse after 2 weeks of steroid therapy

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Conflict of interest: None

Case Report: A 74-year-old woman had 3 weeks of intermittent, antibiotic-resistant fever. The cause of fever was not apparent on CT. She also developed a rash and lymphadenopathy. Blood tests showed leukocytosis and elevated liver enzymes, CRP (15 mg/dl), ferritin (8,412 ng/ml), and IL-18 (3,350 pg/ml). We diagnosed AOSD and started prednisolone 50 mg/day. Her fever decreased and the rash disappeared. Ten days after starting prednisolone, the CRP and ferritin levels decreased. However, after 14 days, the erythema and high fever recurred and the CRP (2.9 mg/dl), ferritin (34,160 ng/ml), liver enzyme, and D-dimer levels increased. The blood tests also showed pancytopenia, and bone marrow examination revealed hemophagocytic histiocytes. We diagnosed AOSD-associated macrophage activation syndrome (MAS). After steroid pulse therapy and cyclosporine administration, the CRP and ferritin levels decreased. She was discharged on hospital day 61. During the disease course, we measured cytokine levels more than once. Discussion: AOSD is rare in elderly people. Marked hyperferritinemia seemed to reflect disease severity. In this case, the patient developed MAS during high-dose prednisolone therapy. We surmised that the early use of combined immunosuppressant therapy contributed to recovery.

P1-299

The characteristics of elderly onset Adult-onset Still's disease

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Conflict of interest: None

[Object] Adult-onset Still's disease (AOSD) is a systemic inflammatory disease characterized by fever, rash, and arthralgia. In recent years, elderly onset cases have been frequently reported. We investigated the clinical features of elderly onset AOSD from two University hospital cohorts. [Methods] The clinical features of patients who developed AOSD at 65 years or older (elderly cases) were compared to those who developed AOSD before age 65. [Results] From 1994 to October 2017, eighty one patients were diagnosed with AOSD. Among them, 21 patients (25.9%) were elderly cases. In recent 10 years, elderly cases were increased (12 out of 35 cases, 34.2%), as compared to those before 2007 (9 out of 46, 19.6%). Serum ferritin levels and serum LDH levels were significantly higher, and pulmonary lesions such as pleurisy (90.1% vs 9.1%) and DIC (28.6% vs 8.3%) were more frequent in elderly cases. More patients were treated by steroid pulse therapy (57.1% vs 18.3%) and immunosuppressive agents (76.2% vs 50.0%) in elderly cases. [Conclusions] In elderly onset patients, AOSD showed high activity and intractable disease, as a result more intense treatments were provided.

P1-300

Certolizumab pegol in refractory adult Still's disease: an observational study of 5 cases

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Conflict of interest: None

[Object] To evaluate the efficacy of certolizumab pegol (CZP) in the treatment of adult Still's disease (AOSD) refractory to conventional therapy. [Methods] We extracted AOSD patients given CZP from our medical record between 2013 and 2017. Patient's clinical characteristics, clinical course and the efficacy of CZP were evaluated. [Results] Five patients with the diagnosis of AOSD according to the Yamaguchi criteria after exclusion of other possibilities (infectious disease, malignancy etc.) were treated with CZP. Two patients were recurrent cases. All patients had typical clinical symptom and serological sign of inflammation (leukocytosis and raised serum CRP, ESR, and ferritin levels). Two of them had hemophagocytic syndrome. All Patients were treated with pulse steroids, high dose glucocoticoid (GC) and immunosuppressant (methotrexate, cyclosporine or tacrolimus). Three patients had given tocilizumab (TCZ), one of them switched from TCZ because of insufficient efficacy. In all patients, clinical symptom and serological variables resolved within 4 weeks after beginning of CZP administration. The dose of GC reduced less than 10 mg/day without recurrence within three months. [Conclusions] CZP may be an option for the treatment of refractory AOSD patients.

P1-301

Hypereosinophilia associated with steroid-resistant adult onset Still's disease

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Conflict of interest: None

A 44-year-old woman who had experienced fatigue and cold-like symptom since March 2017 developed fever and edematous erythema in May 2017; her laboratory data showed elevated white blood cell count of 10900 cells/μL and hypereosinophilia (eosinophil count, 2180 cells/μL). Serum ferritin level was also high (5854 ng/mL). Computed tomography (CT) showed lymphadenopathy, splenomegaly, and slight thoracicoabdominal fluid. Her skin biopsy showed individual cell keratinization and neutrophil infiltration at the outermost epidermal layer, which consistent with atypical rash of adult-onset Still's disease (AOSD). We ruled out another disease that may cause hypereosinophilia. She was thus diagnosed with AOSD. We then started oral administration of prednisolone 60 mg (1 mg/kg) daily; however, her disease was steroid-resistant. We then administered cyclosporine, after which her symptoms and laboratory findings were improved. Two AOSD patients who presented with hypereosinophilia were previously reported, and their clinical and histopathologic patterns were very similar to that of our case. It can be the characteristics for AOSD patients with hypereosinophilia to show atypical rash, steroid resistance, and good response to cyclosporine.

P1-302

A case of adult onset Still disease developed after acute calcific tendinitis of the longus colli

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Conflict of interest: None

[Case] The patient was a 57-year-old woman who had sore throat, neck pain, arthralgia and fever for 10 days before admission. Synovial fluid from her knee joint revealed crystal components different from pyrophosphoric acid calcium crystal / sodium urate crystal. Cervical MRI revealed edematous swelling of the longus coli on the front of the cervical spine (C1-C2 level). Although there were no calcification findings with MRI, she was diagnosed as acute calcific tendinitis of the longus colli due to the presence of crystals in synovial fluid. Since NSAIDs was ineffective, she was treated with short-term use of predonisolone (PSL), which improved her symptoms. After discharge, she had elevated CRP level and fever again. She was re-hospitalized at 3 weeks after discharge. At that time, elevated serum ferritin level (22,622ng/ml) was observed. She was diagnosed as adult onset Still disease (AOSD), fulfilled Yamaguchi's criteria. Treatment with PSL 50 mg per day was started and then her symptoms were improved. [Conclusion] The pathology of sore throat in AOSD diagnostic criteria is still unclear. We experienced a case of AOSD developed after acute calcific tendinitis of the longus colli. This case has suggested that sore throat in AOSD might be caused by inflammation of longus colli.

P1-303

A case of adult-onset Still's disease presenting hemophagocytic syndrome associated with Kikuchi's disease

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Conflict of interest: None

Kikuchi-Fujimoto's disease (KFD) and adult-onset Still's disease (AOSD) are rare inflammatory conditions with some overlapping features. We herein report a case of a 23-years-old female with KFD (confirmed by a cervical lymph node biopsy). Although high-dose predonisolone (PSL) rapidly induced remission, she experienced recurrences repeatedly on treatment tapering. After that, she was admitted to the hospital because of high fever, sore throat, arthritis, cervical lymphadenopathy. Serum ferritin level was elevated and the bone marrow examination revealed hypocellularity with an increase of hemophagocytosis with mature forms. Given that the patient also met criteria for AOSD, a final diagnosis of KFD/AOSD co-occurrence was made with hemophagocytosis. Methylpredonisolone pulse (1000mg×3days) and PSL therapy (60mg/day) led to remmision. Although KFD is usually self-limitted illness, it can be refractory when AOSD complicate with.

P1-304

Clinical study of Adult-onset still's disease with high dose and rapid reduction (HDRR) glucocorticoids (GCs) therapy

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Conflict of interest: None

(Clinical meaning) GCs therapy for AOSD is not standardized. I reported the clinical trial of AOSD treated with HDRR of GCs. (Case1) 39 year-old female had 39, sore-throat, lymph nodes swelling, arthritis, and pink eruptions in back of both and hip. (Case2) 61 year-old female had 39°C, sore-throat, arthritis and pink eruptions in near right elbow and both thighs. (Case3) 72 year-old female had difficulty walking.37°C, sore-throat, arthritis, and pink eruptions in jaw and back of hands. Clinical datas of all showed CRP, WBC and Ferritin are highly elevated and slight liver injury. Biopsy of lymph node, Ga scintigraphy and other exams showed no particular. They were diagnosed AOSD. (Treatment) A. starts GCs120mg/day and reduced 20mg every 3days. (Total GCs 1960mg and 31days B. starts GCs 120mg/day and reduced 20mg with every 3day until 60mg and after 10% reduction in every week. (total GCs 3940mg and 100days) C. starts GCs 40mg/day with 4weeks and after that 10% reduction with 2weeks. (total GCs 3990mg and 154days) (result) case1 and 2 went with B and case3 came along A with no side effects of GCs. (Discussion) Treatment of AOSD has been C. in the past, but cause of AOSD is hypercytokinemia, the treatment of AOSD and Connective vascular diseases must be differenciated.

P1-305

Newly diagnosed cancer in patients with polymyalgia rheumatica

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Conflict of interest: None

[Objectives] To analyze cancer complications in polymyalgia rheumatica (PMR). [Methods] Data were collected retrospectively from medical records of patients newly diagnosed with PMR in our center from April 2010 to September 2016. [Results] We evaluated a total of 60 patients: mean age 78.5 ± 9.3 years, 63.3% women, prednisolone dose 14.6 ± 3.5 mg/d, C-reactive protein 8.1 ± 6.2 mg/dL, erythrocyte sedimentation rate 98 ± 28 mm/1h, and one case with giant cell arteritis comorbidity. Nine cases (15%) had a history of cancer prior to PMR diagnosis (five cases of prostate cancer, four other cases). One patient was found to have colorectal cancer during hospitalization at PMR diagnosis. During outpatient visits, five cases were newly diagnosed as cancer (two gastric cancer, one lung cancer, one prostate cancer, and one ureter cancer). Two other cancer cases were diagnosed after remission or self-discontinuation (one cholangiocarcinoma and one gallbladder cancer). [Conclusions] The possibility of malignancy in PMR should be considered not only at the time of diagnosis but also when a symptom suspected of relapse is identified.

P1-306

Investigation on factors predicting relapse of polymyalgia rheumatica

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Conflict of interest: None

Object: To identify predictive factors for relapse in patients with polymyalgia rheumatica (PMR). Methods: Patients diagnosed with PMR and treated for more than 1 year in our department were subjected. Predictive factors for relapse defined if a patient required increase in PSL ≧ 5 mg or adding concomitant immunosuppressant were detected using comparative and ROC analyses. [Results] Among 68 patients with PMR, 31 relapsed within one year of treatment, whereas 37 did not. No specific differences in baseline characters were identified between both groups. In the non-relapse group, ESR after 52 weeks was significantly lower than the relapse group (13 ± 11 vs 26 ± 21 mm/h, p <0.01). Among 25 patients whose data were available (12 with and 13 without relapse), no differences were found in change in PSL and CRP, however, significant difference was identified in decrease in ESR (57 ± 31 vs 36 ± 26 mm/h, p <0.05), as well the decrease rate (75% vs 31%: median, p <0.05) between initiation and 2 weeks after treatment. 40% reduction in ESR was identified as optimal cut-off value to predict for relapse within 52 weeks with sensitivity of 75% and specificity of 92.3%. Conclusions: Reduction in ESR in first 2 weeks of treatment was identified as a predictor for relapse in PMR.

P1-307

Liver dysfunction in cases of polymyalgia rheumatica or remitting seronegative symmetrical synovitis with pitting edema: case series of a total 38 patients

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Conflict of interest: None

[Objective] To study clinical profiles of polymyalgia rheumatica (PMR) and remitting seronegative symmetrical synovitis with pitting edema (RS3PE) in special reference to elevated serum levels of ALP and other liver enzymes. [Patients (Pts)] Twenty seven Pts with PMR (15 males, 12 females) and 11 Pts with RS3PE (5 males, 6 females) under our care since April 2016 were studied. [Results] Mean onset ages were 68.8±9.1 (48-93) years in PMR Pts and 71.5±11.7 (55-90) years in RS3PE Pts. Of these, 10 PMR and one RS3PE Pts were referred because of sustained inflammation despite therapy, and the remaining Pts were newly diagnosed in our division. Elevated levels of serum ALP before therapy were found in 6/22 (27%) of the PMR Pts and 6/10 (60%) of the RS3PE Pts, and were normalized rapidly after starting steroid therapy. Most Pts with elevated serum ALP showed high CRP levels > 10mg/dl and had active disease that required PSL-dose > 15mg/day. Elevated serum ALP may originate from cytokine-induced apoptosis of hepatobiliary cells as described in the literature. [Conclusions] Serum ALP elevation may be characteristic of active cases of untreated PMR or RS3PE, and useful data for diagnosing these diseases in cases having normal hepatobiliary imaging.

P1-308

Clinical considerations of 100 cases of polymyalgia rheumatica including 23 cured cases

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Conflict of interest: None

[Object] At the 60th annual general assembly, we presented, with bibliographic consideration, 70 cases of polymyalgia rheumatica (PMR). In this time, we present 100 cases of PMR including 23 cured. [Methods & Results] One hundred cases of PMR in our department from April 2007 are clinically analyzed. The average age of onset is 71.3 (cured, 68.4, non-cured, 72.2), the ratio of males to females is 1:1.70. All patients internally got PSL therapy, maximally 20mg (average 13.5mg) per day. Fifty four cases (54%) had a relapse in the course, and 23 cases (23%) got cured during mean period of 26.5 months. In the intractable cases, immunosuppressant drugs such as MTX (3 cases), azathioprine (7 cases) were administered concurrently, and 6 cases were treated with tocilizumab (TCZ). PSL dose could easily reduce in all cases with TCZ, and three cases finally withdrew from PSL therapy. [Conclusions] In our 100 cases of PMR, 23 patients got cured, and TCZ ameliorated six intractable cases including three withdrawal from PSL.

P1-309

Clinical characteristics and prognosis of polymyalgia rheumatica (PMR)

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Conflict of interest: None

PMR is an inflammatory disease that affects the shoulder and pelvic girdles in aged persons. To clarify the clinical feature, ultrasonography (US) findings, and response to glucocorticoid (GC), we reviewed recent-onset PMR patients. [Method] Thirty four patients (M/F=11/23) who were diagnosed as PMR after 2014 were reviewed. Clinical symptoms including shoulder and pelvic pain, peripheral arthritis, and swelling of hands, bursitis (BS)/tenosynovitis (TS) of shoulders by US, and response to GC, and rate of GC-free were investigated. [Results] The mean age was 72.6 years. Two patients with malignancy, but no giant cell arteritis was observed. Clinical features include shoulder pain 100%, pelvic pain 71.9%, peripheral arthritis 73.5%, and swelling of hands due to TS 33%. Either BS or TS was demonstrated by US in 58.6% of patients. Subacrominal BS was most common (44.8%). Mean dose of prednisolone was 13.5mg/day at the start of therapy and was tapered to 5.0mg at the next year and 4.2mg at the second year. Rate of GC-free patients in one year later and 2 years later was 11.5% and 41.2%, respectively. [Summary] In addition to typical shoulder pain, peripheral arthritis and swelling of hands was common in PMR patients and about 40% of patients became GC-free within 2 years.

P1-310

The comparison of flare rate during steroid treatment between polymyalgia rheumatica and RS3PE syndrome

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Conflict of interest: None

[Object] Polymyalgia rheumatica (PMR) and RS3PE (remitting seronegative symmetrical synovitis with pitting edema) syndrome can easily achieve remission by steroid treatment in general, but sometimes they flare during tapering steroid. We compared the flare rate between PMR and RS3PE syndrome. [Methods] 27 PMR patients and 19 RS3PE syndrome patients were diagnosed from January 2012 to October 2017 after exclusion of malignancies and infections, and we investigated them retrospectively. [Results] In the 27 PMR patients and 19 RS3PE syndrome patients, 8 and 15 patients were men and mean age was 76.7 (57-91 years old) and 75.2 (57-91 years old) for each. 18 PMR patients and 3 RS3PE syndrome patients flared in observation period. The average amount and duration period of steroid use at flare time were prednisolone 7.4 (2-12.5) mg/day and 2.3 (1-3) mg/day, 7.1 (1-28) months and 14.3 (10-17) months for each PMR and RS3PE syndrome, and they were significantly different ($P=5.9\times10^{-5}$, log rank test). PMR patients easily flared up and they used immunosuppressants thereafter. [Conclusions] PMR and RS3PE syndrome are said to be similar disease, but we can consider them as completely different disease from their response to steroid.

P1-311

Analysis of risk factors associated with relapse in patients with polymyalgia rheumatica

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Conflict of interest: None

[Object] In polymyalgia rheumatica (PMR), female sex, high erythrocyte sedimentation rate (ESR) and peripheral arthritis were associated in some studies with higher relapse risk. [Methods] Fifteen patients were enrolled who fulfilled the 1979 Bird criteria and were administered prednisolone (PSL) for more than six months. Elevation of CRP or ESR, or exacerbation of myalgia were defined as relapse. [Results] The average age was 73.7 years. Male female ratio was 4:11. Thirteen of them were associated with peripheral arthritis. The average CRP and ESR before treatment was 5.86 mg/dl and 84 mm/h, respectively. The average of initial PSL dose was 12.7 mg/day. The average CRP was 8.61 mg/dl in seven relapsed (RE) and was significantly higher than in eight non-relapsed (NR) patients (3.45 mg/dl). The average ESR was 104 mm/h in RE and was higher than in NR (69 mm/h), but not significant. Initial PSL dose was 13.6 mg/day in RE and was slightly higher than in NR (11.9 mg/day), but not significant. Male female ratio and number of peripheral arthritis were the same level. The average duration of treatment was 26.9 months in RE and was significantly longer than in NR (19.6 months) despite the same final PSL doses. [Conclusions] CRP at onset may be one of the risk factor of relapse in PMR.

P1-312

A case of pyogenic spondylitis that was initially suspected of polymyalgia rheumatica (PMR)

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Conflict of interest: None

PMR is a systemic inflammatory disease of unknown etiology. The diagnosis of PMR poses many challenges since there are no diagnostic tests that are specific for this condition. We reported a case of pyogenic spondylitis that was initially suspected of PMR. A 86-year-old woman was suffered from fever, low back and lower leg pain 25 days before she came to our hospital. The previous doctor diagnosed urinary tract infection because of elevation of CRP level and detection of E. coli in her urine. Although she had received antibiotics, her symptoms continued. The previous doctor suspected she had PMR because of no abnormal findings of blood culture, serological test, and imaging including lumbar MRI. After starting steroid, her clinical symptoms were slightly controlled, but her lower back pain lasted and CRP remained positive. She was consulted our hospital. PET/CT revealed high uptake in fifth lumbar vertebra and sacrum and MRI revealed the findings of pyogenic spondylitis in the same place. E. coli was not detected from aspirate of this part, but was detected from the blood culture after discontinuation of antibiotics. We diagnosed with purulent spondylitis. By administration of antibiotics, both symptoms and examination data had improved, and steroid had been tapered and stopped.

P1-313

A case of gastric cancer in the patient with rheumatoid arthritis and a history of remitting seronegative symmetrical synovitis with pitting edema (RS3PE) syndrome associated with lung cancer: Pathological comparison

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Conflict of interest: None

[Introduction] RS3PE syndrome is known to be associated with malignant tumors. We report a patient with rheumatoid arthritis (RA) who was diagnosed as a gastric cancer and had a history of RS3PE syndrome associated with lung cancer. [Case] A 81-year-old male with RA has sustained the remission by methotrexate and salazosulfapyridine. His affected duration of RA was 12 years. He was referred to our polyclinic for the symptoms of arthralgia, edema of both hands and lower legs, and elevation of inflammatory markers. Chest X-ray and CT scan demonstrated a nodule in the right lung hilar. Upper lobectomy of his lung was performed after diagnosis of lung cancer by bronchoscopy. After surgery and chemotherapy, edema of both his upper and lower limbs disappeared. Pathologic diagnosis was adenocarcinoma. VEGF and IL-6 antibodies were expressed immunohistochemistry on the section of his lung cancer. One year after the surgery of his lung, he had realized loss of appetite. Endoscopic examination showed gastric cancer, although it had not shown any symptom of RS3PE. Fundusectomy was performed after diagnosis of it and pathologic examination had diagnosed adenocarcinoma of stomach. VEGF and IL-6 antibodies was not expressed immunohistochemistry on the section of his stomach cancer.

P1-314

Two cases of chronic polyarthritis induced by nivolumab

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Conflict of interest: Yes

Nivolumab can cause autoimmune disorders including rheumatoid arthritis (RA). We described the first cases with nivolumab-induced chronic polyarthritis, similar to seronegative RA, in Japan. Case 1. A 64-year-old man, suffering from polyarthritis for 5 weeks, was referred to us. He had received 7 courses of nivolumab for 5 months for melanoma. The patient's and physician's global assessment (VAS) was 70/70; TJC, 12/68; SJC, 6/66; mHAQ, 1.25, and CRP, 1.1 mg/dL. RF, anti-CCP antibody and ANA tested negative. The score of the classification criteria for RA was 7, with SDAI of 26.1. Case 2. An 81-year-old man was referred for polyarthritis. Four years previously, he underwent left upper lobectomy for lung cancer. One and a half years previously, nivolumab was started for intra-pulmonary metastasis. One year after nivolumab, he developed oral erosions and finger arthritis, leading to discontinuation of nivolumab. One month later, he was diagnosed with adrenal cortical insufficiency, and was treated with cortisol. A month before the referral, he developed polyarthritis. The patient's and physician's GA (VAS) was 50/50; TJC/SJC 0/11; mHAQ 0.125, and CRP 8.2 mg/dL. RF, anti-CCP antibody and ANA tested negative. The score of the criteria was 7, with SDAI of 26.2.

P1-315

A case of pachydermoperiostosis misdiagnosed as rheumatoid arthritis

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Conflict of interest: None

[case] A 73-year old woman, who had been suffering bilateral knee pain for six months, was diagnosed as having rheumatoid arthritis. Although She had been treated with methotrexate and golimumab, her symptom did not improved and was referred to our hospital. No arthritis was obvious by physical examination and ultrasonography. Instead, a diagnosed of pachydermoperiostosis was made by the presence of furrowing of skin over face, thickening of skin over feet, clubbing with terminal widening of fingers, periosteal thickening by X-ray and bone scintigraphy. Then, the anti-rheumatoid agents were terminated and analgesic medications were initiated. [clinical significance] Pachydermoperiostosis is a rare disorder of skin and bones, which is characterized by the well-defined clinical features. Recently, its pathogenesis has been defined that some genetic predispositions lead to prostaglandins overexpression. The differential diagnosis with arthritis is clinically important when arthralgia is present. The propagation of the disorder is desirable.

P1-316

A case of the arthritis associated with Cold Agglutinin Disease

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Conflict of interest: None

[Case] A 64-year-old man with severe anemia. He was diagnosed as Cold Agglutinin Disease (CAD) / hemolytic anemia with B cell lymphoma. PSL 20 mg was administered, but the improvement was poor. For B cell lymphoma, Rituximab 375 mg/m^2 was started. Edema of the upper and lower limbs, swelling and pain of the multi-joint appeared from February. After 3 month, he was admitted to the our hospital because the labo date comes worse, Hb 5.3 g/dL, CRP 13.14 mg/dL, RF 94.7 U/mL, MMP-3 491.6ng/mL. Joint echo indicated active synovitis on hand and finger joints, retention of fluid in hip joint and patellar fossa, synovial thickening in the ankle joints. Increasing PSL and SASP 1000mg provided limited improvement, and iguratimod was difficult to continue. So Tofacitinib 10 mg was started, and arthritis almost disappeared. [Discussion] It has been reported that CAD sometimes associated with connective tissue disease such as RA, SjS, scleroderma, SLE etc. In this case, RA like arthritis was seen. In the cases of rheumatoid arthritis associated with CAD, it is reported that advanced immunosuppressive therapy is sometimes required. In this case, Rituximab was unavailable and MTX can not be used because of B-cell lymphoma, a good response was shown by using molecular targeted drugs.

P1-317

Amyloid A (AA) amyloidosis secondary to rheumatoid arthritis (RA) may be treatable but is still difficult to manage in daily clinical practice

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Conflict of interest: None

[Object] RA with AA amyloidosis is decreasing, however, we in clinical practice often encounter difficult-to-treat patients who have no inflammatory markers but who do have AA amyloidosis symptoms. **[Methods]** (1) We enrolled 15 RA patients with AA amyloidosis and divided into two groups depending on the therapy duration: less (n = 7) or more (n = 8) than 18 months. (2) Peritoneal dialysis was selected and immunohistochemical analysis was done. **[Results]** (1) The short-term group had a longer RA disease duration (P = 0.025), was diagnosed with AA amyloidosis earlier (P = 0.006), and visited us from farther distances (P = 0.016). Tocilizumab was administered, but the levels of rheumatoid inflammatory markers and proteinuria were worse (P = 0.017 and P = 0.032, respectively). (2) *Mycobacterium mucogenicum*, *M. phocaicum* and *Bacillus cereus* were detected under peritoneal dialysis. (3) Anti-fPRL1 and -CD68 antibodies demonstrated positive staining in phagocytes surrounding the AA amyloid deposits. **[Conclusions]** We encounter RA patients at the terminal stage of AA amyloidosis in the referrals, who lack high-quality rheumatologic services. Improved medical care and opportunities for healthier lives are required. Phagocytes seem to have important immunologic roles in AA amyloid fibril degenaration.

P1-318

A case of thoracicoabdominal fluid due to secondary amyloidosis complicated with rheumatoid arthritis, successfully treated by Tocilizumab (TCZ)

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Conflict of interest: None

[Case] A 77-year-old-woman was admitted to our medical center for abdominal distention. She was with rheumatoid arthritis for 40 years, taking 2.5mg of PSL and 1000mg of SASP. 9 months before hospitalization, AA amyloidosis of colon being proved pathologically. Abdominal distention gradually progressed since then. A month before hospitalization, 2L of ascites was aspirated, and 20mg of furosemide and 25mg of spironolactone were started. Her abdominal distention, however, got worse, she needed to have abdominocentesis regularly and was referred to our medical center. Laboratory data include WBC 6180 /μl, Alb 2.8 g/dl, CRP 2.71 mg/dl, ACPA276 U/l, SAA 28.4μg/ml. Massive ascites and pleural efdfusion were proved by CT. 320 mg of TCZ was administered on 8th day. Abdominal distention and appetite loss were gradually reduced. She left the hospital on 13th day. A month later, she was well without further aspiration of ascites. [Discussion] Although there are some reports describing that TCZ improves AA amyloidosis of digestive tract, it is not clear if TCZ could control ascites and pleural effusion caused by AA amyloidosis in its end stage. This case is of particular value for considering it.

P1-319

A case report of the kidney and bladder amyloidosis

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Conflict of interest: None

A 64-year-old female was diagnosed with rheumatoid arthritis in 1993. She presented gross hematuria from April, 2016 and received the urology department of our hospital. She was followed up for interstitial cystitis, but microscopic hematuria with proteinuria lasted afterwards. She presented gross hematuria from November, 2016 again and this event caused anemia (Hb5.5g/dl). Bladder mucous membrane biopsy was done in December, 2016, and bladder amyloidosis was diagnosed, and she was consulted to the department of rheumatology. Kidney biopsy was done in January, 2017, and kidney amyloidosis was diagnosed. I introduced tocilizumab (TCZ) from February, 2017, and hematuria, proteinuria was relieved six months later. I report the case that the bladder and kidney amyloidosis merger rheumatoid arthritis.

P1-320

Rapidly progressive systemic amyloidosis in a case of rheumatoid arthritis

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Conflict of interest: None

A 53-year-old woman had been treated for rheumatoid arthritis (RA) by bucillamine and 6mg/week (w) of methotrexate (MTX) over 10 years. On the prior admission because of subileus, she was diagnosed with gastrointestinal (GI) AA amyloidosis (AAa) based on endoscopic random biopsy for GI mucosa. The GI motility was improved after conservative therapy. MTX up to 12mg/w ameriolated arthralgias for several months, despite sustained inflammation with around 5 mg/dL of serum CRP levels. She did not choose tocilizumab (TCZ) therapy from economical reason. Furthermore, she withdrew attending a hospital. After no medication for 3 months, she came back to us having anasarca due to nephrotic urine protein at 18 g/Cr, severe arthritis and pneumatosis intestinalis (PI). Serum data showed 15 mg/dL of CRP and elevated levels of biliary enzymes. Renal AAa was proven by biopsy. High-dose steroid therapy with antibiotics and diuretics lead to resolution of anasarca. The PI disappeared by day 27th from the admission, thereafter we started TCZ therapy combined with MTX. [Clinical significance] AA amyloidosis in a case of RA progressed rapidly into multiple organs after a short-term withdrawal of MTX.

P1-321

Clinical and genetic analysis of the patients mimicking familial Mediterranean fever

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Conflict of interest: None

[Object] The differential diagnosis is important for the patients with familial Mediterranean fever (FMF) as the disease-specific markers are not existed. We aimed to evaluate the diseases to watch out for differential diagnosis of FMF. [Methods] We analyzed clinical features and genetic mutations about 22 patients initially suspected as having FMF but diagnosed as other disease after the analysis of the *MEFV* gene mutation.

[Results] The diagnosis of these 22 patients were as follows; malignant tumor (n=5), infectious disease (n=4), Behçet's disease (n=4), adult-onset Still's disease (n=2), and sarcoidosis, palindromic rheumatism, calcium pyrophosphate dihydrate deposition disease, Crohn's disease, PFAPA, myeloradiculitis, and intercostal neuralgia (n=1). Eleven patients (50%) fulfilled diagnostic criteria. Colchicine treatment was effective for 8 patients (most of them had the colchicine effective disease such as Behçet's disease) but then ineffective for 7 patients. Although known *MEFV* gene mutation were identified in 11 patients, exon 10 mutations were not found. [Conclusions] Fulfilling the diagnostic criteria is important for the appropriate diagnosis. Patients not having the mutation in exon 10 and refractory to colchicine treatment may be needed to re-examine other diseases.

P1-322

Clinical study of 22 patients with Familial Mediterranean Fever in our hospital

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Conflict of interest: None

[Objectives] Familial Mediterranean Fever (FMF) is the most frequent autoinflammatory syndrome and the number of FMF is reported to be increased in Japan. We studied clinical features and genetic background of patients with FMF in our hospital between 2007 and 2015. [Methods] We analyzed the clinical features, and gene mutations of 11 autoinflammatory syndrome in 22 FMF patients. [Results] All patients experienced fever. 7 patients had a family history of periodic fever. Thoracic pain, abdominal pain and arthralgia were observed in 8,12 and 10 patients, respectively. *MEFV* gene mutations were found in 5 patients as follows: one in exon10 (M694I), 5 in exon3 (P369S/R408Q), 6 in exon2 (E148Q, L110P/E148Q, R202Q/G304R, R202Q), 1 in exon5 (S503C), and 2 in E148Q/P369S/R408Q. Administration of colchicine exhibited a good therapeutic effect for all patients. Gene mutations identified in other 10 autoinflammatory syndrome were found in 7 patients in *NLRP3*, *NOD2*, *PSTPIP1* and *PSMB8*. [Conclusion] The clinical features of FMF in our hospital coincide with the national epidemiological survey of FMF in Japan. One-third of FMF patients have the gene mutation of other autoinflammatory syndrome. Further study is needed to analyze the clinical meaning of multiple gene mutations in patients with FMF.

P1-323

Four cases of familial Mediterranean fever diagnosed in primary care clinic after more than 10 years from disease onset

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Conflict of interest: None

Familial Mediterranean fever (FMF) is characterized by self-limited attacks of fever and serositis. It is thought as a relatively rare disease in Japan. However, because of insufficient perceptions of disease and self-limited symptoms, frequently recognized that some cases have not been diagnosed even after a long period from disease onset. We report 4 cases of 2 families diagnosed as FMF in our primary care clinic who were not diagnosed over 10 years after disease onset.

P1-324

A case of elderly-onset familial Mediterranean fever

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Conflict of interest: None

Abstract A 80-years-old Japanese woman had suffered for 3 years from systemic scleroderma complicated with interstitial pneumonia and was treated by prednisolone and azathioprine. She hospitalized our department because of periodic fever, polyarthritis and rash around the eyelids. A origin of fever could not be identified by the examination including blood/urine culture, cytomegalovirus antigen test, contrast CT and transesophageal echocardiography. Her clinical manifestations rapidly improved after colchicine treatment. The *MEFV* gene analysis revealed a heterozygous variant in exon2 (G304R). The duration of her fever attack exceeded over 72 hours, but we diagnosed with atypical FMF based on joint pain, erysipelas-like rash, remission of her fever by colchicine and a *MEFV* mutation. Even though it is challenging to diagnose with elderly onset FMF, it should be considered in the differential diagnosis of elder patients presenting with periodic fever.

P1-325

Two familial mediterranean fever variant cases of heterozygote of MEFV exon S503C

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Conflict of interest: None

Familial mediterranean fever (FMF) is an autoinflammatory disease characterized by periodic fever and serositis. Recently, FMF variant cases showing atypical febrile period and clinical symptoms have been reported. [Case 1] 66 years old, male. He had been suffering from arthralgia, fever continuing for 1 week, chest pain since 2012. He had developed persistent aseptic meningitis with unknown cause since 2014. He was heterozygote for MEFV S503C. Colchicine did not improve the symptoms sufficiently. Etanercept enables him to obtain a remission. [Case 2] 28 years old, female. She experienced unknown febrile attacks in 2008, 2011. In December 2016, She presented fever for 2 weeks, pericardial and pleural effusion. Close examinations denied most of connective tissue diseases. She was heterozygote for S503C. She has been free from symptoms without a treatment. [Discussion] S503C heterozygosity in MEFV is rare. Previous reports have shown the frequency of S503C heterozygosity is 0.1% to 0.6% and clinical details has not been available. The febrile periods of our cases are relatively longer than typical FMF. Of interests, both of our cases developed chest pain which seems uncommon in FMF variant. Our cases might contribute to an elucidation of the pathophysiology of S503C heterozygote.

P1-326

Aberrant splicing mechanism of PYCARD/ASC in Japanese patients with palindromic rheumatism (PR)

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Conflict of interest: None

[Object] We previously found the *PYCARD/ASC* splicing variant lacking exon2 (Δexon2) in Japanese patients with palindromic rheumatism (PR). As we also found rs8056505 A→G SNP, here we investigated the relationship between rs8056505 A→G SNP and this splicing variant. [Methods] Splicing variant mRNA production was examined under IL-1β 0-20 ng / mL condition by exon trapping method using THP-1 cells and pSPL3 vector containing rs8056505 wild type A or mutant G allele. Sequence analysis of rs8056505 was also performed using DNA obtained from healthy donors including four patients expressing heterozygous Δexon2 variant, one donor expressing homozygous Δexon2 variant and four donors expressing homozygous wild type. [Results] Δexon2 mRNA dominantly expressed in case with rs8056505 G allele as compared with A allele. IL-1β stimulation didn't affect the expression pattern. rs8056505

G allele was found heterozygously in two donors expressing heterozygous Δexon2 variant. [Conclusions] Our results suggest that rs8056505 G SNP contribute the production of *PYCARD/ASC* Δexon2 splicing variant.

P1-327

A case of TNF receptor associated periodic syndrome (TRAPS) successfully treated by Canakinumab

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Conflict of interest: None

Patient is a 30 year old, female. She had periodic fevers since 1987. In 1995, oral steroid treatment was started, and she was admitted to Kyushu University Hospital in 2000. Genetic analysis revealed the C70S mutation of the TNFRSF1A gene and she was diagnosed as TRAPS. The effect of steroids declined. After Etanercept (ETN) treatment started in 2005, symptoms were improved. But periodical fevers appeared again since 2014 and gradually worsened. ETN was switched to Canakinumab in 2017. She became afebrile quickly after the initiation of it, and inflammatory findings also improved. TRAPS is one of the representative autoinflammatory disease caused by genetic mutation of type1 TNF receptor. Although its pathophysiology has not been elucidated, there are several pathological hypotheses such as cooperative theory of wild type/mutant type TNFR and the abnormal intracellular transportation of mutant TNFR. Among them, the effectiveness of IL-1β inhibitor for TRAPS had been reported, and Canakinumab is approved for TRAPS in December 2016 in Japan. In this case, although anti-TNF treatment become ineffective, the symptoms were improved by Canakinumab promptly. Since they are thought to help clarify the pathology and treatment of rare disease TRAPS, we will report literature review.

P1-328

A 12-year-old girl of TNF receptor associated periodic syndrome successfully treatedby canakinumab

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Conflict of interest: None

[Case] A 12-year-old girl [P.H.I] She had a fever accompanied by preceding abdominal pain at the age of 1 year and 9 months, Repeated similar episodes, diagnosis of TRAPS was confirmed by TNFRSF1A gene C55R heterozygote at 2 years and 10 months. Although it was controlled with PSL at the time of fever attack, it gradually became difficult of dose reduction of PSL, and she was showing short stature and central obesity. At 10 years old, ibuprofen began and it could supress fever attack, but periodic ocular conjunctival hyperemia, thoracoabdominal pain, leukocytosis, elevation of CRP and SAA could not be controlled. The symptoms almost disappeared by adding of colchicine, and steroid reduction became possible, but periodic leukocytosis, elevation of CRP and SAA continued. [Progress] Because control of inflammatory condition was insufficient, administration of canakinumab was started at the age of 12 years. By 150 mg of canakinumab every 4 weeks, the inflammatory condition is controlled, then colchicine and ibuprofen are discontinued and the dose of PSL was further decreasing. [Summary] Not only sufficiently suppress the disease activity by canakinumab, but also the quality of life of her, including the cancellation of the medicine for internal use, was improved markedly.

P1-329

A novel NOD2 gene mutation in early-onset sarcoidosis

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Conflict of interest: None

[Background] Early-onset sarcoidosis is systemic inflammatory granulomatosis. The most common manifestation of the disease is arthritis. Here, we describe a case without arthritis of early-onset sarcoidosis with a novel mutation. [Case presentation] An 8-year-old girl presented with granulomatous panuveitis and skin lesions. Genetic analyses revealed that the patient had a novel *NOD2* mutation (D512V), and a diagnosis of early-onset sarcoidosis was made. She showed the absence of arthritis. [Conclusions] Our results suggest that the D512V mutation may be associated with the absence of arthritis. In cases of idiopathic granulomatous panuveitis even without arthritis, early-onset sarcoidosis should be considered in the differential diagnosis.

P1-330

PYCARD/ASC variant lacking exon2 up-regulates NLRP3 inflammasome

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Conflict of interest: None

[Object] We previously found a *PYCARD/ASC* variant mRNA lacking exon2 in patients with palindromic rheumatism (PR). To clarify the contribution to the pathogenesis of PR of this variant, we investigated NLRP3 inflammasome function *via* this variant as compared with wild type. [Methods] PBMCs were obtained from healthy donors expressing heterozygous or homozygous wild type *PYCARD/ASC*. We generated THP-1 cells expressing variant or wild type recombinant PYCARD/ASC. These cells were treated by using 0.5 μM PMA, then stimulated with 100 μg/mL MSU. IL-1β in conditioned medium was measured by using ELISA. We also performed immuno-precipitation by using total proteins of recombinant THP-1 cells to compare the interaction ability of ASC with NLRP3 or Caspase-1 as compared with wild type. [Results] IL-1β significantly increased in case with heterozygous PBMCs without stimulation as compared with wild type. IL-1β significantly increased in case with THP-1 cells expressing variant ASC with MSU stimulation as compared with wild type. Binding ability of variant ASC with both NLRP3 and Caspase-1 increased as compared with wild type. [Conclusions] Our results suggest that the variant PYCARD/ASC activates inflammasome as compared with wild type and may contribute to the pathogenesis of PR.

P1-331

Functional analysis of a PYCARD/ASC variant lacking exon2 in NLRC4 inflammasome

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Conflict of interest: None

[Object] We previously found the PYCARD/ASC variant mRNA lacking exon2 in Japanese patients with palindromic rheumatism (PR). To investigate the effect of this variant in NLRC4 inflammasome, we examined 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 (0.5μM), followed by stimulation with 100ng/mL flagellin. IL-1β concentrations in conditioned medium were measured by using ELISA. Total proteins were extracted and interaction analysis be-

tween ASC and NLRC4 or Caspase-1 was performed by co-IP. [Results] IL-1β production and inflammasome activation rate were significantly increased in the case with wild type ASC dose dependently ($P<0.05$) as compared with Δexon2 variant. Binding rate of ASC and NLRC4 was increased in the case with Δexon2 variant as compared with wild type. [Conclusions] Our results suggest that the variant PYCARD/ASC interfere with the NLRC4 inflammasome activation.

P1-332

Adult-onset Still's disease complicated by hemophagocytic lymphohistiocytosis during pregnancy

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Conflict of interest: None

[Case] A 40-year-old Japanese woman presented with fever of unknown origin, cervical lymphadenopathy, erythema at 34 years old. She was diagnosed as having Adult-onset Still's disease (AOSD) in a clinic. The treatment was initiated, including glucocorticoid and cyclosporine. At 40-yead old, she was pregnant for the first time, and taking cyclosporine was discontinued. Treated with Prednisolone 8mg, there was no recurrence. She presented with fever, fatigue, jaundice at 35weeks of pregnancy. Investigations revealed thrombopenia, billirubinemia, liver enzyme elevation, hyperferritinemia, splenomegaly, and hemophagocytosis in bone marrow. She was treated with steroid pulse therapy, and intravenous immunoglobulin therapy, cyclosporine under a diagnosis of hemophagocytic lymphohistiocytosis (HLH) and exacerbation of AOSD. There was no subsequent recurrence. [Discussion] Several study reported pregnancy-related HLH and exacerbation of AOSD during pregnancy. In particular, they demonstrate a high rate of exacerbation during second trimester of pregnancy and post partum. In our patients, there was exacerbation in third trimester of pregnancy and no symptoms at the onset. The patient with AOSD should require a close monitoring during and after pregnancy.

P1-333

A Case of neuro-Sweet disease Requiring Differentiation from acute neuro-Behçet disease

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Conflict of interest: None

Case: Neuro-Sweet disease (NSD) is relatively rare. We treated an NSD patient whose case required discrimination from acute neuro-Behçet disease (NBD). A 55-year-old Japanese man had herpes keratitis 2 weeks before hospitalization and was treated by an ophthalmologist. Tongue pain, tongue biloba, and oral ulcer appeared 1 week prior to his admission and did not improve despite treatment. An approx. 38°C fever continued from 2 days pre-admission, and he was examined at our E.R. and admitted to our hospital. He lost consciousness 1 week post-admission. Increased protein and cell number were shown by a cerebrospinal fluid test, and head MRI revealed meningoencephalitis. Acute NBD was suspected, and he was transferred to our department. We initiated steroid pulse therapy; the symptoms of consciousness disturbance and fever improved promptly. Based on pathology and skin findings and HLA-B54 positivity, we diagnosed NSD. **Clinical Significance:** NSD and NBD are related diseases, and it is often difficult to distinguish them. The main differences are skin findings, head MRI findings, HLA typing, and pathological findings, but as these diseases' therapeutic reactivity and prognoses differ, they must be differentiated.

P1-334

About two elderly people who had a diagnosis of CDS because found calcification around the odontoid process of the axis on CT and posterior neck pain

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Conflict of interest: None

Case 1. 77 years old man. He has the past of cerebral hemorrhage and the alcoholic liver damage, and takes antihypertensives. There was a pain around the posterior neck and he came to hospital because meningitis was doubted. In blood sampling, the CRP value is 8.95 and found calcification around the odontoid on CT. According to the prescription of NSAIDs, pain improved quickly. Case 2. 84 years old woman. She has the past of cerebral artery stenosis and duodenal ulcer, and takes cilostazol and PPI. She came to hospital because pain was recognized in the posterior neck. The CRP value is 8.76 and found calcification similarly. It took 10 days to ameliorate the symptoms because she didn't take NSAIDs but acetaminophen due to the past. There are many reports that CDS has a high proportion of elderly women, CRP increases in blood collection, and NSAIDs are effective. Although CDS have calcification around the odontoid, it is not a CDS because there is calcification. Calcification around the odontoid is also observed in psoriatic arthritis, ankylosing spondylitis and tumors of chordoma and meningioma. Therefore, it should be noted that it is not necessarily treated with NSAIDs just because an elderly woman who has posterior neck pain recognizes calcification around the odontoid on CT.

P1-335

TNF-alpha augments uric-acid induced interleukin-1beta and IL-18 secretion in human neutrophils

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Conflict of interest: None

[Object] Gout is an inflammatory arthropathy due to the deposition of uric acid (monosodium urate: MSU) crystals in synovial tissue. MSU leads to activate nucleotide-binding oligomerization domain-like receptor family pyrin domain containing 3 (NLRP3) inflammasome and following IL-1beta secretion via caspase-1 activation in human monocytes. However, priming signals for NLRP3 inflammasome pathway had not been completely elucidated in sterile inflammatory arthritis including gout. In this study, we investigated the role of TNF-α on MSU-mediated IL-1β induction in human neutrophils. [Methods] Human neutrophils were stimulated with MSU, in the presence or absence of TNF-α priming. The cellular supernatants were analyzed for IL-1β, IL-18 and caspase-1 by ELISA. [Results] TNF-α stimulation induced pro-IL-1β mRNA expression, however, MSU stimulation alone did not induce pro-IL-1β mRNA expression in neutrophils. TNF-α alone or MSU stimulation did not result in efficient IL-1β secretion. Whereas MSU stimulation to TNF-α-primed neutrophils resulted in a marked IL-1β as well as IL-18 secretion. [Conclusions] Priming of human neutrophils with TNF-α promotes uric acid-mediated NLRP-3 activation and IL-1β secretion in the absence of microbial stimulation.

P2-001

Characteristics of Elderly onset of rheumatoid arthritis (EORA) patients in NinJa 2016 database registry

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Conflict of interest: None

[Objectives] Recently, the patients of rheumatoid arthritis (RA) were aging, therefor the assessment of the characteristics of older ages of RA

patients were interested. [Methods] In 15341 of patients of NinJa 2016 registry, age over 75 years old were subjected. They were divided to three groups due to the age of disease onset, the onset age under 65yo: Group A, 65yo to 74yo: Group B, and over 75yo: group C. Each group was divided to two groups by their gender. [Results] The standardized incidence ratios (SIRs) of malignant tumors was estimated. SIR of Group A, Group B, Group C was 1.40, 0.92, and 0.98 in male, whereas SIR was 1.03, 0.74, and 0.63 in female groups A, B, and C, respectively. The ratios of death during one year were deferent between male and female, that is the ratios were 4.8%, 3.7%, and 3.7% in male Groups of A, B, and C, whereas 1.5%, 1.1%, and 1.1% in female, respectively. The ratios of positive smoking history were 71.0%, 64.2%, and 58.1% in male Groups of A, B, and C, and 10.9%, 9.9%, and 10.1% in female, respectively. [Conclusion] In the female group of EORA, SIRs were lower than in male group, and in group of younger onset RA (YORA) in age more than 75yo. The reason of the results could not explain in this study, and father study was desirable.

P2-002

Elderly onset RA in the most advanced ageing prefecture in Japan

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Conflict of interest: None

[Object] To determine the impact of age on early-onset rheumatoid arthritis in Shimane prefecture. [Methods] This study included 100 consecutive outpatients with a disease duration of <1 year (median age, 65 years; 74% women). On the basis of the ROC curve orientated by anti-CCP antibody positivity, the suggested cutoff age was 70 years. Therefore, we defined EORA as early RA with disease onset at the age of >70 years. [Results] In EORA, involvement of the shoulder was common and that of the PIP and MTP joints was less frequent. Although the baseline disease activity was not different, Health Assessment Questionnaire (HAQ) score and CRP level were significantly higher in EORA than in younger-onset RA (1.23 ± 0.81 vs 0.57 ± 0.52, $p < 0.03$ and 3.02 ± 3.72 vs 1.64 ± 2.29 mg/dL, $p < 0.03$, respectively). As for the treatment outcome after 12 months, no statistically significant differences were found between EORA and younger-onset RA in the rate of DAS index remission. However, the rate of HAQ score remission was significantly lower in EORA than in younger-onset RA (65% vs 89.6%, $p < 0.03$). [Conclusions] The cutoff age of 70 years for EORA was suitable for the most aging prefecture in Japan. To prevention of functional disability is important for elderly people.

P2-003

Clinical features of elderly-onset rheumatoid arthritis in patients in the Akita Orthopedic group on Rheumatoid Arthritis registry

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Conflict of interest: None

[Object] With the population aging, the prevalence of elderly-onset (≧60 years of age) rheumatoid arthritis (EORA) is increasing. EORA shows variable clinical characteristics, requiring careful diagnosis and treatment. We studied patients with EORA aged ≧65 years extracted from the Akita Orthopedic group on Rheumatoid Arthritis (AORA) registry. [Methods] We investigated 832 EORA patients from among 2,238 registered patients in the 2017 AORA registry. [Results] The average age of EORA patients was 77 years, (198 men, 634 women; [1: 3.2]), and the average duration of illness was 7.7 years. The methotrexate (MTX) use rate was significantly lower and the salazosulfapyridine use rate was higher in EORA patients than in those with young-onset (<60 years of age) rheumatoid arthritis (YORA). The biological disease-modifying antirheumatic drug (bDMARD) use rate was significantly different between EORA patients and YORA patients (15.6% vs. 30.9%). However, there was no significant difference in disease activity and in the frequency of merger of past disease between the two groups. [Conclusions] EORA patients aged ≧65 years in the AORA registry had significantly lower rates of MTX and bDMARD use than those of YORA patients, but the disease activity was comparable.

P2-004

Incidence of medication in patient with rheumatoid arthritis and dementia

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Conflict of interest: None

[Object] To evaluate the incidence of medication in patient with rheumatoid arthritis and dementia. [Methods] Seven hundred ninety-nine patients applied for nursing-care insurance from April 1, 2016 to March 31, 2017 were objected in this study. We defined the criteria " I or above" of bedridden and demented elderly was established by the Ministry of Health and Welfare as patients with dementia. We evaluate the incidence of rheumatoid arthritis with dementia and the medication for rheumatoid arthritis such as NSAIDs, csDMARDs, bDMARDs, prednisolone and so on. [Results] The incidence of rheumatoid arthritis with dementia was 1.8%. Methotrexate and prednisolone were used in 8 patients (72.7%) and 7 patients (64%), respectively. However, bDMARDs was just prescribed 2 patients. They were dosed with Methotrexate at 5.1 mg per week and prednisolone at 3.4 mg per day. The dosage of prednisolone in patient with rheumatoid arthritis and dementia was higher than that of other patients without dementia. [Conclusions] We conclude that more prednisolone was used in rheumatoid arthritis with dementia.

P2-005

Change in the rate of pneumococcal vaccination and difference in clinical characteristics between rheumatoid arthritis patients with and without vaccination based on the IORRA cohort

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Conflict of interest: None

[Objective] To examine change in the rate of pneumococcal vaccination and difference in characteristics between rheumatoid arthritis (RA) patients with and without vaccination from 2012 (before routine immunization) to 2016 (after routine immunization system). [Methods] Change in the rate of pneumococcal vaccination was calculated based on patients' self-report in the IORRA from 2012 to 2016. The difference in characteristics between RA patients with and without vaccination in 2016 were evaluated. [Results] The rate of vaccination for the past 5 years increased from 18.3% in 2012 to 24.1% in 2016, and from 35.0% to 45.7% in the patients over 65 years old, respectively. This rate in 2016 was similar with national estimated rate (43%). Among 2,673 patients over 65 years old in 2016, the number with and without vaccination was 1,121 and 1,331, respectively. Female (%), average age, RA duration, mean DAS,

steroid use (%), and MTX use (%) were not statistically different between the 2 groups. bDMARDs use was significantly different in patients with (18.0%) and without vaccination (12.5%) ($p<0.01$). [Conclusion] The rate of pneumococcal vaccination with Japanese RA patients increased especially in over 65 years old. The vaccination rate was significantly high in the bDMARDs users.

P2-006

Obesity, fatty liver, and hyperlipidemia complications in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] Obesity, hyperlipidemia complications, fatty liver, and diabetes were investigated in patients with rheumatoid arthritis. [Subjects and Methods] The study subjects were patients with favorable response to and continued treatment with DMARDs for >6 months between January 2014 and December 2015 to investigate obesity, hyperlipidemia, fatty liver, and diabetes complication rates with respect to each drug. MTX, Tac, TCZ, ABA, IFX, ETN, GML, ADA, and CZP were to 84, 23, 59, 30, 27, 19, 19, 12, and 9 patients, respectively. Those with body mass indexes >25 were regarded as obese, and hyperlipidemia was assessed using the JAS standard. [Results] The complication rates of obesity, hyperlipidemia, fatty liver, and diabetes of each drug were 11.1-33.3%, 42.1-60.0%, 17.4-42.4%, and 0-16.7% respectively. The complication rate by each drug ranged from 54.8% to 77.8%. Despite no significant difference before and after the treatment intervention, obesity and cholesterol levels tended to decline. [Discussion and Conclusion] RA treatment aims to reach and maintain the clinical remission level, but the complication rates were high in this study, suggesting the future need for measures to prevent complications.

P2-007

Clinical futures of rheumatoid arthritis in patients with chronic kidney disease

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Conflict of interest: None

Object: To investigate the clinical future of rheumatoid arthritis in patients with chronic kidney disease. Methods: Subjects were 136 RA patients from our outpatient clinic. Patients were categorized into two groups according to estimated glomerular filtration rate (eGFR): CKD+ (eGFR < 60 ml/min/1.73m^2) and CKD- (eGFR ≧ 60 ml/min/1.73m^2). Clinical future was evaluated in both groups. Results: The mean age of subjects was 63.7±14.4 years, and the number of women was 94 (69.1%). The mean duration of RA was 2.9±1.9 years, and the number of RF positive and ACPA positive patients were 77 (56.6%) and 64 (47.1%), respectively. The number of patients in each group was as follows: CKD+ 24 (17.6%); CKD-, 112 (82.4%). The mean age of CKD+ was significantly higher than that of CKD-. Female patients were fewer in CKD+ compared to CKD-, and mean duration of RA was longer in CKD+ compared to CKD-. The ACPA positive rate was lower in CKD+ compared to CKD-, but there was no significant difference in RF positive rate between two groups. MTX was prescribed to a lower proportion of CKD+ than to CKD- and glucocorticoids were prescribed to higher proportion of CKD+ than to CKD-. Conclusion: There were many elderly men with ACPA negative in patients with CKD+, and corticosteroids were mainly prescribed.

P2-008

The prevalence of chronic kidney disease (CKD) in patients with RA, the administration of DMARDs, and the remission rate of the patients with or without CKD: Retrospective study from data of our hospital

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Conflict of interest: None

[Object] To estimate the prevalence of chronic kidney disease (CKD) in patients with RA and the administration of DMARDs. We also evaluated the remission rate of the patients with or without CKD. [Methods] We retrospectively analyzed the charts of 68 patients who had been diagnosed as RA since 2013 and received treatment continuously for more than one year. [Results] The patient's background was as follows: male, 32.3%; the average age, 66.7, the average time from onset until diagnosis, 6months. The prevalence of GFR stages was: stage G1, 29.4%; G2, 45.6%; G3a, 14.7%; G3b, 8.8%; G4, 1.5%; and G5, 0.0%; CKD (eGFR<60), 25.0%. The number of patients using each DMARD at 52 weeks was: MTX, 42 patients (four of whom had CKD); SASP, 12 (8); IGU, 6 (3); TAC, 1 (0); TOF, 2 (0); PSL, 11 (4). bDMARDs were used as follows: TCZ, 1 patient in G3a; ABT, 4 in G3b; and in the group without CKD, GLM, 5; CZP, 3; ETN, 3; ABT, 1. The DAS28CRP remission rate at 28 and 52 weeks was: 47.1%, 75.0% in the CKD group and 62.7%, 73.5% in the group without CKD. [Conclusions] The prevalence of CKD in our study was 25%, which was higher than 13% in the general population. RA patients with CKD require limited drug selection, but could achieve remission at the almost same rate by using appropriate kinds of DMARDs.

P2-009

Correlations among knee joint disability in rheumatoid arthritis patients

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Conflict of interest: None

[Object] Knee joint disability in rheumatoid arthritis (RA) is thought to be an important factor in decreasing quality of life. The purpose of this study is to clarify factors related to knee joint disability in RA patients. [Methods] A total of 447 female RA patients (mean age; 63.7 years) were recruited in KURAMA cohorts. Clinical data included age, disease duration (DD), Steinbrocker stage and class, anti-CCP, RF, CRP, MMP-3, DAS28-CRP, and Pain-VAS. Knee function was assessed by the scores of the Japanese Knee Osteoarthritis Measure (JKOM) questionnaire. The correlations between JKOM and each factor were evaluated by univariate and further multiple regression analyses. [Results] A total of JKOM had a median value of 17 points, a interquartile range of 5.5 to 43.5 points. Univariate analyses showed that age, DD, stage, class, anti-CCP titer, CRP, MMP-3, DAS28-CRP, and Pain-VAS were significantly correlated with JKOM. Multiple regression analysis with JKOM as the objective variable revealed that Pain-VAS, age, MMP-3 were extracted as a significant factor. [Conclusions] Pain is an essencial factor in knee joint symptoms of RA patients. MMP-3 is closely related to knee joint symptoms, and it is considered that patients with high MMP-3 should pay particular attention to knee joints.

P2-010

Comparison of background, treatment and RA disease activity between groups divided by cut-off value of weighted joint score using the NinJa database

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Conflict of interest: None

[Objective] The joint scoring system developed (Ono K., Ohashi S., Oka H., Tanaka S., et al., *Mod Rheumatol*, 2015) was used to investigate background factors and treatments for maintaining physical function. [Methods] 13,135 subjects (10,578 females, 2,557 men) from NinJa 2015 were examined. The cutoff value 3 or more in the joint score was defined as the physical function declining group and the less score was defined as the maintained group. [Results] The average value of the declining group vs maintained group is 66vs64 years of age, duration of disease 16years vs 12years, tender and swollen joints 5.8vs0.7, 3.4vs0.8, PtPainVAS 3.8vs1.9, PtGVAS 3.9vs2.0, DrVAS 2.6vs1.1, mHAQ 0.7vs0.3, CRP 0.9vs0.4, ESR 34vs24, DAS28 3.4vs2.2, DAS28CRP 3.3vs1.9, SDAI 14.2vs4.6, CDAI 13.3vs4.3, RF 138vs89, ACPA 110vs104, PSLamount 4.2vs3.9, and MTXamount 8.4vs8.3. The maintained group had more men, lower Stage/Class, lower MTX, PSL, NSAIDs, biologics usage rate, smoking rate, and unemployment rate. [Conclusions] In the high joint score group, the diseased years were long, the disease activity was high and the physical function was impaired although the administration rate of each drug was high, suggesting that it is important that adequate treatment be performed at the early stage of RA.

P2-011

Discrepancy of global assessments between patient and doctor is associated with depression and anxiety in patients with rheumatoid arthritis -Analysis of NinJa 2016 database-

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Conflict of interest: None

Objectives: We reported before the prevalence and factors associated with depression (Dep) and anxiety (Anx) in RA patients (pts) using NinJa database of 2012 to 2014. We aimed to analyze with NinJa 2016 including whether discrepancy in global assessments (GA) between patient and doctor (bP-D) is associated with Dep and Anx. **Methods:** We analyzed RA pts with results from the Hospital Anxiety and Depression Scale (HADS). For Dep, a Dep group (DG) with score ≧11 and non-DG with score <10. Differences in clinical data were analyzed between groups. For Anx the same. **Results:** 9,021 RA pts in 32 hospital were enrolled. The frequency of DG in 2016 was 9.6% (9.4% in 2014) an that of AG 5.6% (4.6%). In multivariate analysis, work and SDAI remission were observed as negative factors for DG (respectively, p<0.001, OR 0.566, 95%CI 0.478-0.670 and p<0.005, 0.708, 0.564-0.888). Further, DAS28CRP and discrepancy of more than 20mm of GA of patient above that of doctor were observed as risk factors (respectively, p<0.001, 1.321,1.206-1.447 and p<0.001, 1.636,1.391-1.924). Shown as above, discrepancy of GA bP-D is suggested to be associated with Dep and Anx in RA pts. **Conclusion:** Discrepancy of GA bP-D supposed to be associated with Dep and Anx in RA pts.

P2-012

Comparison of background, treatment, comdition and RA disease activity between women and men patients using the NinJa 2015 database

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Conflict of interest: None

[Objective] To examine gender differences in RA patients using NinJa 2015, we compared background, condition, treatment, disease activity, etc. [Methods] Of the 15,115 subjects registered in NinJa 2015, 13,135 subjects (10,578 females, 2,557 men) with no missing data were subjected to a t test and a chi-squared test for comparative study on the NinJa endpoint. [Result] Class & Stage distribution in male vs. female (1/2/3/4) is Class (44.9/40.9/12.3/1.9%vs34.1/46.4/17.0/2.5%), Stage (32.6/33.6/19.1/14.7%vs23.8/26.2/20.0/30.0%), indicating a significant difference. The average value of each item is 67vs64 years old, age of onset 56vs50 years, diseased years 10years vs 14years, the number of tender and swollen joints 1.6vs2.2 and 1.3vs1.5, PtPainVAS 2.1vs2.5, PtGVAS 2.2vs2.5, DrVAS 1.3vs1.5, mHAQ 0.3vs0.4, CRP 0.7vs0.5, ESR 22vs27, DAS28 2.2vs2.6, DAS28CRP 2.2vs2.3, SDAI6.5vs7.4, CDAI 15.8vs6.9, RF 131vs94, ACPA 127vs100, PSL amount 4.4 vs 3.9, and MTX amount 9.0vs823, which were all significant differences. Surgical history, steroid, DMARDs, MTX and biological agent usage was high, however, there was no difference in NSAIDs and tacrolimus usage rate. [Conclusions] This study suggests that it is important to adequately treat women especially in the early stage of RA suffering.

P2-013

Prevalence of hallux valgus and flat foot in rheumatoid arthritis

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Conflict of interest: None

[Object] The rheumatoid feet may cause deformity of hallux valgus (HV) and flat foot. The purpose of this study was evaluate the prevalence of HV and flat foot by disease duration. [Methods] This study included 211 patients (422 feet); mean age 67.2 years, mean disease duration 12.1 years. The feet were categorized into 3 groups by disease duration. The short term group (S) in 6 years and less, the middle term group (M) in 7-11 years, and the long term group (L) in 12 years and more included 120 feet, 146 feet, and 152 feet. We defined HV as HV angle ≧20 °and flat foot as calcaneal pitch (CP) angles <20°. The HV angles and CP angles were measured at baseline and 3 years from baseline. [Results] The prevalence of HV were 43.3% in S, 37.2% in M, and 50.0% in L at baseline. The proportion of increased HV angles were 48.3% in S, 53.4% in M, and 48.1% in L and The proportion of increased CP angles were 45.8% in S, 59.5% in M, and 51.9% in L at 3 years from baseline. In the characteristics at baseline, the value of rheumatoid factor was significantly high in M, and the body weight was significantly heavy in S. [Conclusions] The deformity of rheumatoid feet affect pain and gait. The HV and flat foot were existed and tended to worse half patients regardless of the

disease duration.

P2-014

Environmental factors, family history, comorbidity and sex contributing to susceptibility of rheumatoid arthritis: a cross-sectional study

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Conflict of interest: None

[Object] To compare environmental factors, family history and comorbidity contributing to rheumatoid arthritis (RA) susceptibility between male and female. [Methods] We enrolled 284 cases (male 58, female 226) of rheumatoid arthritis who attended our hospital until October 2017. In cross-sectional study we analyzed the data according to sex, age at the onset, smoking history, inspiration history, inhalation exposure, comorbidity of autoimmune diseases, family history, rheumatoid factor (RF), anti-cyclic citrullinated peptide antibody (ACPA) and interstitial lung disease (ILD). [Results] The age at the onset was 21-94 years (median 55.5 years) in female, and 24-83 years (median 65 years) in male. Male patients were significantly more likely to have smoking history than female patients regardless of age at the onset (83% vs 29%, P<0.01). Male patients without any smoking history, inhalation exposure, family history or comorbidity of autoimmune diseases were significantly fewer than female patients (10% vs 52%, P<0.01). In male patients sensitivity of RF was significantly higher in patients with smoking history (P<0.05) whereas that of ACPA and comorbidity rate of ILD were not significant. [Conclusions] Male patients without any factor contributing RA susceptibility are rare.

P2-015

Early arthritis cohort study for prediction of rheumatoid arthritis in healthy islanders: the 3rd report

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Conflict of interest: Yes

Aim: Autoantibodies have been observed in healthy subjects up to 10 years before they developed RA. 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. Informed consent were performed. To screen for early RA, we have been done as follows: (1) serum ACPA measure, (2) the questionnaires about arthralgia with finger and/or wrists, (3) the family history of the rheumatic diseases. The high-risk subject was defined as 2 out of 3 previous variables, and they were recommended to visit the rheumatologist for further exams. After 2015, ACPA positive subjects without arthralgia were included in the high-risk group. Results: We had obtained informed consents from 5339 subjects, ACPA positivity was 2.0 %. One hundred twenty eight subjects were required for further exams. Only 62 subjects (48 %) visited the rheumatologist, and final diagnoses were as 10 RA, 52 non RA (23 Osteoarthritis, 6 undifferentiated arthritis, 3 Spondyloarthropathy, 20 others). Current and past smoking rate was 30.0 %. Conclusions: During 4 years, ACPA positivity was 2.0 % in healthy islanders. Long-term follow-up is necessary to clarify the course of early arthritis.

P2-016

Changes of clinical practice over time for patients with rheumatoid arthritis receiving methotrexate in Japan

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Conflict of interest: Yes

[Object] To describe time trends of clinical practice for patients with rheumatoid arthritis (RA) receiving methotrexate (MTX). [Methods] We used Registry of Japanese Rheumatoid Arthritis Patients on Biologics for Long-term Safety (REAL, patient entry 2006-2011) and Clinical Outcomes of Japanese Rheumatoid Arthritis Patients in Real World Commencing Targeted Therapy (CORRECT, patient entry 2012-2017) database, and compared patients newly starting MTX between these two databases regarding baseline characteristics, RA treatments, changes of disease activity, and incidence rates (IRs) of serious adverse events (SAEs) in 3 years. [Results] Patients in the CORRECT group had shorter disease duration (REAL, 1.0 year; CORRECT, 0.4 year) and lower proportion of patients with Class 3 or 4 (REAL, 9.9%; CORRECT, 7.9%). The median dosage of MTX in 3 years was 6-8 mg/week in the REAL group, 8-10 mg/week in the CORRECT group. The percentage of patients with DAS28CRP <2.6 at 0.5,1,2,3 year was 64.4%,68.7%,75.8%,71.3% in the REAL group, 54.5%, 70.0%, 77.5%, 81.0% in the CORRECT group. The IRs (/100 patient-years) of SAE in the two groups were similar (REAL, 7.36; CORRECT, 7.63). [Conclusions] This study showed changes of clinical practice for Japanese RA patients with MTX in the real world.

P2-017

Clinical Practice for female patients with rheumatoid arthritis who desire to bear children, pregnancy and lactation in NinJa 2016

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Conflict of interest: Yes

[Object] To clarify the actual condition of female RA patients with who desire to bear children, pregnancy and lactation. [Methods] By using National Database of Rheumatic Diseases in Japan (NinJa) in 2016, we examine the wish to bear children, pregnancy and lactation in female RA patients under age 50 years. Patients were divided into 6 groups; group A (under age 25, n=23), B (25-29, 42), C (30-34, 86), D (35-39, 175), E (40-44, 324) and F (over age 45, 421), and examined the relationship between their wishes and their disease activities or treatments. [Results] Prevalence of the patients who desire to bear children was 17.4% in group A, 11.9% in B, 25.6% in C, 22.3% in D, 11.7% in E, and 1.4% in F. Their median age was 38 yrs. In comparison with the patients who don't desire to bear children, CDAI in those desire it was lower in group C, but higher in group D and E. Usage rate of steroid was also higher in group D and E, and that of etanercept or certolizmab pegol was significantly higher in group D, E and F. However, there were no differences in the disease duration or mHAQ. Eight patients in pregnancy (n=16) or in lactation period (n=10) were treated with biologics. [Conclusions] Actual condition of female RA patients was different depending on the wish to bear children.

P2-018

Pregnancy outcomes in 41 women with rheumatic diseases in our clinic

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Conflict of interest: None

To evaluate the obstetric outcomes of pregnancies with rheumatic disease, we retrospectively assessed pregnancy outcomes of 41 women with rheumatic diseases, seen at our clinic for the period between 2007 and 2017. Mean gestational age at delivery was 32.9 (±0.9). The most rheumatic diseases were as follow: systemic lupus erythematosus (18 cases), Sjogren's syndrome (7 cases), mixed connective tissue disease (5

cases) and other diseases (12 cases). At the time of delivery, 22 cases were treated with corticosteroids and 9 cases were treated with immunosuppressants. Three cases were treated with more than two immunosuppressants and there was no congenital anomaly of the newborns. A case was stopped mycophenolate mofetil at the 6 weeks pregnant and she had a baby with no congenital anomaly. In conclusion, 24% of the patients with rheumatic diseases were treated with immunosuppressants, and most patients had healthy babies except two.

P2-019

Present issues and problems of steroid therapy for polymyalgia rheumatica (PMR)

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Conflict of interest: None

[Object] To investigate the present issues of steroid therapy for PMR and elucidate the problems. [Methods] 72 patients diagnosed as PMR and started prednisolone (PSL) during June 2005 and December 2014 were included. Remission and PSL withdrawal rates in 1,3,6 months,1,2 years after treatment for 63 patients who could follow more than 3 months from the start were investigated, and the background of patients who achieved remission in one month after the start and those who did not were also examined. Adverse events occurred in the entire course of all 72 patients were examined. [Results] Of the 63 patients,39 patients achieved remission (62%) in one month and 50 patients (79%) in two years. PSL could be discontinued in 20 cases (32%). CRP at the start was extracted as an independent predictor for remission, and the cut-off point was CRP 6.2mg/dl. In the entire course,15 infections,6 malignant tumors,6 cardiovascular events,19 musculoskeletal or nervous system disorders appeared.A number of adverse events related to PSL occurred;4 hypertension,26 dyslipidemia,12 diabetes mellitus. [Conclusions] Although PSL was effective for PMR, the remission rate remained at only about 80%, and since many adverse events related to steroids occurred, a new treatment strategy not dependent on PSL is expected.

P2-020

Fundamental study on the role of TGF-beta in bone destruction of RA

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Conflict of interest: None

[Object] TGFβ is present in the bone matrix and is released in large amount in association with bone resorption and exerts its action locally. The effects of TGFβ on osteoclasts (OC) are yet to be clarified. Then, We examined the effect of TGFβ on RANKL-induced osteoclastgenesis using human peripheral blood monocytes (PBM). [Methods] Monocytes were isolated from the peripheral blood of healthy volunteers by the MACS magnetic beads method. Osteoclastgenesis was evaluated based on both the TRAP staining positive multinucleated cell number and the ability to form bone resorption pits on osteoplates. [Results] From 10 pg / ml, TGFβ1 suppressed osteoclastgenesis in a concentration-dependent manner. When gene expression of cathepsin K was examined by RT-PCR method, it was strongly induced by RANKL and significantly suppressed by TGFβ1. When TGFreceptor II (TGFRII) was added to the culture, the inhibitory effect of TGFβ1 was significantly released. when peripheral blood T cells were stimulated with immobilized anti-CD3 antibody, TGFβ1 was strongly induced. [Conclusions] TGFβ strongly suppresses induction of human OC. In the RA bone erosion locus, activated T lymphocytes and TGFβ released with bone resorption may suppress bone resorption locally.

P2-021

Exploring involvement of Inter alpha trypsin inhibitor heavy chain 4 in the pathology of GPI induced arthritis (GIA) mice and patients with rheumatoid arthritis (RA)

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Conflict of interest: None

Background/Purpose: We recently identified inter alpha trypsin inhibitor heavy chain 4 (ITIH4) was one of the major citrullinated proteins in serum, which is associated with disease activity in peptide (pGIA) RA. The aim of this study was to clarify the involvement of native and citrullinated ITIH4 in pathology of arthritis. **Methods:** 1) Immunohistochemistry of ITIH4 was performed in pGIA joints. 2) ITIH4 was assessed by semi-quantitative Western blotting in synovial fluid from untreated RA and osteoarthritis (OA) patients. 3) The concentration of plasma ITIH4 was examined by sandwich ELISA in RA patients healthy control (HC). **Results:** 1) ITIH4 was observed in the pGIA joints of Day14, while not in the joints of Day0 and Day28. 2) ITIH4 was detected in synovial fluid of both RA and OA. The relative intensity was significantly higher in RA patients. 3) Average plasma ITIH4 concentration was tend to be higher in RA patients compared with HC. There was no correlation between ITIH4 concentration and CRP value or DAS28-CRP. **Conclusion:** It was suggested that native ITIH4 increased in inflamed joints, but serum ITIH4 level itself did not correlat to disease activity. Further analysis on citrullinated ITIH4 is now in progress.

P2-022

Characterization of human tolerogenic dendritic cells generated with protein kinase C inhibitor and induction from patients with autoimmune diseases

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Conflict of interest: None

[Object] Tolerogenic dendritic cells (tDCs) are a promising therapeutic tool for specific induction of immunological tolerance. Human tDCs can be generated ex vivo using various compounds. We found that DCs (PKCI-tDCs) treated with protein kinase C inhibitor (PKCI) had potent tolerogenic properties. In this study, we describe the characterization of PKCI-tDCs and examined whether PKCI-tDCs could be generated from patients with autoimmune diseases. [Methods] We compared the tolerogenic properties of tDCs treated with PKCI, dexamethasone, vitamin D3, rapamycin (Rapa), IL-10, TGF-β, and PPARγ and retinoic acid. Moreover, we tried whether PKCI-tDCs could be generated from patients with rheumatoid arthritis (RA) or primary Sjögren's syndrome (pSS). [Results] All tDCs had a semi-mature DC phenotype and were stable against proinflammatory stimuli. PKCI-, TGF-β-, and Rapa-tDCs showed CCR7 expression and migration to CCL19, but other tDCs showed little or none. PKCI- and IL-10-tDCs induced functional regulatory T cells more strongly than other tDCs. Furthermore, PKCI-tDCs were generated from patients with RA and pSS not only before but also after treatment with agents such as methotrexate and prednisolone. [Conclusions] PKCI-tDCs may be most useful for tolerance-inducing therapy.

P2-023

A novel regulatory mechanism of Helios expression in CD4+ T cells

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Conflict of interest: None

[Object] Recently, we have reported that Tocilizumab treatment increases Helios expression in $CD4^+$ T cells in rheumatoid arthritis (RA) patients. However, the mechanisms that regulate Helios expression in $CD4^+$ T cells remain uncertain. The purpose of study was to elucidate a

novel regulatory mechanism of Helios expression in CD4+ T cells. [Methods] We searched for genes whose expression was inversely correlated with *Helios* expression in CD4+ T cells of RA patients by DNA microarray analysis. We then examined the role of identified molecules in Helios expression. [Results] *ZFP36* family molecules including *ZFP36, ZFP36L1, and ZFP36L2* were identified as genes whose expression was negatively correlated with the expression of *Helios*. TCR-mediated stimulation down-regulated Zfp36l2 expression but up-regulated Helios expression in CD4+ T cells in both humans and mice. Forced Zfp36l2 expression reduced Helios expression and down-regulated suppressive function in murine induced regulatory T cells (iTregs). Zfp36l2 caused Helios mRNA destabilization in an AU-rich element-dependent manner. [Conclusions] Zfp36l2 directly suppresses Helios expression and regulates suppressive function in iTregs.

P2-024

Ablation of Shp-1 in DCs induces autoimmune sialadenitis: characterization of the inflammatory cells in the salivary glands

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Conflict of interest: None

[Object] A tyrosine phosphatase Shp-1 is a negative regulator of signaling in hematopoietic cells and is expressed in immune cells including dendritic cells (DCs). To analyze the function of Shp-1 in DCs, we generated Shp-1 conditional knockout mice (CKO) in which *Shp-1* gene is specifically deleted in CD11c+ cells and found that CKO develop autoimmune tubulointerstitial nephritis (TIN). Since TIN is the most common renal manifestation of Sjögren's syndrome, we analyzed salivary glands of CKO to confirm the presence of sialadenitis. [Methods] We performed histological examination of salivary glands of CKO at the age of 40 weeks, then the single cells prepared from collagen-digested salivary glands were analyzed by flow cytometric analysis (FCM). [Results] Histological study showed CKO exhibited infiltration of inflammatory cells with periductal foci in salivary glands. Most of infiltrated cells were stained with CD4, B220 and F4/80. FCM revealed B cells increased in the salivary glands of CKO. A distinct B cell subset, B-1 cells, which are an important source of natural antibodies, also increased in the salivary glands of CKO. [Conclusions] DC-specific ablation of Shp-1 causes autoimmune sialadenitis characterized by the marked accumulation of B cells including B-1 cells.

P2-025

Expression of IL-29 in peripheral blood mononuclear cells in rheumatoid arthritis

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Conflict of interest: None

Objective: Among the cytokines produced from immunocompetent cells, interleukin (IL) -10 shows a high value in the serum of rheumatoid arthritis (RA) patients. IL-29 is known to have the characteristics of IL-10. We reported high levels of IL-29 in serum of RA and the possibility of playing a role in peripheral blood mononuclear cells (PBMC). In this study, the involvement of the expression of IL-29 in synovial tissue of RA and the adhesion ability to monocyte line was investigated. Methods: 1. Fluorescent immunostaining was performed to examine IL-29 expressing cells in synovial tissue of RA. 2. To identify the cells producing IL-29, human monocytic cells (THP-1), PBMC, human umbilical vein endothelial cells (HUVEC), synovial fibroblasts (fibro) were stimulated with TNF- IL-29 in the serum was measured by ELISA. 3. To identify the role of IL-29 on monocytic cells of RA, the adhesion ability of TH-1 stimulated with IL-29 to fibro was measured by Adhesion Assay. Results: 1. It was significantly expressed in monocyte lineage cells in synovial tissue of RA. 2. IL-29 was significantly higher in THP-1 · PBMC. 3. The ability of IL-29 to adhere to monocyte cells increased and increased with time. Conclusion: It was suggested that IL-29 may play an important role in monocytic lineage cells.

P2-026

Tumor necrosis factor-alpha induces expression of eotaxin-1/CCL11 and CCR3 from fibroblast-like synoviocyte in rheumatoid arthritis

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Conflict of interest: None

[Object] We investigate the expression of CCL11 and CCR3 in rheumatoid arthritis (RA). [Methods] CCL11 levels were determined in serum from healthy control (HC) and RA using ELISA. We measured CCL11 and TNF-α levels in synovial fluids (SFs) from osteoarthritis (OA) and RA using ELISA. To investigate CCL11 and CCR3 expression on fibroblast-like synoviocyte (FLS), cells were left unstimulated or were stimulated with TNF-α or CCL11. After stimulation, CCL11 levels in conditioned medium were measured by ELISA and mRNA levels of CCL11 and CCR3 were measured by qPCR. CCL11 expression on FLS was demonstrated by immunohistochemistry. [Results] CCL11 levels in the serum from RA were higher than those from HC. CCL11 levels in SFs from RA were higher than those from OA and were positively correlated with TNF-α levels. CCL11 mRNA expression and CCL11 secretion in FLS were time-dependently increased by TNF-α. CCR3 mRNA expression was also induced time-dependently by TNF-α. CCL11 mRNA was positively correlated with CCR3 mRNA. We confirmed that CCL11 expression on FLS was increased with TNF-α stimulation using immunohistochemistry. CCL11 induced CCR3 mRNA expression and CCL11 mRNA expression was self-induced by CCL11. [Conclusions] These data suggest CCL11 and CCR3 may play an important role in RA.

P2-027

Decreased inflammasome activation in healthy subjects treated with benzbromarone

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Conflict of interest: None

[Object] We investigated the effect of uric acid lowering therapy on inflammation in vivo in human, mainly focusing on the inflammasome activation. [Methods] Healthy adults who had no underlying disease were enrolled. They administrated benzbromarone (150 mg/day), a uricosuric agent, for two weeks. We collected the blood samples before and after administration and plasma and peripheral blood mononuclear cells (PBMCs) were separated. Inflammatory cytokines (IL-1β, TNFα, IL-8, IL-6, IL-18) in plasma were measured. PBMCs were cultured and stimulated with LPS and/or cholesterol crystals. [Results] The participants were 4 male and 4 female. The average of plasma uric acid level dropped from 6.0 mg/dl to 1.9 mg/dl by administration of benzbromarone ($p<0.01$). In vivo plasma IL-18 level was significantly decreased: before administration 273.2 ± 58.9 pg/ml, after administration 248.2 ± 52.7 pg/ml ($p=0.038$). However there were no differences in plasma Il-1β, TNFα, IL-6 and IL-8 level. Ex vivo both IL-1β ($p<0.01$) and TNFα ($p<0.01$) secreted from PBMC were significantly suppressed by administration of benzbromarone. [Conclusions] It indicated that benzbromaron itself or the effect on lowering serum uric acid level have the anti-inflammasome effect in human.

P2-028

Biological experiments and theoretical modeling reveal effects of human parvovirus B19 on the infected dendritic cells and their immune response

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Conflict of interest: None

[Object] We analyze the influence of human parvovirus B19 (B19) on monocyte-derived dendritic cells (MDDC) in in vitro culture. Then, we investigate the significance by constructing a theoretical model for presented antigens on dendritic cells (DC) and proliferation of the relevant T cells with high or low affinity T cell receptors (TCR). [Methods] 1. After $CD14^+$ monocytes from the peripheral blood of a healthy people were induced into MDDC and cultured with B19. We analyzed the change of cell surface molecules on these DCs and the production of IL-12p40. 2. We constructed a toy model representing antigens on DCs and calculated the probabilities of proliferation of T cells with high or low specificity using Mathematica. [Results] 1. In vitro culture, addition of B19 decreased the expression of HLA and co-stimulatory molecules in MDDC and IL-12p40 production from MDDC was decreased. 2. The theoretical analysis showed that the possibility of selective proliferation of T cells with high affinity increases under the conditions where HLA expression is down-regulated on DC. [Conclusions] Reduction of the expression of HLA in DC by B19 can increase specificity of proliferating T cells with high affinity TCR. We suggest the pathological significance of down-regulation of HLA in DC by B19.

P2-029

A study on the contribution of autoantibody-inducing CD4 T cell (aiCD4 T cell) help to the B cell maturation and possible autoantibody formation in SLE

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Conflict of interest: None

[Object] Autoantibody-inducing CD4 T (*ai*CD4 T) cell is indispensable for the 'self-organized criticality theory' which induces SLE. We previously showed that this *ai*CD4 T cell belongs to $CD45RB^{lo}122^{lo}$ CD4 T cell subpopulation. We here analyze the B cell population and assess our contention that autoantibody-inducing CD4 T cell (*ai*CD4 T cell) helps B cell maturation. [Methods] BALB/c mice were repeatedly immunized with OVA and SLE was induced. Cell surface marker of Bcell was detected using flow cytometry and analyzed its population. [Results] After repeated twelve times immunization with OVA, follicular B (Fo B) cell and germinal center B (GC B) cell were significantly increased ($P<0.05$), whereas marginal zone B cell was significantly decreased. Furthermore, activation markers of the B cell were increased, and in particular, CD80 was significantly increased ($P<0.05$). [Conclusions] The result showed that Fo B cell and GC B cell and the activation markers of B cell, as well, were significantly increased in the OVA-stimulated mice, which is compatible with the contention that *ai*CD4 T cells helps the maturation of B cells into germinal center B cells to enhance autoantibody formation in SLE.

P2-030

TNF-alpha modulates expression of p27Kip1 via c-Myc in RA-FLS

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Conflict of interest: None

[Object] TNF-α accelerates the proliferation of RA fibroblast-like synoviocytes (RA-FLS), however, the detailed mechanism remains unclear. In this study, we investigated the expression of c-Myc and $p27^{Kip1}$ to reveal the role of TNF-α in RA-FLS. [Methods] TNF-α accelerates the proliferation of RA fibroblast-like synoviocytes (RA-FLS), however, the detailed mechanism remains unclear. In this study, we investigated the expression of c-Myc and $p27^{Kip1}$ to reveal the role of TNF-α in RA-FLS. [Results] TNF-α decreased the expression of c-Myc while increased the expression of $p27^{Kip1}$. [Conclusions] As previously reported, the expression of $p27^{Kip1}$ was modulated by c-Myc *via* FOXO3a. Our results indicate TNF-α increased the expression of $p27^{Kip1}$ by down-regulating c-Myc in RA-FLS.

P2-031

Clinical and functional significance of STEAP4-splice variant in CD14+ monocytes in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] 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). The aim of this study is to elucidate the role of STEAP4 and its variant (v-STEAP4) in RA. [Methods] 1) We identified v-STEAP4 by sequencing, and compare the expression of STEAP4 and v-STEAP4 in $CD14^+$ monocytes from RA patients. 2) We investigated the correlation between the expression of STEAP4 or v-STEAP4 and clinical information. 3) We produced STEAP4 or v-STEAP4 overexpressing monocytic cell lines. 4) We analyzed intracellular localization of STEAP4 and v-STEAP4. [Results] 1) Exon3 splicing form v-STEAP4 and STEAP4 were more highly expressed in RA. 2) The expression of v-STEAP4 was positively correlated with RF and CRP, and STEAP4 was positively correlated with ESR and CRP. 3) The production of IL-6 by LPS was suppressed via decreased p-STAT3 by v-STEAP4 overexpression, while TNF-α was increased via degradation of IκBα. 4) V-STEAP4 was localized in nucleus, whereas STEAP4 was localized in endosome. [Conclusions] V-STEAP4 was identified in patients with RA, and might have a regulatory role in arthritis via the suppression of IL-6, probably due to the specific localization in nucleus.

P2-032

Histone methylation profiling in peripheral white blood cells of Behcet's disease

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Conflict of interest: None

[Object] Although a line of evidence has suggested genetic and environmental contributions to Behcet's disease (BD), epigenetic mechanisms may play pivotal roles in the pathogenesis as well. We examined the histone modifications of peripheral white blood cells (WBCs) in BD. [Methods] Peripheral WBCs were obtained from 28 patients with BD, 11 other connective tissue disease patients and 16 healthy controls (HC). Peripheral WBCs were classified as below: CD4+T cells, CD8+T cells, γδTcells, neutrophils, regulatory T cells, 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. Particularly, histone methylation in γδT cells correlated with the disease activity of BD. In addition, the similar results were also observed between active and inactive phases in the same patients. The change of histone methylation inγδT cells was specific to BD on compared with other connective tissue diseases. [Conclusions] Differences in histone modifications were detected in peripheral WBCs in BD patients. 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.

P2-033

Development and functions of B cells in anti-CCP IgM transgenic mice

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Conflict of interest: None

[Object] Anti-citrullinated protein antibodies (ACPAs), including anti-cyclic citrullinated peptide (CCP) antibody, are specifically produced in rheumatoid arthritis (RA). Induction of neo-antigens by citrullination and breach of B cell tolerance might be involved in ACPA production, but the detailed mechanisms remain unknown. Since Tsuda et al. have cloned an anti-CCP antibody and defined its specificity (Tsuda R, Arthritis Rheum, 2015), we generated transgenic mice expressing the antibody to analyze B cell tolerance. [Methods] Variable region of the human anti-CCP antibody genes are inserted into vectors generated to express mouse IgM (kindly provided by Prof. Amagai, Keio University). The gene fragments encoding the chimeric heavy and light chains were injected into fertilized eggs of C57BL/6 mice. [Results] CCP-specific B cells were detected in the bone marrow and lymphoid organs of the transgenic mice. Most of those in the periphery were CD93-negative mature B cells and were follicular B cells expressing CD23 but not CD21. While the expression levels of surface IgM were maintained, the transgenic B cells responded insufficiently in response to IgM crosslinking. [Conclusions] CCP-specific B cells seem to be tolerated, suggesting exposure to the antigens even in normal conditions.

P2-034

Development of rheumatoid arthritis stress control scale (RASCS) of rheumatic patients

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Conflict of interest: None

[Object] RA stress control scale (RASCS) was developed to measure how RA patients deal with stress in daily life and relief their pain. [Methods] The 350 people was randomly selected from the membership of the Japan Rheumatism Friendship Association and a questionnaire survey was done. Obtained data was shared with the item of family and others by the question form and was put to factor analysis. [Results] The factor analysis showed that factors are divided into 8; 1st: environmental adjustment (contributing rate of the dispersion, 12.1%), 2nd: relation with a doctor (10.2%), 3rd: management of a meal and sleep (8.2%), 4th: acquisition of knowledge about rheumatism (6.9%), 5th: management of a nap (rest) (6.0%), 6th: aggressive relaxation (6.0%), 7th (family factor): handle to pain and discomforts (30.8%), 8th (family factor): role awareness (13.2%). Cumulative contribution rate of family factor was 44.0% and of others was 49.4%. Reliability of the measure (α value) of family factor was 0.77 and of others was 0.59. [Conclusions] In order to develop RASCS, a questionnaire survey to RA sufferers was done and 8 factors are given as the factor which leads to painful reduction. It should be necessary to select the items carefully and improve the reliability of the scale (RASCS).

P2-035

The effect of stress-activated protein kinase (SAPK) inhibitors in fibroblast-like synoviocytes (FLS) isolated from rheumatoid arthritis (RA) synovial tissues

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Conflict of interest: None

[Objective] To investigate how mRNA expression, protein production of IL-6 and MMP-3, and phosphorylation of SAPK change in FLS isolated from RA synovial tissues. **[Material and Method]** Synovium was isolated from 3 RA patients who were performed total knee arthroplasty and FLS were isolated and cultured. These cells were incubated for 3h and 24h with c-jun N-terminal kinase inhibitor (JNKI) and p38mitogen-activated protein kinase inhibitor (P38MAPKI) (5 and10μM) in SAPK inhibitors. This study were assayed by real time PCR, and by Western blotting. **[Result]** The expression of IL6 mRNA (24h) with JNKI (10μM) increased to 3.5 times as compared to control, but the expression of MMP-3 mRNA (24h) decreased to 0.7 times. The expression of IL-6 protein (24h) did not change, but the expression of MMP-3 protein and JNK's phosphorylation (both 3h and 24h) decreased. The expression of IL-6 mRNA (24h) with p38MAPKI (10μM) decreased to 0.2 times, and MMP-3 decreased to 0.63 times. The expression of IL-6 protein (both 3h and 24h) decreased, and MMP-3 protein (24h) also decreased slightly. But the expression of p38MAPK's phosphorylation did not change. **[Conclusion]** The results in this study suggest that JNKI inhibits MMP-3 production in FLS, and that p38MAPKI inhibits both IL-6 and MMP-3 production.

P2-036

Clinical utility of valued life activities scale (VLA) as one of the patient-reported outcomes (PRO) in clinical practice of Rheumatoid Arthritis

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Conflict of interest: None

[Object] Among individuals with RA, patient-VAS (pt-VAS) and HAQ are commonly used as patient-oriented scales. However, both scales do not always reflect disabilities of their daily lives sufficiently. Recently, valued life activities scale (VLA) and shortened version of VLA (S-VLA) are reported as useful measurement of high level functioning including participating in social and recreational activities (1). [Methods] To investigate the clinical importance of S-VLA in Japan, we translated S-VLA questionnaire into Japanese and analyzed the results using Kyoto University Rheumatoid Arthritis Management Alliance (KURAMA) cohort. [Results] 199 subjects were included. Female were 83.8%, mean age was 64.6 years, mean duration of RA was 11.9 years, and mean DAS28-CRP score was 2.29. In univariate analysis, S-VLA ($r=0.6223$, $p<0.0001$), HADS-Depression score ($r=0.2639$, $p=0.0002$) showed positive correlations with pt-VAS. In multiple regression analysis, S-VLA (standardized $\beta=0.6220$, $p<0.0001$), HADS-Depression score (standardized $\beta=0.1841$, $p=0.0064$) showed independent correlations with pt-VAS while other indicators did not show significant correlations. [Conclusions] This study suggests the utility of S-VLA in Japan.

P2-037

MTX treatment in early stage is important for good prognosis of RA

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Conflict of interest: None

[Object] To bring out the outcome of five-year treatment, 247 patients with rheumatoid arthritis (RA) were collected from NinJa databases of 2012 to 2016. They all had visited the hospital of NinJa group within 2 years from disease onset. **[Methods]** 247 patients were divided to two groups (RL group: Remission or Low disease activity, MH group: Mod-

erate or High disease activity) according to their DAS28CRP data of 2016. **[Results]** Numbers of RL group was 205 and MH was 42. There were no significant differences between two groups concerning the age of RA onset, stage, CRP, RF, ACPA data, usage of GC and biologics, e.g. of the first year. On the other hand, DAS28CRP score, TJC and MTX usage of the first year had shown the significance. **[Discussions and Conclusions]** Although in the decades of T2T, it is difficult to treat RA patients ideally. It seems to be important that the patients with RA should be treated intensively with MTX from early stage.

P2-038

The efficacy of Remi-Check Q (infliximab Kit) in our clinic RA patients

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Conflict of interest: None

[Object] We have judged the dose escalation and the shortening of the duration of infliximab (IFX) by clinical manifestations. In the RISING study, it has been shown that more than 1μg/ml of IFX trough level, but we could not measure in clinical practice. Recently, we became able to measure IFX trough level by Remi-check Q (RCQ). We examined the efficacy of the RCQ in our clinic RA patients. [Methods] We determined IFX trough level by RCQ in 12 infliximab treated patients in our clinic. We compared the clinical manifestations with the result of RCQ. [Results] Patients were 62.6±13.3 years, male to female ratio 2:10, disease duration was 16.4±6.0 years, stage classification (stage 1; 2 cases, stage 2; 5 cases, stage 3: 5 cases), mean MTX was 8.33±1.87 mg/week, IFX administration period was 9.5±2.5 years. 9 cases of RCQ were positive, 3 cases of negative (Biosimilar in 1 case). Patients VAS and DAS 28 were improved in 6 of 9 patients with positive RCQ. In a negative case, we observed a worsening finding on the US (1 case). [Conclusions] RCQ was considered one of the useful judgment materials for increasing the amount and shortening the period. However, there are cases where clinical efficacy is poor even in RCQ positive cases, and accumulation of future cases is necessary.

P2-039

A study of bone destruction, hand function, and QOL in patients with rheumatoid arthritis

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Conflict of interest: None

[Background and objective] Hand lesions impair QOL in rheumatoid arthritis (RA) patients. The Disabilities of the Arm, Shoulder and Hand (DASH) is useful for assessing disability and treatment effects. We studied factors affecting hand function by DASH. [Method] We randomly extracted 160 RA outpatients satisfying the ACR 1987 classification criteria and sent questionnaires. We reviewed medical records to evaluate characteristics and treatment effects using DASH. [Result] The response rate was 99.4%, and 125 patients were evaluable using DASH. There were 24 men. The mean age was 66.0 years; mean disease period, 13.2 years. Five patients were untreated, 20 treated with steroids, 102 treated with csDMARDs, and 53 treated with bDMARDs. Mean DASH score was 32.2. DASH scores were significantly lower in male, young, and low-stage patients. Scores were significantly higher in patients on bDMARDs. DASH scores were significantly higher in patients with imaging changes in joints, especially in those with finger (particularly right thumb interphalangeal joint) more than wrist changes. [Conclusion] Reduced finger function in patients with more changes in finger joints than wrists suggests that early diagnosis and treatment may lead to upper extremity function retention.

P2-040

How do patients with rheumatoid arthritis evaluate their global assessment?

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Conflict of interest: None

[Object] We previously found that Japanese rheumatologists changed their strategy to ask patient global assessment (PtGA) according to the patients' understanding ability. To clarify how patients themselves evaluate PtGA, a focus group study was conducted. [Methods] During the period of August and September, 2016, a 90-minute focus group was held four times. The participants discussed about how to evaluate their conditions of rheumatism, how to evaluate the therapeutic effect freely. Totally, 34 women and 4 men, average age 56.1 ± 10.9 years old, and disease history 9.39 ± 9. 36 years joined the study. [Results] Many RA patients evaluated their PtGA based on pain, swelling, inconvenience of daily life, the mood of the day, comprehensively. However, they felt confusing because the criteria of how to evaluate PtGA was unclear. Most patients set "when most painful after onset" as 100, but the standard of 0 varied. Many patients had experienced a divergence between PtGA and CRP, and were eager that their doctor would understand the divergence. [Conclusions] It is necessary to be discussed about how to evaluate PtGA between doctors and patients at the start of treatment. By utilizing PtGA as a communication tool, it would facilitate establishment of good doctor patient relationship.

P2-041

Investigation of hand function required for self-administration of pen-type injector / autoinjector for subcutaneous injection

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Conflict of interest: None

[Object] Among the self-injectable devices of biologic agents, pen-type injector / autoinjector are useful for patients who have a strong fear of needle because they are easy to use and have a structure in which needles cannot be seen. However, dysfunction of hands is a problem for administration. Therefore, in this study, the hand function required for self-administration was examined. [Methods] 199 patients with rheumatoid arthritis (RA) in our hospital were investigated whether a button could be pushed using 3 kinds of demonstration injector. Age, sex, disease duration of RA, DAS28, patient VAS, BMI, the range of pronation and spination, HAND20 and grip strength were evaluated. [Results] There were 37 patients who could not push any device. Compared between the 37 patients and the patients who could push all devices, there was a significant difference in all parameters ($p < 0.001$). The most correlated factor was grip strength ($r = 0.414$). The cut-off value of grip strength for pushing the button was 13 kg. The patients who could not push any device were inferior to those who could push all in all items of HAND20. [Conclusions] Grip strength and HAND20 were useful as hand function evaluation of RA patients and can be an indicator of introduction of pen-type injector / autoinjector.

P2-042

Pattern change of EuroQOL 5 Dimension (EQ5D) and factors that have correlation with EQ5D in Rheumatoid arthritis patient who are underwent b- or ts-DMARDs

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Conflict of interest: None

(Object) EuroQOL 5 Dimension (EQ5D) is standard index for evaluating Quality of Life (QOL) in estimating cost/effectiveness (C/E) of drug. In rheumatoid arthritis (RA) treatment, it is important to evaluate the C/E of anti-rheumatic drug such as biologics (BIO) and JAK inhibitors (JAK-i), and to assess the EQ5D pattern change in administration. (Methods) RA patients who were underwent BIO or JAK-i from January

2007 to June 2017 was enrolled. Pattern change of EQ5D from start to 3 months after administration were evaluated, and factors that candidate to have correlation with each parameters of EQ5D, such as in patient's background, and monitored parameters were statistically evaluated with multivariate linear regression analysis. (Results) 151 patients were recruited. In patients who had evaluated as EULAR good response, all patterns of EQ5D had demonstrated to be improved. For each dimension of EQ5D, most significant factors that demonstrated significant correlation were Patient's Global Assessment (PGA) and modified Health Assessment Questionnaire (mHAQ). (Conclusions) BIO and JAK-i can be suggested that can attain good QOL as long as it has been evaluated good response. The other important landmark for the evaluation of good QOL is PGA and mHAQ.

P2-043

The remission achievement rate of functional assessment in rheumatoid arthritis patients with Treat to Target strategy

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Conflict of interest: None

[Object] Our final and realistic treatment goal in RA is not to receive uneasy in everyday life and a social activity. Now, T2T strategy became the standard strategy of the RA treatment, we think that the achievement of CR in early RA is relatively easy. We investigate the achievement rate of the functional remission receiving RA treatment with T2T strategy, and clarify the present situation. [Methods] In 411 RA patients, who continued to treat more than three months during a consecutive period until March 2017 from January 2016, we investigated them and examined in each parameter with the functional assessment (HAQDI and EQ5D5L). [Results] The ratio of HAQDI≦.5 was 64%. We recognized statistical significance for the functional remission achievement in their disease duration, weight, DAS at the last evaluation, MTX and GCs use situation, the former medicine treatment, stage, class, smoking history, HAQ-DI at the first our consultation. And, we indicated statistical significant difference in EQ5D-5L scores at the last observation day between the achievement of HAQDI≦.5 and the non-achievement. [Conclusions] We propose that the practice of both functional evaluations of an everyday life and the social activity is the only method that can contribute to good outcome.

P2-044

Long term effectiveness and safety of biologics for highly aged RA patients

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Conflict of interest: Yes

[Object] Biologicals treatment is carried out to old RA patients, but the validity and the safety over the long term are not clear. [Patient and Methods] In 4 establishments of participation, continuity rate of 48 cases who were newly treated with biologics after 75 years old was investigated. Effectiveness and safety of 15 patients who have finished continuing treatment over 4.2 years were examined. Adverse event was compared with the contrasting group. [Results] Continuity rate for 3 years of 48 patients was 68%, and cancellation reasons were infection in 7 patients, neoplasm in 2 and lack of effect in 2. DAS28-CRP average were 2.14, 2.27, 2.25, 2.53, 2.42 respectively 4.64 before introduction, MHAQ were 0.46, 0.51, 0.54, 0.60, 0.65 respectively 1-4 years later from 0.75, but mHAQ was deteriorating gradually after the 2nd year. Severe adverse events were admitted in 11 patients out of 15 patients, there were many cases of infection and/or pneumonia and cases of fall, bone fracture and osteoporosis. and there were clearly more cases than in the contrasting group. [Conclusions] Treatment effectiveness of biologics to highly old RA patients showed the same effect of younger RA patients. There was a lot of adverse event and caution should be exercised.

P2-045

Lower limb function and quality of life in patients with rheumatoid arthritis using Timed UP and GO (TUG) test

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Conflict of interest: None

[Object] We examined the lower limb function and QOL in patients with rheumatoid arthritis using the TUG test. [Methods] there was 26 RA patients. The average age of patients was 74 years old, the disease duration was 23 years, and the DAS28-CRP was 2.12. Using HAQ and SF-36, we investigated the ADL, QOL and the background for the lower limb malfunction group that exceeded TUG 13.5 seconds, which was regarded as falling risk, (referred to as group P) and the favorable group (referred to as group G). [Results] The average TUG was 11.5±4.3 seconds. The average age of the group G (19 patients) and the group P (7 patients) was 74±5, 76±5 years old (p=0.37), the BMI was 22±4, 23±3 (p=0.33), the DAS28-CRP was 2.09±0.7, 2.2±0.7 (p=0.61), the disease duration was 21±13, 28±10 years (p=0.24), the HAQ was 0.73±0.7, 1.68±0.7 (p<0.01), respectively. By multivariable analysis, the risk of the lower limb malfunction was the HAQ, and the odds ratio was 4.09 (95% CI 1.03 to 16.9). According to the SF-36, P group was significantly inferior in physical function and social life function. [Conclusion] Lower limb function in RA was strongly related to ADL such as HAQ over the age and the disease activity. Some patients well-controlled disease activity have a high risk of falling.

P2-046

Golimumab treatment retention rate and the factor influencing retention rate in patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] In this study, we investigated the retention rate of golimumab (GLM) treatment and the factors influencing the retention rate in patients with rheumatoid arthritis (RA). [Methods] We assessed the retention rate in accordance with the age, presence or absence of methotrexate (MTX), and predonizolone (PSL) combination in 101 patients with RA. [Results] Owing to the age distribution at 65 years and subsequent analysis, the mean age of patients under 65 years (56 patients) was 52.0 years, and the retention rate was 67.3%. On the contrary, the mean age of patients 65 years or older (23 patients) was 70.5 years, and the retention rate was 68.2%. The presence of MTX combination revealed that the mean MTX dose of 68 patients was 8.75 mg/week and the retention rate was 85.3%. In addition, the retention rate of 17 MTX-free patients was 76.5%. Furthermore, the presence of PSL combination revealed that the mean PSL dose of 58 patients was 5.01 mg/day and the retention rate was 66.1%. The retention rate of 34 PSL-free patients was 94.1%. Notably, PSL-free patients had a significantly high retention rate. [Conclusion]

The age and the presence or absence of MTX combination did not influence the GLM retention rate. PSL combination acted as a reduction factor in the retention rate.

P2-047

Analysis of RA patients in clinical remission by tocilizumab with low-field magnetic resonance imaging

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Conflict of interest: None

[Object] In RA patients achieved clinical remission, we clarify the association of low-field MRI (compacTscan; cMRI) inflammatory findings with structural damage progression. [Methods] The patients treated with Tocilizumab (TCZ), and who achieved DAS28-ESR (DAS) remission, were enrolled. 1) We analyzed baseline cMRI findings at remission. 2) We compared 1. clinical findings, 2. disease activity, 3. cMRI findings, between progressing bone erosion score group (PG) and non-progressing group (non-PG), retrospectively. [Results] 1) We examined 24 patients. At remission, there were cMRI findings of bone marrow edema (BME) in 41.7% patients, and of synovitis in 75.0%. 2) PG was 8 (47.9±21.5 years old) and non-PG was 16 (53.8±10.4 years old). 1. There was no significant difference in CCP+ rate between two groups. 2. DAS at starting TCZ in PG was higher than in non-PG (5.38±1.04 vs 3.81±1.19, $P<0.05$), however there was no significant difference in DAS at remission between two groups (1.75±0.77 vs 1.63±0.68, $P=0.58$). 3. At remission, BME score (3.0±3.7) and synovitis score (13.4±14.2) in PG were significantly higher than those (0.4±0.8 and 3.2±3.3) in non-PG ($P<0.05$). [Conclusions] In patients treated with TCZ, MRI findings in clinical remission seem to predict subsequent structural damage progression.

P2-048

Significance of Measurement of Trough Value in Infliximab-administered RA Patients

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Conflict of interest: None

[Objective] To examine whether to determine the effectiveness of infliximab by measuring the trough value and to verify the method of use such as future dose and change of administration period. [METHODS] IFX trough values were measured using Infliximab RemiCheckQ and future methods of use were examined. For disease activity evaluation, DAS28-ESR and SDAI were used. Measurements were made on 13 cases of 3 males and 9 females. Average age 68.9 years, average disease duration 29.6 years, average weight 51.4 kg, IFX average dose 8.68 mg/kg. The current mean disease activity was DAS28-ESR 2.65 SDAI 4.19 at the current mean administration interval of 8.6 weeks. [Results] 10 out of 13 cases were positive and 3 cases were negative. The average disease activity of 3 negative subjects was DAS 28-ESR 3.13, SDAI 5.75, 10 positive cases were 2.51 and 3.72, in negative 3 cases the disease activity tended to be high. The average dose was 7.43 mg/kg in the negative group and 9.06 mg/kg in the positive group. [Conclusion] Suggesting the possibility of prolonging the period and decreasing the dose for positive cases. Especially remission status was obtained for two cases with an administration interval of 12 weeks, and it seems that it may be tried to decrease the dose.

P2-049

mHAQ less than 0.5 is no longer target to treat in elderly rheumatoid arthritis patient

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Conflict of interest: None

(Object) Ageing have deep influence on modified Health Assessment Questionnaire (mHAQ) in rheumatoid arthritis (RA) treatment. The impact of effect of Ageing on mHAQ is statistically evaluated. (Methods) 516 RA patients who have been treated for more than 3 years, were enrolled. Patient's Age, mHAQ, 28-joints disease activity score with C-reactive protein (DAS28), Sharp/van der Heijde Score (SHS), pain score with visual analogue score (PS) were monitored since first consult (BL). Relationship between mHAQ and the other parameters including number of comorbidities (Com) at BL and last observational year period (FU), and its change were evaluated with multiple linear regression analysis (MLR). After correction that minimize effects of parameters other than Age, relationship between mHAQ and Age was also evaluated with MLR. (Results) At BL, Age, DAS28, and PS demonstrated significant correlation with mHAQ, while Age, SHS, PS, and Com demonstrated significant correlation at FU. After correction, Age demonstrated significant correlation with mHAQ, and its correlation coefficients (CC) was 0.013. (Conclusions) Age have deep influence on mHAQ. When patient's age exceeds 63, mHAQ increases 0.013 with one year. We should treat in according to T2T strategy being aware of patient's age.

P2-050

New tool for assessing patient general health - My Weather Note for Patients- might predict disease progression earlier than physician's estimates in patient with rheumatoid arthritis treated by Abatacept

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Conflict of interest: None

(Purpose) to compare new tool with conventional scales. (Methods) We evaluated patients' own general health scale per week by using "My weather note", which divided to sunny-very good, partly cloudy-anxious, cloudy-hard, rain-pretty hard and thunderstorms-the hardest. In this report, we assessed patients with rheumatoid arthritis treated by Abatacept. At the same time, the monthly clinical evaluation by physicians (DAS28-ESR, CDAI, CRP, RF) and other patient evaluations (HAQ-DI, RAPID3) were compared. We also evaluated quality of life by SF36K at the base line and three months after. (Results) Thirteen patients (average age 71.3 years and 149 months of disease duration) was investigated. The average of DAS28-ESR was 5.5, MMP3 337 ng/ml and patient VAS 61.6. ABT was injected subcutaneously except for one patient. The wether index responds almost equal to patient VAS duling ABT therapy. It appears to show the improvement of patients' general health about 2 weeks, which is earlier than Physicians evaluation concerning clinically improving group. (Conclusion) "My weather note" is a new tool for assessing patients' general health and might predict disease activity by conventional scales.

P2-051

Evaluation of the usefullness of Remicheck Q

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Conflict of interest: Yes

[Objective] The aim of this study is to evaluate the usefullness of Remicheck Q Kit. [Methods] We used Remicheck Q for patients with rheumatoid arthritis (RA) and examined the judgment method and results. [Results] There were 14 RA patients, 39 to 72 years old, 56.9 years old on average. According to the attached document, Remicheck Q was used by diluting patient serum 5-fold and judging by color development of the line. Of the 14 cases, the line of RemiCheck Q developed 13 cases, and it was judged that IFX serum concentration was 1 μg/ml or more except for 1 case. The line developed color within a few minutes after the diluted sample passed through. It was thought that there was a difference in concentration depending on case from IFX dose and administration interval, but there was no difference in coloring time and coloring intensity

of Remicheck Q line. The time required for determining the IFX serum concentration was about 30 minutes (centrifugation, specimen dilution, and judgment) after blood collection. [Conclusions] Remicheck Q can conveniently determine IFX serum concentrations and is considered a useful test method when considering the next treatment strategy at the time of efficacy reduction.

P2-052

Comparison of remission rate and subsequent attenuation of treatment between seropositive and seronegative patients with inflammatory arthritis receiving remission induction therapy with methotrexate

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Conflict of interest: None

[Aim] To compare remission rate and subsequent attenuation of treatment between seropositive and seronegative patients with inflammatory arthritis (IA) receiving remission induction therapy with methotrexate. [Methods] Patients with IA who started to receive methotrexate within 2 years after the onset of persistent symptoms of arthritis in Early Arthritis Clinic in NCU Hospital. Patients were classified as having rheumatoid arthritis (RA) according to the ACR /EULAR 2010 classification criteria for RA. Patients with established diagnoses including other connective tissue diseases were excluded. Patients positive for rheumatoid factor and/or anti-CCP antibodies and those negative for both of them were classified as seropositive (SP) and seronegative (SN), respectively. [Results] 188 patients with IA (162 RA and 26 undifferentiated arthritis; 49 SN and 139 SP) could be included. SN group was associated with higher age, higher disease activity, lower rates of concomitant other synthetic DMARDs and biologics, higher rate and dosage of glucocorticoids, and higher rate of successful tapering and discontinuation of methotrexate compared to SP group. [Conclusions] Serological finding predicts necessity for maintenance therapy and its intensity after successful remission induction therapy.

P2-053

IL-6 is an independent predictive factor for drug survival after dose escalation of Infliximab in patients with rheumatoid arthritis

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Conflict of interest: Yes

[Object] We aimed to investigate factors predictive of increased serum IFX concentration with improvement of disease activity, as well as better 1-year continuation rate after dose escalation, in RA patients who showed inadequate response to 3 mg/kg of IFX. [Methods] In 42 patients allotted to administration of IFX, 13 patients showed adequate response and 29 patients required dose-escalation after inadequate response. DAS28, mHAQ, serum level of CRP, IL-6, IL-17, anti-infliximab antibody titers and IFX concentration before and after dose escalation were examined. [Results] Multivariate analyses revealed that a serum IL-6 level of less than 4.0 pg/ml at baseline was the only factor predictive of clinically beneficial increase of serum IFX concentration. ROC analysis revealed that 5.16 pg/ml of IL-6 was the cut-off value. One-year drug survival rate of patients with IL-6 levels less than 5.16 pg/ml and greater than or equal to 5.16 pg/ml at baseline was 83.3% and 30.8%, respectively (Log-rank test, p=.011). [Conclusions] The results indicated that a baseline serum level of IL-6 below 5.16 pg/ml might be a predictive factor for a clinically beneficial increase of serum IFX concentration with improvement of disease activity and better 1-year continuation rate after IFX dose escalation.

P2-054

Evaluating the clinical features of seronegative rheumatoid arthritis to obtain their appropriate management

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Conflict of interest: None

[Object] To establish good management of seronegative (sero-) rheumatoid arthritis (RA), we evaluated their clinical features. [Methods] Newly-diagnosed RA patients in our hospital from Apr. in 2016 to Mar. in 2017 were stratified as sero- or seropositive (sero+). We retrospectively compared the clinical features, therapeutic regimens, and therapeutic response after 6 and 12 mo. between the two groups. [Results] We analyzed 109 patients (age 64 (20-95) y.o., female 64%, RF positivity 63%, ACPA positivity 61%). The sero- group contained more elderly patients and showed higher swollen and tender joint counts, higher CRP level, lower fulfilment of the 2010 criteria, higher US application rate, higher PSL usage than the other group. The sero- group responded well to treatment and reached remission after 12 mo. similar to the sero+ group. There were no inter-group differences in usage of anti-rheumatic drugs through the treatment period as well as PSL usage rate and PSL dose after 12 mo. [Conclusions] Because patients with sero- RA have a high risk for disability due to old age and high joint inflammation, prompt diagnosis is needed with applying US examination and transient PSL use as initial therapy accompanied by anti-rheumatic drugs may be considered to obtain rapid therapeutic response.

P2-055

Circulating gliostatin (thymidine phosphorylase) correlates with serological feature and response to IL-6 inhibitor therapy in patients with RA

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Conflict of interest: None

[Objective] Gliostatin (GLS) is known to have angiogenic and arthritogenic activities. We previously demonstrated significantly higher concentrations of GLS in the sera and synovial fluids of patients with rheumatoid arthritis (RA) compared to those with osteoarthritis or normal controls. Tocilizumab (TCZ) is a humanized monoclonal antibody against the interleukin-6 receptor. In this study we examined serum GLS concentrations of RA patients treated with TCZ. [Patients and methods] We evaluated serum MMP-3, CRP and GLS levels, and the disease activity score 28 (DAS28-ESR) in 14 RA patients (11 females and 3 males) treated with TCZ for more than 12 weeks. Among these patients the means of age and disease duration of RA were 57 years old and 14 years, respectively. [Result] The mean of DAS28-ESR was 4.76 at baseline, and that was improved to 2.50 after TCZ therapy for 12 weeks, the mean of MMP-3 (182.3ng/ml) improved to 86.2, the mean of GLS levels (2.03) decreased to 0.90ng/ml, respectively. [Conclusion] Serum GLS levels were reduced by TCZ treatment, and those were correlated with clinical outcomes in RA.

P2-056

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] In 73 RA patients who started GLM at our hospital, from 0 to 52 weeks of administration, and multivariate analysis was performed on factors contributing to remission. In addition, 13 cytokines before and at the 52th week were measured and the relationship with the effectiveness was examined. [Results] DAS28-CRP at 0 week, 4 weeks, 52 weeks significantly decreased from 4 weeks ($p<0.001$), and at 52 weeks 56.1% achieved clinical remission. and the combined dose of methotrexate (MTX) in two groups of remission and non-remission in multivariate analysis ($p<0.001$). The amount of combined MTX was high ($p<0.001$) was extracted as a contributing factor to achieving clinical remission. IL-6 at 52 weeks was significantly decreased ($p<0.00001$), correlated with reduction rate and disease activity improvement rate. [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.

P2-057

A Scoring System to Predict Treatment Response of TNF Inhibitors for Rheumatoid Arthritis (RA) patients

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Conflict of interest: None

[Object] To make a predictive scoring system for treatment response of TNF inhibitors (TNFi). [Methods] RA patients treated with TNFi (certolizumab pegol or adalimumab) in 4 sites are enrolled in this retrospective observational study during the period from July 2013 to February 2017. We analyzed factors associated with discontinuing TNFi, generated ROC curve as predictive model of the persistence rate at 24w of TNFi. Additionally we compared treatment response between TNFi group and tocilizumab (TCZ) group depending on the obtained scoring system. [Results] Corticosteroid user (PSL > 5mg/day) ($p=0.009$), DAS28-CRP > 4.0 at baseline ($p=0.005$) and past history of biologics use ($p=0.006$) were found as predictive factors of TNFi discontinuation. AUC of ROC curve was 0.755 (95% CI: 0.659-0.851), and the persistence rate at 24w in score 0, 1, 2 and 3 were 93.2%, 74.3%, 49.4% and 0%, respectively. Using a threshold of ≦ 1 scores, sensitivity was 42% and specificity was 92%. In patients with ≧ 2 score (TNFi 22 patients, TCZ 61 patients), TCZ group has longer persistence rate as compared with TNFi group ($p<0.001$). [Conclusions] High score predicted lower response rate of TNFi in score-dependent manner. TCZ was available for the high scored patients.

P2-058

Predictors of radiographic progression in patients with rheumatoid arthritis by using magnetic resonance imaging and ultrasound

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Conflict of interest: None

Object: To clarify the predictors of radiographic progression in patients with rheumatoid arthritis. Methods: Thirty three patients with RA were enrolled and observed for 12 months. They were evaluated by using US synovitis score, semi-quantitative exam by grey-scale and power Doppler (PD) every 3 months. MRI and radiograph were done every 6 months. Synovitis, bone edema and bone erosion were assessed by the Rheumatoid Arthritis Magnetic Resonance Imaging Scoring system (RAMRIS). Radiographic progression was defined as ΔGenant-modified Sharp score (GSS)>0.5. After univariate analysis, multivariate analysis was performed to establish the predictors for radiographic progression. Results: Median of disease duration was 9 months and that of DAS28-CRP was 4.20 at baseline. Radiographic progression was found in 12 patients. A univariate analysis showed GSS score and RAMRIS scores at baseline and 6 month, and US scores at 3 month and 6 month were associated with radiographic progression. Multivariate analysis revealed RAMRIS bone edema score at baseline and a synovitis of PD≧2 at 3 month and 6 month were predictors of radiographic progression. Conclusions: Our findings suggest RAMRIS score at baseline and PD≧2 after 3 month were useful to predict radiographic progression.

P2-059

Real-world effectiveness of Tocilizumab in rheumatoid arthritis: detection of predictor of achieving low disease activity

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Conflict of interest: None

[Object] To analyze the efficacy of Tocilizumab (TCZ) for rheumatoid arthritis (RA) patients and to determine the predictors of achieving low disease activity (LDA) in real-world clinical practice. [Methods] Patients have received TCZ and could calculate DAS28-ESR (3) at 24 week were included in this study. The patients were categorize into 3 group by biological therapy before this study (i.e. TNF group, ABT group, naïve group). Logistic regression was perfumed to determine the predictors of achieving LDA at 24 week. [Results] 101 patients (TNF group; n=18, ABT group; n=33, naïve group; n=33) were included in this study. The mean DAS28-ESR (3) at baseline was 4.85±1.31 and 9 (8.9%) patients achieved LDA. DAS28-ESR (3) improved significantly at 24 week (2.37±1.28 ($p<0.01$)), and 76 (75.2%) patients could achieve LDA. Disease duration (OR 0.76, 95% CI (0.644-0.917), $p<0.01$) and prednisolone dose (OR 0.698, 95% CI (0.509-0.957), $p=0.026$) were identified the predictors of LDA at 24 week in all patients, age (OR 1.38, 95% CI (1.00-1.92), $p=0.05$) and disease duration (OR 0.375, 95% CI (0.147-0.972), $p=0.044$) in TNF group, female (OR 33.36, 95% CI (1.75-634.1), $p=0.02$) in naïve group. [Conclusions] We concluded that female might be the predictor of achieving LDA of naïve group in real-world clinical practice.

P2-060

Factor analysis for therapeutic goal used Short Form-36 (SF-36) in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To evaluate factors for QOL assessment we prospectively analyzed three-component model of Short Form-36 (SF-36) v2TM in patients with rheumatoid arthritis (RA). [Methods] We measured the SF-36 in 252 patients with RA. We analyzed the relationship between three-components, physical component (PCS), mental component (MCS), and role/social component summary (RCS) and RA clinical disease activity, HAQ-DI, Total Sharp score, comorbidities in patients with RA. Three component summaries standardized by standard Japanese score50±10. We compared SF-36 score data from other countries and other diseases. [Results] Both of PCS (34.1±1.4) and RCS (37.8±16.6) was lower than MCS (48.7±9.1) in 252 patients with RA before treatment. Low RCS score concerned with ACPA positive, low HAQ-DI, and long disease duration by multi-variate analysis. On the other hand RCS score recover was related with low HAQ-DI, short disease duration by multi-variate analysis. [Conclusions] These data suggested that RCS in SF-36 was a useful analytical tool in health related quality of life of Japanese patients with RA.

P2-061

The relationships between the efficacy of MTX and MTX metabolic enzymes SNPs

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Conflict of interest: None

(Object) The efficacy of MTX depends on patients characteristic more than MTX doses. MTX (folate analogue) enters cells through RFC1 (reduced folate carrier-1) and are metabolized via dihydrofolate reductase (DHFR), Thymidylate synthase (TS). (Methods) MTX monotherapy 89 patients and MTX+biologics 81 patients We evaluated the relationships between clinical efficacy and RFC1, TS, DHFR in these patients cross sectional. Multiple regression analysisi were performed. Few patients were seriously evaluated by m-RNA of RFC1. (Results) RFC1 has the most strong relation with RA treatment efficacy comparing other SNPs. Ther were no relationships of DAS28 with all SNPs. (Conclusion) Other studies reported the importance of DHFR as a marker of side effects but our results revealed RFC1 has the relation with RA treatment efficacy. We conducted serious study m-RNA of RFC1 for more RA patients.

P2-062

Study of next treatment option in rheumatoid arthritis patients who had inadequate response to biologic DMARDs (BIO)

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Conflict of interest: None

[Objective] RA treatment is available for 8 biologics, and it is discussed how to use them properly, but there are few ones explicitly stated. Therefore, our hospital creates a Bio flowchart, adheres to it and is in charge of treatment. As a result, the clinical remission rate of 1st-Bio is 73%, but there are 27% patients who can't remission. The results of the following treatment options in 1st-Bio treatment failure were examined. [Method] Among the cases administered Bio treatment, In accordance with the Bio flowchart that made in our hospital 140 patients whose 52 weeks or more have passed since the final treatment change was applied Respectively at Apr 2009 to Oct 2016. We compared and evaluated remission rate of next treatment option and remission rate at 1st-Bio of our facility. [Result] The remission rates of next treatment options were ADA + IGU 82.8%, GLM 55%, TCZ 59.1%, ABT 32.4%. [Conclusion] By using our flowchart and To perform treatment without delay, it was confirmed that the clinical effect even if 1st-bio treatment was failure.

P2-063

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

[Object] To analyze the effect of early introduction of ADA (within 3 M from the introduction of MTX) and BF in RA patients. [Methods] Among 169 patients (M35, F134) who received ADA, 42 (M11, F31) 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 30 patients (M4, F26, age 54.0±14.9 years, disease duration 11.8±22.7 months) who were followed up more than 52 W. [Results] DAS28-CRP decreased from 4.64±1.35 to 1.73±0.48 ($p<0.001$). 25 patients achieved CR (83.3 %), and 12 patients (40%) achieved BF. One patient relapsed and re-started ADA, but achieved CR and BF again with the adjustment of csDMARDs. MTX (mg/W) was significantly increased from 7.3±1.9 to 8.8±3.2 ($p=0.00579$). The numbers of csDMARD other than MTX were 0.9±0.6 to 1.4±0.8 ($p=0.00574$). One patient discontinued bucillamine due to proteinuria. PSL (mg/day) was 6.1±3.6 to 2.8±1.7 ($p=0.00247$). Three patients with CR did not want BF. Five patients with sustained CR wanted BF and discontinuation of ADA was already scheduled. [Conclusions] Early introduction of ADA was effective and it might be a good choice in terms of medical cost due to BF.

P2-064

The trial to use moderate glucocorticoids for treating early rheumatoid arthritis patients to arrive at early remission (modified COBRA slim)

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Conflict of interest: None

[Object] In some cases, they are difficult to treat patients whose disease activity of rheumatoid arthritis are high. We sometimes use medium dose glucocorticoids before using cDMARD and evaluated those effectiveness. [Methods] 32 patients (10 men and 22 women, mean age 65.7 years) were enrolled between April 2010 and April 2017. After patients entered the hospital, hiro de cortisone sodium succinate (glucocorticoids) 100mg were injected for 3 days before used cDMARD. C-reactive protein (CRP) levels, the Disease Activity Score 28-CRP (DAS28-CRP), durations till remissions, final DMARDs, numbers and reasons to use bDMARDs were evaluated. [Results] After glucocorticoids injection, the average of CRP decreased from 5.2 mg/dl (0.1-16.5) to 1.4 mg/dl (0.1-4.4) and the average of DAS28- CRP decreased from 4.80 (3.48-6.05) to 3.46 (1.59-5.43) ($P<0.05$). Durations till remissions were 4 months (1-11 months). 18 patients were treated with only cDMARDs and 14 patients were treated with bDMARD. Response to glucocorticoids injection relates whether patients were treated with bDMARD ($P<0.05$). [Conclusions] Glucocorticoids injection were effective to reduce inflammations in early time. The bad response to glucocorticoids injection show the possibility to use bDMARD.

P2-065

Three cases of RA receiving tocilizumab more than 15 years

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Conflict of interest: None

The efficacy and safety during very long-term administration of tocilizumab (TCZ) are not well known. Here, I present three cases of RA receiving TCZ more than 15 years. [Case 1] A woman born in 1967 developed RA in December 1990. She was treated with prednisolone (PSL) at 5 mg daily in combination with gold sodium thiomalate (GST), iguratimod, or bucillamine. From November 2001, administration of TCZ started (DAS28ESR 6.30). [Case 2] A man born in 1938 developed RA in August 1998. He had high fever from October and was treated with PSL at

30 mg daily. Though salazosulfapyridine and MTX were added, polyarthritis remained. From August 2001, administration of TCZ started (DAS28ESR 5.10). [Case 3] A woman born in 1937 developed RA in August 1996. She was treated with D-penicillamine and GST. From May 1999, 5 mg daily of PSL was added. She participated in the clinical trial of infliximab from July to August. Thereafter, RA flare occurred. MTX 6 mg/w + PSL 10mg/d was not effective. From July 2001, administration of TCZ started (DAS28ESR 8.52). [Results] After administration of TCZ, all patients achieved remission soon. Swollen joint count (28) has been almost zero. Bone destruction was prevented. [Conclusion] Long-term use of TCZ maintains remission and prevents bone destruction.

P2-066

A study of 40 early rheumatoid arthritis (RA) patients who have achieved a drug-free remission at high rates

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Conflict of interest: None

[Object] A drug-free remission can be achieved by inducing apoptosis in all of her TNF-producing cells on the basis of the "transmembrane TNF" theory proposed by Dr.Takahiko Horiuchi of Kyushu University. At our clinic, a drug-free remission has been achieved at high rates as described below. [Method] A TNF-α inhibitor and MTX were concurrently administered to 40 early RA patients suffering from the disease for not more than six months and untreated with an antirheumatic drug. The dose of the biological drug was increased to promptly lead the patients to a deep remission, which was then maintained for not less than nine months. After one year of the treatment, the patients were kept drug-free and followed up for another year while periodically having blood tests. [Results] Thirty seven of the 40 early RA patients became drug-free within one year, and 33 of them did not have a recurrence by the end of the second year. In the four patients who had a recurrence after a drug-free remission, treatment with the biological drug and MTX was immediately resumed, leading them to become drug-free again within one year. [Conclusions] Our method allows 88 percent of them to become drug-free within one year, and is therefore superior to methods in which MTX is administered as the anchor drug.

P2-067

Analysis of the Efficacy, safety and drug retention rates of tocilizumab in elderly patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To compare the efficacy and safety of tocilizumab (TCZ) between elderly and younger patients with rheumatoid arthritis (RA). [Methods] We retrospectively evaluate the efficacy, safety, and retention rates of TCZ by classifying 93 patients with RA into two groups of 57 younger (under 65 years) and 36 elderly (65 years old and over) patients. [Results] Characteristics of patients; younger / elderly: onset age (mean) 41/60 years old, duration of disease 9/11 years, DAS28-ESR4 5.4/ 5.4, HAQ-DI 0.94 /1.54, dose of MTX 7.6 / 2.9 mg/ week, dose of PSL 2.8 / 2.7 mg/day. Lower dose of MTX and higher HAQ-DI were observed in elderly compared with younger patients. In effectiveness, DAS28-ESR4 and HAQ-DI significantly decreased in both groups for one year after initiation of TCZ therapy. TCZ continued in 43 younger (75.4%) and 29 elderly patients (80.6%). Retention rates were not significantly different between two groups. The reasons terminated TCZ; younger / elderly: severe adverse events 4 (7.0%) / 1 (2.8%) cases, lack of efficacy 5/0 cases. Number of patient with lack of efficacy increased was higher in younger group. [Conclusions] Efficacy, safety and drug retention rates of TCZ in the elderly patients were not inferior to younger ones with RA.

P2-068

Safety and effectiveness for Long term strategy in elderly Rheumatoid arthritis

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Conflict of interest: None

[OBJECTIVE] As for the RA, recommended T2T and complications or multiple drug various problems about the treatment for the old RA (following EORA). In EORA treatment of biological preparation (following BIO) examined treatment in our house. [METHODS] Randomly selected the EORA patient received in two years from June 2015 to June 2017 65 years or older. I examined patient background of Bio group and Non-Bio group, disease activity, HAQ change. [RESULTS] 22 BIO group (ABT GOL ADA) age 74.0 y o, 22 N-BIO group 74.6 y o HAQ significantly decreased in Bio group 24 months later. (0.91 → 0.60) DAS-CRP decreased together in BIO group for 24 months for 12 months (3.27 → 2.31). The liver and renal disease exacerbation and the serious infectious disease merger were not in both groups. [CONCLUSION] Treatment in consideration of CKD, complications including the cognitive functional decline is necessary for an elderly person, but it control HAQ and am connected by what the treatment that included BIO in positively in EORA is high in disease activity intervenes in for extension of the healthy life expectancy. But consider the safety management such as an infectious disease or the vaccination enough, and it is important to support patient education by the team medical care that did including a nurse.

P2-069

The experiences and perceptions of conventional synthetic disease-modifying antirheumatic drugs -induced interstitial pneumonitis - Comparison between rheumatologists and physicians other than rheumatologists by web -based survey

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Conflict of interest: None

[Object] To compare the experiences and perceptions of conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) -induced interstitial pneumonitis (IP) between rheumatologists who had specialist qualifications through Japan College of Rheumatology and physicians other than rheumatologists (non-R). [Methods] We performed a web-based questionnaire survey of Japanese physicians involved in rheumatoid arthritis (RA) treatment by csDMARDs. Respondents were asked about experiences of csDMARDs-induced IP, perceptions of IP risk and their clinical care. [Results] Valid responses were obtained from 184 physicians. We compared rheumatologists (66) with non-R (118). 48% of non-rheumatologists were practicing general medicine. Rheumatologists had significantly longer clinical experiences, and were assigned to more patients than non-R. 85% respondents stated they experienced csDMARDs-induced IP. 53% of rheumatologists and 27% of non-R experienced death caused by csDMARDs-induced IP. Comparing the content of medical care provided by two groups, less rheumatologists performed auscultation in outpatient settings. [Conclusions] Most of the physicians caring for RA patients experienced csDMARDs-induced IP. Rheumatologists may need to listen to patients' chest with a stethoscope.

P2-070

The efficacy of Tocilizumab therapy in rheumatoid arthritis

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Conflict of interest: None

[Object] To evaluate the efficacy in tocilizumab therapy with rheumatoid arthritis (RA) and an inadequate response to biologic disease-modifying antirheumatic drugs (DMARDs). [Methods] This study comprised 16 patients with rheumatoid arthritis intolerant to biologic DMARDs. Patients received tocilizumab therapy with or without metho-

trexate for 12 months. The outcomes were assessed with the disease activity during 12 months study period, using the 28-joint Disease Activity Score based on the erythrocyte sedimentation rate (DAS28 ESR) and Clinical Disease Activity Index (CDAI). [Results] DAS28ESR (from 3.6 to 1.4) and CDAI (from 7.7 to 1.2) decreased significantly from baseline to Week 52. DAS28ESR Remission achieved in 6 cases at Week 52. Tocilizumab monotherapy was also effective with RA patients of in adequate response to antiTNF inhibitor therapy. The retension rate of tocilizumab at 52 weeks was 90%. The average dose of methotrexate tapered from 9.7mg to 8.3mg. The average dose of glucocorticoid also tapered from 7.5mg to 2.8mg. [Conclusions] These results suggested that tocilizumab therapy is effective in patients with RA of an inadequate response to other biologic DMARDs.

P2-071

The examination of long-term efficacy of Abatacept (ABT) on patients with rheumatoid arthritis (RA) ~ by SWEET cohort

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Conflict of interest: None

[Object] We investigate the predictive factors for long-term clinical response to ABT on RA patients. [Methods] We evaluated their DAS28-ESR and DAS response at 12 and 24 weeks, 1, 2, 3, 4 and 5 years of 48 RA patients who started ABT treatment through Oct 2010 to Aug 2012. We compared their clinical / serological background and early DAS response between DAS-improved group and DAS-unchanged group. The same comparison was done between ABT-continuing group and dropout group. [Results] The mean DAS28-ESR at starting was 5.11, and it dropped to 3.70 after 5 years. The drug retention rate for 5 years was 32.5%, and the drug dropout rate due to inefficiency was 55.0%. There were significantly more naïve patients and more seropositive patients about both RF and anti-CCP antibody in DAS-improved group than in DAS-unchanged group at 1 year. No significant association was found in any backgrounds between these groups at 3 year and 5 year, however early DAS response was significantly associated with DAS improvement. There were significantly more patients with concomitant use of MTX and more good responders at 24 week in ABT-continuing group than in dropout group at 5 year. [Conclusions] Our study suggested that early DAS response may be important as predictive factors for long-term efficacy.

P2-072

Usefulness Remicheck Q in the RA patients with infliximab treatment

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Conflict of interest: None

[Object] Remicheck Q (Remi Q) is an in vitro diagnostic kit that determines whether serum IFX concentrations are less than 1 μg/mL or not less than 1 μg/mL by immunochromatography, and which help us to determine the appropriate dose of infliximab (IFX) in the patients of rheumatoid arthritis (RA). In this study, we investigated whether there were clinical differences between patients in Remi Q positive cases and negative cases. [Methods] Remi Q was used immediately before IFX administration to RA patients who were treated with IFX in our hospital. We divided patients into two groups, the Remi Q positive group and the negative group, and compared their background, serological marker, HAQ, comprehensive disease activity evaluation, and medication details at that time. [Results] In 34 cases (1 male, 33 females), the average age was 59.7 years ± 13.0 years. 25 were Remi Q positive (73.5%). CRP (0.11 vs 0.67 mg / dl, p =0.01) and DAS 28-CRP (1.94 vs 3.21, p =0.03) were significantly lower in the Remi Q positive group. There was no difference between the two groups in terms of disease duration, IFX administration interval, MTX amount, and RA treatment contents other than MTX and IFX. [Conclusions] We should use Remi Q for the patients with high CRP and/or DAS28-CRP during IFX.

P2-073

Short-term follow-up for early seronegative mono-, oligo- and poly-arthritis

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Conflict of interest: None

[Object] The aim of this study is to investigate the short-term follow-up for seronegative rheumatoid arthritis. [Methods] We retrospectively examined 576 rheumatoid arthritis (RA) patients since January 2012 until August 2015. Patients included in this study were diagnosed for seronegative RA and treated for at least 1 year. There were 32 patients, including 14 males and 18 females, were aged at 31 to 82 years old (averaged:55 years old). Patients were divided into three groups by the number of affected joints at first visit: mono-arthritis (MA), oligo-arthritis (OA) and poly-arthritis (PA) groups. MMP-3 level (ng/ml), DAS28-ESR, SDAI, and CDAI at first visit were compared to at one year later in each groups. Statistical analysis was made by *t*-test, and values of $p < 0.05$ were considered statistically significant. [Results] Averaged MMP-3 level in each groups decreased from at first visit to at one year later, but there were no statistically significance ($p = 0.981$, 0.170, and 0.553), Disease activity was improved from moderate to low in MA and OA, and also from high to low disease activity in PA. [Conclusions] MMP-3 level and disease activity could be improved on the patients with seronegative mono- or oligo-arthritis as same as poly-arthritis by treating adequately in early phase.

P2-074

Changes in Th subset of rheumatoid arthritis patients after ABA discontinuation and possibility of prediction of relapse

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Conflict of interest: Yes

[Object] Immunological changes after ABA withdrawal and factors affecting relapse were examined in RA patients with sustained low disease activity. [Methods] Twelve patients with RA who had low disease activity (below LDA) persisted with ABA treatment were included. Peripheral blood Th subset (Th1, Th2, Th17, Th17.1) at 0 wks, 8 wks, 16 wks, 24 wks after ABA discontinuation was analyzed by multicolor flow cytometry. In addition, serum IL-6 and TNFα were measured and the effect on relapse (moderate disease activity (MDA) or more) was examined. [Results] During follow-up for 24 weeks, 7 cases relapse. During the course, IL-6 (median 0 wks 3.4 pg / ml, 24 wks 3.0 pg / ml), TNFα (1.37 pg / ml, 1.60 pg / ml) did not change markedly and Th1 (19.5%, 18.4%), Th2 (2.5%, 2.7%), Th17 (1.6%, 1.8%), Th17.1 (0.23%, 0.15%) also showed no significant change. The patient group was divided into Th17.1-high and Th17.1-low group by median, and the period until relapse was analyzed. The relapse rate was significantly higher in Th17.1-high group (Log-rank, $p < 0.05$). [Conclusions] There was no significant change in the Th subset after ABA cessation. In this study, it was suggested that the proportion of IFN-γ-producing Th17 cells (Th17/1) at the time of ABA withdrawal may be a predictor of relapse.

P2-075

Sustained remission in rheumatoid arthritis patients from NinJa database

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Conflict of interest: None

[Object] To analyze the sustainability of remission in clinical settings and clarify the predictors for sustained remission using NinJa database. [Methods] Among the patients registered in NinJa, the data of patients who were in remission in 2003 (group A) and 2010 (group B) were analyzed. The Kaplan-Meier curves were used to assess the survival rate of remission. We stratified the patients according to age; gender; disease duration; mHAQ; use of biologics, methotrexate, corticosteroids, and NSAIDs at baseline. Log-rank test was used to assess the difference in survival rate. [Results] Number of patients were 427 (12.8%) in group A and 1568 (28.1%) in group B. The average remission time was 2.93 years in group A and 3.28 years in group B. Survival rate was significantly higher when patients were male, disease duration < 5 years or without NSAIDs in group A. In group B, survival rate was significantly higher when patients were male or under 65 years, those without NSAIDs or corticosteroids, and mHAQ ≦ 0.5. The survival rate decreased as Steinbrocker stage and class advanced. [Conclusions] The average duration of remission was around 3 years and recently induced remission tended to sustain longer. Male and disease duration < 5 years were predictor of sustained remission.

P2-076

Outcomes of etanercept therapy in elderly rheumatoid arthritis patients: an investigation of the Akita Orthopedic Group on Rheumatoid Arthritis registry

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Conflict of interest: None

Objective: We aimed to investigate the continuation rate for ETN therapy, reasons for discontinuation, and therapeutic effects among elderly RA patients Methods: Among 237 AORA-registered patients starting ETN therapy between January 2009 and August 2016, data for the 31 patients who were ³75 years old at the initiation of therapy were evaluated. We evaluated the 1-year cumulative continuation rate for ETN therapy, and investigated the characteristics of patients who discontinued treatment. We evaluated efficacy in 26 patients based on EULAR criteria. Results: The 1-year cumulative continuation rate for ETN therapy was 80.5%. Twenty patients discontinued treatment. The reason for discontinuation was 9 adverse events and 4 lack of efficacy. A mean age of 80.4 years at the start of treatment, with a mean disease duration of 14.3 years, 20.0% of patients switching from another biologic agent, and a comorbidity rate of 75.0%. Efficacy was noted for 54.8% of all patients with 52 weeks of ETN therapy. Conclusion: Retention rate and efficacy were considered satisfactory in elderly RA patients receiving ETN therapy. The risk of adverse events was suggested to increase with increasing age, declining ADL, and presence of comorbidities.

P2-077

Ten-year outcome of biologic agents in patients with rheumatoid arthritis in clinical practice

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Conflict of interest: None

[Object] The development of biologic DMARD (bDMARD) has improved the management of rheumatoid arthritis (RA). But data on the long-term effects of bDMARDs are not so many. So, the aim of this study is to evaluate the ten-year outcome of bDMARDs in patients with rheumatoid arthritis. [Methods] RA patients treated in our hospital between 2005~2007 were investigated and 30 patients were enrolled. 28 patients were treated with Etanercept (ETN) and 2patients treated with Infliximab (IFX). At baseline, average DAS28-CRP was 5.17 and serum MM-3 was 443. [Results] There were 19 patients who continue to visit our hospital for treatment (16 patients who continue first-line bDMARDs, retention rate was 53%), and 8 patients who died. The disease activity in patients who continue bDMARDs at the time of last visit was good, average DAS28-CRP was 2.06 and serum MMP-3 was 80.3. The patients who discontinued bDMARDs were significantly elderly than patients who continue (respectively, 68.4 years old, 58.0 years old, p=0.02). [Conclusions] In this study, the overall 10-year drug retention rate for RA patients treated by bDMARDs results comparatively good, but outcome of patients who discontinued bDMARDs were severe.

P2-078

Efficacy of iguratimod plus TNF inhibitor in rheumatoid arthritis patients who MTX cannot use

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Department of Rheumatology, Seirei Hamamatsu General Hospital

Conflict of interest: None

[Object] 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 IGU+Bio therapy in RA patients who had MTX intolerance at the author's institution. [Methods] Subjects were 5 patients who had MTX intolerance from August 2012 to March 2017. Previous treatment Bio. was ADA. Baseline characteristics were Mean age 59.2 years, mean duration of illness 100.0months, corticosteroid use 20.0% (mean 3.0mg/day). The course of DAS28, SDAI, CDAI and remission rates were analyzed. [Results] Mean DAS28-ESR, SDAI, CDAI were decreased trend from the initiation of IGU treatment at 24 weeks (3.29→2.30, 5.88→1.88, 5.46→2.68). Remission rates of DAS28-ESR, SDAI, CDAI were 40%, 80%, 80% at 24 weeks. [Conclusions] IGU+Bio might be a new RA treatment option for aiming remission in patients who had MTX intolerance.

P2-079

Analysis of tocilizumab subcutaneous injection for patients with rheumatoid arthritis

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Conflict of interest: Yes

[Objective] In this study, cases of using tocilizumab (TCZ) subcutaneous injection were examined. [Subjects] The features of TCZ subcutaneous injection were examined for rheumatoid arthritis (RA) cases into which TCZ subcutaneous injection was introduced so far. [Results] There were 12 cases, 2 males and 10 females. The age was 40 to 83 years old, and the average age was 60.9 years old. Six cases were BIO naive cases, and there were two cases of change from TCZ infusion to TCZ subcutaneous injection, and in 5 cases from prior BIO. Transition from TCZ infusion to subcutaneous injection, acquisition of subcutaneous injection

technique was also smooth, and the effect was also equal to or higher than drip. In 3 cases in which the effect was insufficient during the follow-up observation with TCZ subcutaneous injection, the administration interval was shortened to one week, and the expected effect was obtained, and thereafter it was possible to return to administration at intervals of two weeks met. [Discussion] As a result of examining RA cases with TCZ subcutaneous injection, the number of cases was small, but it was considered to be a drug which can increase the drug effect by shortening the administration interval when the effect is weak.

P2-080

Prognostic factors for abatacept retention in our department

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Conflict of interest: None

[Object] We report the retention rate of abatacept (ABT) to rheumatoid arthritis (RA). [Methods] 80 subjects who administered ABT to RA in our department from September 2010 to November 2016 were evaluated. [Results] 64 females, average age 67.6 years, mean disease duration 11.3 years (2 years or more 63 cases) were characterized. The seropositivity was 43 cases of anti-CCP antibody (ACPA) ≧ 100 U / ml, 45 cases of RF ≧ 45 IU/L, and 35 cases of both positive. In induction, 68 cases of administered methotrexate (MTX) (average 8.4 mg / week), intravenous infusion was performed for 63 cases (5 cases was changed to subcutaneous injection (sc)), sc was 17 cases. The bDMARD naive was 39 cases. We evaluated 67 cases excluded except for less than 3 months of ABT use and the patients introduced to other clinic. The retention rate of one year was 70% and the median duration of retention was 2.31 years. The ACPA positive, ACPA and RF double positive group, the initial transfer group predominantly had high persistence rate. The ACPA and RF double positive group with MTX contributed to retention rate. [Conclusions] The high retention rate of ABT could be expected in seropositive cases, especially in double positive cases with MTX, or initial introduction cases.

P2-081

The clinical course of abatacept treatment selected for safety reasons

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Conflict of interest: None

[Object] 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] 84 RA patients who underwent ABT treatment at our hospital were enrolled in this study. We compared disease activities, drug retention rate and adverse events (AEs) between patients selected for safety reasons (Subject group) and another group (Control group). [Results] 66 patients were included in subject group. In the baseline data, there was no significant difference between Subject group and Control group, except for age, stage, class. The change of the disease activity after the initiation of treatment was equivalent in both groups. Drug retention rate at 3-year was 50.8% in Subject group and 55.4% in Control group, whereas discontinuation rate due to IRs in Subject group was higher than that in Control 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.

P2-082

Comparison of Three Kinds of Biological Agents (Tumor Necrosis Factor Inhibitor Golimumab, Interleukin-6 Inhibitor Tocilizumab and T-cell Co-stimulation Modulator Abatacept) in Patients with Rheumatoid Arthritis Patients from Daily Clinical Practice Data

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Conflict of interest: Yes

[Object] TNF inhibitor, IL-6 inhibitor and T-cell co-stimulation modulator are 3 major bDMARDs. The objectives of this study is to investigate the differences among bDMARDs with different mode of action. [Methods] This retrospective study used RA patients who start one of 3 kinds of bDMARDs (GLM, TCZ or ABT) from Toyohashi RA Database (TRAD). Patients' characteristics and drug continuation rate were investigated. Next, we investigated time-course of disease activity, activity of daily living, immunological status (RF) and concomitant drugs. [Results] 60, 65 and 46 patients were treated with GLM, TCZ and ABT, respectively. GLM group presented higher MTX concomitant rate and lower PSL concomitant rate. TCZ group were younger and had shorter RA duration. ABT group were older and had longer RA duration. Drug continuation rate were comparable among 3 bDMARDs with no statistical differences. Comparison of time-course of CDAI showed similar trends. Interestingly, only RF in GLM group significantly decreased time after time. PSL was tapered in all group. MTX was tapered in TCZ group and ABT group. [Conclusions] Baseline patients' characteristics may be one of the important information to choose bDMARDs. Results of drug continuation rate and efficacy were similar.

P2-083

Prevention for progression of rapid radiographic progression and bone marrow edema in early RA patients with RRP associated with bone marrow edema by treatment with biologics

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Conflict of interest: None

[Objective] To study whether biologics treatment prevents the deterioration of bone marrow edema (BE) and rapid radiographic progression (RRP). **[Methods]** Seventeen early RA patients (male 4, female 13) with extensive BE in hand MRI test were enrolled. All patients met RRP criteria, and their clinical demographics were: average age: 64.9 years old, disease duration: 20.8 months, DAS28-ESR: 4.51, yearly modified total Sharp score (mTSS): 17.2/year. After 24 weeks of treatment with biologics, change in DAS28-ESR, mTSS/year, BE in MRI were investigated. **[Results]** BIO with ADA (12 patients), IFX (1), GOL (1), ABT (2), CZP (1) were combined with methotrexate (9.6mg/week). After 24 weeks, DAS28-ESR was reduced from 4.51 to 2.94 by a short-time treatment with biologics. Importantly, apparent reduction of BE was also determined in 70% of patients. Mean mTSS/y from all patients was significantly reduced from 17.2 to 4.4, and consequently, RRP rate was decreased from 100% to 22%. None of patients whose BE was improved by this treatment were categorized in RRP. **[Conclusions]** A short-term usage of biologics reduces progression of BE, and consequently prevents the progression of arthritis into RRP category in 70-80% of early destructive RA despite DMARDs therapy.

P2-084

Continuation Rate of Biological Treatment in Patients with Rheumatoid Arthritis

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Conflict of interest: Yes

[Object] The object of the present study is to investigate continuation rate of biological (BIO) treatment in patients with RA, especially in se-

nile RA patients. [Methods] Toyohashi RA Database (TRAD) was used. 330 RA patients who initiated biological agents in our institute were used. 272 female and 58 male. Continuation rate of biological treatment was analyzed using Kaplan-Meier method. In this study, switching from one biological agent to another was defined as continuation of BIO treatment. [Results] Baseline characteristics at the initiation of BIO treatment: Mean age was 58.1 years. Mean RA duration was 10.9 years. Continuation rate of BIO treatment is 88.4% at 1 year, 82.0% at 3 years, 72.2% at 5 year and 57.1% at 10 years. Next we divided all patients into three groups (A group (n=210): 64 years, B group (n=98): 65-74 years, C group (n=22): 75 years). There were significant differences in continuation rate of BIO treatment between A and B and between A and C, but not between B and C. [Conclusions] 10-year continuation rate of BIO treatment was about 60% in older RA patients. Continuation rate of BIO treatment in senile RA patients was inferior to that in non-senile RA patients.

P2-085

Efficacy and safety of tocilizumab (TCZ) in elderly patients with rheumatoid arthritis (RA)

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Conflict of interest: None

[Object] To assess the safety and efficacy of TCZ in elderly RA patients treated in daily practice. [Methods] We divided RA patients into under 65 years group (<65) (N=39) and over 65 years (≧65) (N=20) by the age of TCZ initiation. We compared transition of SDAI/CDAI, their improvement ratio and TCZ retention between two groups. TCZ retension was estimated with the Kaplan-Meier method. [Results] In <65/≧65 group, SDAI were 27.8/26.4, 15.9/15.0, 10.3/13.9, 9.5/11.6, 9.0/10.9, 9.2/9.8, 7.8/10.0, 8.3/8.7, 7.5/9.1, CDAI were 25.5/24.8, 15.4/14.7, 10.2/13.9, 9.5/11.5, 9.0/10.7, 9.1/9.8, 7.8/10.0, 7.6/8.7, 7.9/8.6, 7.5/8.9 at 0, 1, 2, 4, 6, 12, 18, 24, 30, 36 months. After 1, 2, 4, 6, 12, 18, 24, 30, 36 months, SDAI improvement ratio were 44/42%, 62/45%, 61/53%, 64/57%, 65/60%, 70/59%, 70/63%, 66/64%, 71/63%, CDAI improvement ratio were 41/38%, 59/38%, 58/48%, 62/53%, 63/57%, 68/56%, 68/61%, 66/62%, 69/61%. Cumulative retension were 90/92%, 90/90%, 90/85%, 90/82%, 80/74%, 75/60%, 76/60% at 3, 6, 12, 18, 24, 30, 36 months (P=0.71 Log-rank test). No significant deference was seen between two groups in transition of disease activity and drug survival. [Conclusions] TCZ was safe and effective in elderly RA patients as well as in younger patients under appropriate risk management in daily practice.

P2-086

The efficacy and adverse events of abatacept in patients with rheumatoid arthritis associated with autoimmune diseases or autoantibodies

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Conflict of interest: Yes

[Object] To investigate the characteristics and results of autoimmune disease-associated or autoantibody postive (in addition to RF and ACPA) RA (AA-RA) patients treated with abatacept (ABT). [Methods] Patients characteristics, efficacy, and adverse events were retrospectively investigated in patients with AA-RA and other RA (NAA-RA), who were treated with ABT. [Results] Thirty AA-RA patients (Sjogren's syndrome 7, SLE 6, other diseases 7, anti-nuclear antibody positive 10) and fifty NAA-RA patients were studied. NAA-RA group were younger and more female dominant. Disease duration, ratios of stage III/IV, previous biological therapy, and frequency and dosage of concomittant prednisolone or methotrexate were comparable. At 6 month, both groups showed similar continuation rate, DAS28CRP reduction, and remission rate. The rates of discontinuation due to efficacy or adverse events were similar in two groups. But two patients in AA-RA (both showed anti-SS-A Antibody positive Sjogren's sybdrome) discontinued ABT by an onset of interstitial lung disease and eruption. [Conclusions] AA-RA and NAA-RA showed similar efficacy, continuation rate, and adverse events, but two AA-RA patients developed infrequent adverse reaction in the lung and the skin.

P2-087

Safety and adherence of infliximab in patients with rheumatoid arthritis who started the therapy before and after the dose escalation allowed

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Conflict of interest: None

[Object] Infliximab (IFX) has been approved to rheumatoid arthritis (RA) since 2003. The product has been allowed for dose escalation and/or shortening the interval since July 2009 in Japan. We compared the safety and continuation rates of IFX in RA patients who started IFX therapy before and after the dose escalation allowed. [Methods] The study involved 152 patients. They were divided into 2 groups by the time of initiation of IFX before (group A, n=96) and after July 2009 (group B, n=56). They were evaluated with respect to their clinical characteristics, DAS28, HAQ score, inflammation markers, RA-related markers, medications, and 3-year outcomes and treatment discontinuations. [Results] There were no significant differences in age onset of RA, gender, disease duration, biologics naïve rate, DAS28-ESR4, HAQ, RF and MMP-3 between the groups. Higher dose of methotrexate and lower dose of prednisolone were significant in the group B than the group A. The prevalence of patients who received IFX dose escalation therapy was lower in the group A than the group B for 3 years. Adverse events and continuation rate didn't increase in group B. [Conclusions] In group B, there were more patients with dose-escalation because of inefficacy, and less PSL dose administration, but no superior adhesion.

P2-088

The effects of tocilizumab therapy on articular joints in rheumatoid arthritis patients

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Conflict of interest: None

[Object] The objective of current study is to evaluate the effect of TCZ treatment in patients with rheumatoid arthritis (RA), on articular cartilage. [Methods] Participants comprised 25 patients who met the 2010ACR/EULAR classification criteria. At baseline and at weeks 24 (clinical) and 52 of TCZ treatment, clinical and radiographic data results were obtained. Clinical evaluations were made using the DAS28-ESR. Peripheral blood was obtained at the same time and serum concentrations of cytokines and serum biomarkers for degradation (C2C: Collagen Type II Cleavage) and synthesis (CP2: Procollagen Type II C-Propeptide), and MMP-3 (Matrix Metalloproteinase-3) were analyzed. Biomarker concentrations, cytokine concentrations, MMP-3 and DAS28-ESR between patients with radiographic progression (total sharp (van der Heijde) score (TSS) and with no progression per year were compared. [Results] Comprising 12 patients with no progression of TSS (Group A), and 13 patients with progression of TSS (Group B). Mean serum concentration of MMP-3 (ng/ml) in group A was 269.3 at baseline and 82.8 at 24 weeks in Group A, and 230.9 and 206.3 in Group B. [Conclusions] There were no significantly differences, the serum concentrations of MMP-3 were decreased in group A, from baseline to at week 24.

P2-089

The efficacy of subcutaneous Tocilizumab for patients of Rheumatoid arthritis

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Conflict of interest: None

[Object] We evaluated efficacy of subcutaneous Tocilizumab (TCZ-SC) for patients of Rheumatoid arthritis. [Methods] In this study we included 97 patients (female: 86, male: 11) who were administrated with TCZ-SC over 52 weeks. Efficacy was evaluated based on retention rate and safety as well as SDAI from starting to 52 weeks. The subjects of baseline were as below, age: 63±14 years, disease duration: 17.1±10.3 years, the rate of concomitant methotrexate: 28.9%, duration of administration: 2.6±1.1 years. [Results] The retention rate of TCZ-SC by Kaplan Meier method was 91.7% at 2.5 years. In 9 discontinued cases, the reasons of that were adverse events: 6, insufficient: 3 other: 1. Average of SDAI improved 15.7±12.3 to 9.4±8.3. We divide two groups of patients: changing from TCZ-drip treatment (group D: 52) and starting with TCZ-SC (group S: 45). The retention rate at 2.5 years was 91.7% in group D, 91.5% in group S. Average of SDAI improved 9.6±8.2 to 8.3±6.8 in group D, 22.7±12.5 to 9.4±8.3 group S. There were statistically differences of average of SDAI at starting in 2 groups, but there was no difference of that at 52 weeks. [Conclusions] This study indicated that TCZ-SC has longterm efficacy for patients in rheumatoid arthritis.

P2-090

The MTX dose combined with biological DMARD in patients with RA by NinJa2016 cohort

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Conflict of interest: None

[Object] The purpose of this study is to evaluate the influence of the MTX dose combined with biological DMARD in patients with RA by NinJa2016 cohort. [Methods] In 15343 RA patients registered in Japanese large cohort of NinJa (National Database of Rheumatic Diseases by iR-net in Japan), 3029 patients had the combination therapy with MTX bDMARD or bDMARD monotherapy, respectively. without csDMARD except MTX. We investigated the average dose of MTX and the rate of monotherapy, below MTX 4mg/week, over MTX10mg/week in each groups by observational cohort. [Results] The average dose of weekly MTX was IFX8.26±2.8mg, ADA7.42±3.8mg, GLM6.63±3.9mg, CZP6.70±4.5mg, ETN5.16±4.3mg, ABT3.89±4.3mg, TCZ3.24±4.2mg, respectively. The rate of monotherapy was TCZ57.1%, ABT47.8%, ETN33.3%, CZP25.7%, GLM15.7%, ADA11.1%. The rate of bDMARD with MTX dose below 4mg per week was GLM13.2%, IFX10.2%, ETN10.2%, ABT9.9%, ADA9.7%, TCZ8.1%, CZP3.4%, respectively. The rate of bDMARD with MTX dose over 10mg per week was CZP38.5%, IFX32.9%, ADA32.7%, GLM25.2%, ETN18.5%, ABT13.6%, TCZ11.0%, respectively. [Conclusions] The higher dose of MTX was medicated for RA patients, combined with TNF inhibitor than non-TNF inhibitor, and in TNF inhibitor, anti-TNF monoclonal anitibody than TNF receptor fusion protein.

P2-091

Five years drug survival rate of Tocilizumab for patients with Rheumatoid Arthritis

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Conflict of interest: None

Object: The purpose of this study was to evaluate five years drug survival rate of Tocilizumab (TCZ) therapy for patients with Rheumatoid Arthritis (RA). Methods: Subjects were 140 patients (30 men and 110 women) who had TCZ therapy between May, 2008 and April, 2012. The background of subjects at baseline included the following: age; 58.0±13.0 years, disease duration; 12.4±13.5 years, first biological use; 37.8%. We retrospectively analyzed drug survival rate by Kaplan-Meier method, adverse event and efficiency of TCZ therapy for five years. Results: The five years drug survival rate was 59.8%. Outcomes of patients were continuation (69/140), discontinuation (58/140) and loss following (13/140). The reasons of discontinuation of this therapy were adverse event (26/58), insufficient effect (21/58) and others (11/58). The adverse event were infection (9/26), drug allergy (5/26), interstitial pneumonia (4/26) and others (8/26). The clinical characteristics of 69 patients who could continue this therapy for five years included the following (at baseline, at 5 years, respectively): SDAI; (28.9±13.6, 8.5±6.9), rate of low disease activity (%); (5.8, 42.6), rate of remission (%); (0, 26.5). Conclusions: The five years drug survival rate of TCZ therapy was 59.8%.

P2-092

Clinical efficacy of certolizumab pegol therapy in patients with active rheumatoid arthritis; two years of follow-up ~a Multicenter Registry Study ~

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Conflict of interest: None

[Objectives] To evaluate the clinical efficacy of Certolizumab pegol (CZP) in patients with RA. [Methods] Participants were all patients registered in a Japanese multicentre registry who were treated with CZP and had at least two years of follow-up (n = 98). We reviewed the methods about the improvement of DAS28-ESR and SDAI, and the rate of remission patients at Year2 by LOCF method. [Results] The group of patients included 16 males and 82 females. The mean age was 59.5±14.7 years old; the disease duration was 9.4±8.8 years. The DAS28-ESR improved from 4.84±1.36 at baseline to 3.54±1.35, 3.31±1.46, 33.37±1.47, 3.31±1.43 and 3.28±1.48 at Week 4, 12, 24, Year1 and 2 (all $p<0.001$) significantly. The SDAI improved from 21.2±11.3 at baseline to 11.4±9.0, 9.7±9.0, 9.8±9.1, 9.4±9.1 and 9.2±9.2 at Week 4, 12, 24, Year1 and 2 (all $p<0.001$) significantly. At Week 4, 12, 24, Year1 and 2 the rate of patients who achieved remission were each 28.8%, 37.2%, 32.9%, 33.7% and 34.6% in DAS28-ESR criteria. At Week 4, 12, 24, Year1 and 2 the rate of patients who achieved remission were each 11.7%, 29.3%, 30.5%, 28.8% and 30.8% in SDAI criteria. [Conclusion] This study suggested that the CZP was effective in patients with active RA for 2 years.

P2-093

Serum IL-6 concentrations correlate with swelling joint counts in Rheumatoid Arthritis under Tocilizumab treatment

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Conflict of interest: Yes

[Object] Tocilizumab (TCZ) is an IL-6 receptor blocker that increases serum IL-6 concentrations while normalizing serum inflammatory markers such as CRP. The purpose of this study was to examine the clinical significance of serum IL-6 and its consecutive measurement in CRP-negative patients during TCZ treatment. [Methods] Fifteen RA patients treated with intravenous TCZ who achieved normal CRP levels were included. Clinical assessment and serum IL-6 measurement were performed at each TCZ infusion. We examined the correlation between serum IL-6 concentrations and clinical parameters, and their variation. [Results] Serum IL-6 concentrations were correlated with swollen joint counts (SJC) (r=0.54) and drug dose (r=0.54). Multiple linear regression analysis also showed that SJC and drug dose were independent factors for serum IL-6 concentrations. Delta serum IL-6 concentrations were correlated with delta SJC (r=0.33), delta patient global assessment and delta CDAI. Serum IL-6 concentrations changed in CRP-negative patients during TCZ treatment, and the changes correlated with changes in RA disease activity. [Conclusions] Consecutive measurement of serum IL-6 may serve as an adjunct marker for RA disease activity in cases whose inflammatory markers are not helpful.

P2-094

The efficacy and safety of additional administration of iguratimod (IGU) in patients with RA who showed an inadequate response to tocilizumab (TCZ)

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Conflict of interest: Yes

[Object] To investigate the efficacy and safety of additional administration of IGU in patients with RA who showed an inadequate response to TCZ. [Methods] 31 patients with RA (22 women/ age 60.9 years/ disease duration 14.2 years/ prior TCZ duration 2.9 years/ CDAI 14.7[67.7%>10]/ 25 intravenous [8mg/kg/month]/ 28 secondary/ MTX 3.0mg/week [35.4%]) who showed an inadequate response to TCZ were additionally treated with IGU, and enrolled in this 24-week, retrospective study. [Results] Statistically significant decreases in outcome measures were as follows: SJC from 4.1 at baseline to 1.9 at week 24, TJC from 1.8 to 0.4, patient's VAS from 48.8 to 25.7, CDAI from 14.7 to 4.9, MMP-3 from 218.6 to 112.0 ng/ml, RF from 392.4 to 261.9 IU/mL (Wilcokson test). 20 patients (64.5%) achieved good or moderate response according to the EULAR criteria at week 24. MTX dose decreased from 3.0 to 2.4mg/week. 27 patients (87.1%) continued the treatment for 24 weeks. 2 patients discontinued for infection,1 for digestive symptoms,1 for remission. Mean daily dose of IGU was 41.7mg/day (20 patients 50mg/day [64.5%]).3 patients (9.7%) showed the elevation of AST/ALT but all continued the treatment. [Conclusions] Adding IGU to inadequate responders to TCZ may be promising complementary treatment option.

P2-095

Features and prospects of elderly patients with rheumatoid arthritis (RA) treated with biologics (Bio)

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Conflict of interest: None

[Object] The aim of this study is to clarify the appropriate treatment strategy for elderly patients with RA treated with Bio. [Methods] Of 238 patients with RA treated with Bio were divided into two groups by age. 145 patients under 64 years were grouped as GroupY (GY). 93 patients over 65 years were grouped as Group O (GO). Patients'characteristics, disease duration, rates of treated with MTX and/or PSL, dose of MTX and/or PSL, the number of switching Bio, the continuous rate of Bio, changes of 0 to 6 months in ΔDAS (CRP) and ΔHAQ, and incidences of adverse events were evaluated. Statistical analysis performed by t-paired test. [Results] In GO, rate without MTX and/or with PSL was higher. Doses of MTX and/or PSL and continuous rate of Bio was not different between two groups. Numbers of switching Bio were more often and level of CRP at baseline was higher in GO. ΔDAS was significantly improved in GO. [Conclusions] The elderly patients exhibited higher disease activity at baseline, and switching of Bio were more often performed. Whereas, elderly patients with appropriate effective Bio improved DAS and maintained treatment. Considering with higher incidence of adverse event for elderly, carefully and close observation is required during administration of Bio.

P2-096

The usefulness of abatacept switching for rheumatoid arthritis patients who were in remission with biological DMARDs

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Conflict of interest: None

The maintenance of the remission is extremely important by treatment of rheumatoid arthritis (RA), but it is a problem that an infection risk rises to continuously administer an immunosuppressive drug. About the reduction of the infection risk, glucocorticoid, immunosuppressive DMARDs and biological DMARDs (bDMARDs) reduction or cancellation are selected, but RA control does not rarely turn worse. Therefore we consider that whether reduction of infection risk and maintenance remission of RA is possible by changing occupied bDMARD to Abatacept (ABT). The object is 33 RA patients who achieved remission using bDMARD except ABT. 12 cases (S group, 3 men and 9 women) changed to ABT. 21 cases (C group, 4 men and 17 women) continued bDMARD. The average DAS28-CRP at 0, 52, 104 weeks are 1.85, 1.87, 1.72 (S group), 1.77, 2.03, 1.85 (C group), respectively. For 104 weeks, infectious disease are almost not serious and 0.94 person-year in S group and 0.58 person-year in C group. The infection risk was not reduction, but equal. The remission achievement rate was 50% in S group, 62% in C group, and there was not the significant difference between both groups. It was suggested that the switching to ABT could become one of the option to maintain remission of RA activity.

P2-097

Intensive therapy of infliximab in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To analyze efficacy and safety of infliximab (IFX)-intensive therapy in RA patients who had not responded to conventional IFX therapy. [Methods] In some patients, antibodies to infliximab were assayed by ELISA and serum trough level of IFX was checked from their preserved serum by Remi check Q. [Patients] Six males and 23 females, with a mean age of 58.0 years and, with mean disease duration of 8.12 ± 11.0 years were studied. MTX dose: 7.4 ± 1.5 mg/w, DAS28-ESR4: 5.60 ± 1.08. High disease activity: 19, moderate disease activity;10 [Results] 1) Short interval therapy; 5, High dose IFX therapy; 9, Combination; 15. 2) EULAR Good response (GR); 11, Moderate response (MR); 7, No response (NR); 11. 3) Nine NR cases in IFX-therapy were changed to adalimumab (ADA), etanercept (ETN) and tocilizumab (TCZ). Both ETN and TCZ led MR, while ADA was ineffective. Three patients administered ADA were changed to TCZ (2) and abatacept (1). TCZ showed MR. 4) Antibody to IFX was detected in 3 cases out of 12 pa-

tients. They were all NR patients. 5) adverse events: Cerebral infarction; 1, Herpes zoster; 2, pneumonia; 1, Bacterial infection of pulmonary cyst; 1 [Conclusion] It was suggested that intensive IFX therapy could be useful strategy for conventional IFX-resistant RA.

P2-098

Evaluation of effects after underwent total elbow arthroplasty, and capsulosynovectomy in patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] We evaluated effects after underwent total elbow arthroplasty (TEA), and capsulosynovectomy in patients with rheumatoid arthritis (RA). [Method] We enrolled 20 RA patients who underwent TEA with capsulosynovectomy or only capsulosynovectomy. The patients included 2 males and 18 females with a mean age of 68 years, and disease duration of 23.6 years at the time of surgery. 17 patients underwent TEA with capsulosynovectomy, 3 patients underwent only capsulosynovectomy. Preoperative and postoperative RA disease activity was measured using the Disease Activity Score 28 (DAS28). We investigated preoperative and postoperative dose of MTX and PSL, and use rate of biological drugs. [Results] DAS28 was significantly decreased from 3.58±0.86 preoperatively to 3.04±0.98 postoperatively (P <0.05). There was no significant change between dose of MTX and PSL, and use rate of biological drugs at preoperative and postoperative. [Conclusion] This study suggested that TEA and capsulosynovectomy in patients with RA decrease RA disease activity.

P2-099

Total knee arthroplasty became unnecessary by golimumab therapy in rheumatoid patients: a report of three cases

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Conflict of interest: None

[Object] We report three cases in which TKA for RA became unnecessary by golimumab (GLM) therapy. [Cases] Case 1: A 62-year-old man with a 15-year history of RA was referred owing to progressive destruction of the left knee joint. The DAS28-CRP was 4.51. We recommended TKA, but he requested biologic therapy. Four-weekly subcutaneous injections of 50 mg GLM were started. The pain and swelling disappeared quickly. The DAS28-CRP decreased to 1.79 after 5.2 years of therapy. The Japanese Orthopedic Association (JOA) score improved from 41 to 95. Case 2: A 76-year-old woman with a 2.5-year history of RA received three biologic therapies, but her knee lesions progressed. She cancelled TKA, and 100 mg GLM therapy was started. The DAS28-CRP and the JOA score improved from 5.08 and 65 before the therapy to 1.31 and 95 after 2.6 years of therapy, respectively. Case 3: A 69-year-old woman with a 21-year history of RA received MTX therapy, but the right knee pain and swelling occurred. She preferred 50 mg GLM therapy to TKA. The DAS28-CRP and the JOA score improved from 4.44 and 31 before the therapy to 1.48 and 87 after 4.3 years of therapy, respectively. [Conclusions] Structural knee joint damage was repaired after GLM therapy, and TKA became unnecessary in these cases.

P2-100

Investigation of patients with rheumatoid arthritis receiving biologics presenting with severe infections

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Conflict of interest: None

[OBJECTIVE] The average age of patients receiving biologics is increasing every year, and infectious diseases are one of the most significant factors. We evaluated factors for severe infections that require hospitalization in patients with rheumatoid arthritis receiving biologics. [METHODS] From January 2011 to July 2017, 162 patients with rheumatoid arthritis started biologics with 242 drugs in our hospital, and of these, 26 presented a severe infection requiring hospitalization. We examined their backgrounds and risks. [RESULTS] The frequency of severe infections was 2.0-13.4 events per 100 person-years. Between the severe infection and nonsevere infection groups, significant differences were observed in the age (67.7±11.7 years and 60.1±11.6 years, respectively), height (150.9±8.6 cm and 155.4±8.8 cm, respectively), HbA1c levels (6.35±0.73% and 5.96±0.95%, respectively), and lymphocyte count (1604.9±483.9/microl and 1347.9±528.0/microl, respectively). Of these, patients with >=6.5% HbA1c levels faced independent risks. [CONCLUSION] Irrespective of the presence or absence of diabetes mellitus, controlling blood glucose levels is important for reducing severe infection risks in patients receiving biologics.

P2-101

Analysis of serological changes before and after rituximab therapy

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Conflict of interest: None

[Object] Patient with rheumatoid arthritis, systemic lupus erythematosus, and Sjogren's syndrome (SjS), it is known that rituximab (RTX) diminish more IgM than other immunoglobulins. In this retrospective study, we evaluated the effect of RTX on the serological change. [Methods] Charts of 36 patients whom vasculitis or interstitial pneumonia (IP) was diagnosed 2012 to 2017 were reviewed. We analyzed patients who use glucocorticoids (GC) plus RTX (RTX group) and GC plus other immunosuppression drug (GC/IS group). Collected information included IgG, IgM, IgA, CH50, C3, C4, MPO-antineutrophil cytoplasmic antibody (ANCA), PR3-ANCA. [Results] In RTX group, 15 patients were included (4 granulomatosis with polyangitis, 2 IP with dermatomysosis, 2 microscopic polyangilitis, 2 eosinophilic granulomatosis with polyangiitis, IP with SjS, 1 IgA vasculitis, rheumatoid arteritis, IP with autoimmune features, diffusealveolarhemorrhage) with a mean age of 63.4. 21 patients were included as GC/IS. In RTX group, IgG and IgM decrease (p=0.008, p=0.01). In GC/IS group, IgG, IgA and MPO-ANCA decreased (p=0.004, p=0.001, p=0.03). IgG decreasing rate were high in RTX than GC/IS (p=0.02). There were no changes of complement and PR3-ANCA. [Conclusions] There are possibilities of the IgG and IgM decreased with RTX therapy.

P2-102

Long-term Safety (up to 5.5 years) of Baricitinib (Bari) in Patients (pts) including Japanese (JP) with Moderate to Severe Active Rheumatoid Arthritis (RA): an Integrated Analysis

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Conflict of interest: Yes

[Object] To evaluate long-term safety of Bari in pts with moderate-to-severe active RA including JP. **[Methods]** Incidence rates (IRs, per 100 patient-year: PY) of adverse events (AEs) were calculated using data in ALL BARI RA analysis set which included pts exposed to any Bari dose, and pooled from completed phase 1-3 studies and an ongoing long-term extension study of Bari in RA pts. **[Results]** 3492 pts (514 JP) were exposed to Bari for 6637 total PY (maximum exposure: 5.5 yrs) as of Sep 2016. Compared with previously reported (cut off Aug 2015), there were no increases in IRs of deaths (0.3), AEs leading to discontinuation (4.9), malignancies excluding non-melanoma skin cancer (0.8), major adverse cardiovascular events (0.5), serious infections (2.9), Herpes zoster (HZ) (3.2), lymphoma (0.09), or GI Perforation (0.05). All tuberculosis cases occurred in endemic areas; none in JP. In JP, HZ (6.5) were more frequent than overall pts as with another JAK inhibitor, but HZ IR was similar to previously reported and stable with longer exposure and events were considered manageable. **[Conclusions]** With longer exposure, Bari had an acceptable safety profile in pts with active RA as described in the previous report. Aside from HZ, the safety of Bari was not notably different between JP and overall pts.

P2-103

Changes in hemoglobin (Hb) and other hematologic parameters in patients (pts) with rheumatoid arthritis (RA) from baricitinib (Bari) clinical studies

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Conflict of interest: Yes

[Object] Janus kinase (JAK) 2 regulates erythropoietin (EPO) signaling pathway. Bari is a selective inhibitor of JAK1/2; Hb and other hematologic parameters were thoroughly evaluated in RA pts from Bari clinical studies. **[Methods]** Blood samples were analyzed at baseline (B/L) and at each visit from Bari ph2/3 studies. **[Results]** Hb levels below lower limit of normal (LLN) were observed at B/L in 25% pts. Small declines in Hb were observed in Bari 2 and 4mg at Wk 2 and again at Wk 14, consistent with the volume and frequency of phlebotomy, before returning to B/L levels. Initial decreases in Hb were accompanied by declines in RET. Subsequent increases in Hb were associated with increases in RET after Wk 8. Dose-dependent increases in total Fe, TIBC and EPO were observed in Bari compared with placebo. Hb shifts from normal to <LLN were similar among Bari and PBO (29.3% vs. 25.8%). Shifts in Hb from ≧8 g/dL to <8 g/dL were uncommon and similar across groups (0.1%-0.6%). Hb shifts were similar in Japanese pts. **[Conclusions]** Proportions of RA pts with low Hb did not differ significantly between Bari and PBO. Return to B/L in Hb following initial declines suggests that homeostatic mechanisms counterbalance Bari's pharmacologic effect of JAK inhibition on EPO signaling.

P2-104

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: 52-Week Results

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Conflict of interest: Yes

[Object] We previously reported the results of 12-week treatment phase during phase 1/2, multi-center, open-label, multiple ascending dose study of E6011, a humanized anti-fractalkine monoclonal antibody. This is the report of the 52-week safety, pharmacokinetics and efficacy of this trial (NCT02196558). **[Methods]** Japanese patients with active RA who have shown inadequate response or intolerance to MTX or TNFi received E6011 at week 0, 1, 2, and then biweekly for up to week 10 (Treatment Phase). Subjects who met criteria were received biweekly administrations at the same dose for up to week 52 (Extension Phase). **[Results]** 12, 15, and 10 subjects were enrolled in the 100, 200, and 400 mg cohorts, and a total of 28 subjects entered the Extension Phase. 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 response rates at week 12 and 52 (LOCF) were 75.0 and 58.3%, 80.0 and 73.3%, and 70.0 and 60.0% in the 100, 200, 400 mg cohort. **[Conclusions]** E6011 was safe and well tolerated, and demonstrated durable efficacy for 52-week in active RA with an inadequate response or intolerance to MTX or TNFi.

P2-105

Pain Reduction Is Associated with Improved Work Productivity in Patients With Rheumatoid Arthritis (RA)

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Conflict of interest: Yes

[Object] To assess the relationship between pain reduction and improvements in daily activity and work productivity in patients (pts) with RA. **[Methods]** In this post-hoc analysis of phase 3 clinical trial (RA-BEAM study) of baricitinib, pain was assessed using the patient's assessment of pain (0-100mm visual analogue scale). The Work Productivity and Activity Impairment Questionnaire-RA (WPAI-RA) instrument was used to evaluate the percentage of activity impairment (N=1302, overall), absenteeism (N=521, overall), presenteeism (N=490, overall), and overall impairment in work productivity (OWI, N=490, overall). **[Results]** Pts with a ≧30% pain reduction at Week (Wk) 1 had significantly greater ($p<0.001$) improvement in activity impairment, presenteeism, and work productivity at Wk 12 than those with a <30% pain reduction. For the Japanese cohort, similar trend was observed. With a reduction of ≧50% in pain from baseline, the WPAI-RA scores were -30.1/-3.0/-23.4/-23.1 at Wk 12 and -33.2/-2.5/-26.0/-25.2 at Wk 24 for activity impairment, absenteeism, presenteeism, and OWI, respectively. For the Japanese cohort, similar trends were observed. **[Conclusions]** Pain reduction was associated with improvements in regular daily activity and work productivity in pts with RA.

P2-106

Efficacy Response to Baricitinib (Bari) Based on Baseline Characteristics and Historical or Pre-existing Conditions at Baseline in Patients (pts) with RA Who Are Inadequate Responders to Conventional DMARDs (cDMARDs) and Biological DMARDs (bDMARDs)-naive

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Conflict of interest: Yes

[Object] To investigate the effect of baseline characteristics and historical or pre-existing conditions at baseline on efficacy outcomes in pts with RA who are inadequate responders to cDMARDs and bDMARDs-naive, treated with Bari. **[Methods]** 1684 pts (803 for Bari 4mg, 881 for placebo [PBO]) were included from 5 randomized trials. This pooled data analysis evaluated efficacy outcomes (ACR50, DAS28-CRP≦3.2, change from baseline in HAQ-DI) at Week (Wk) 12 in Bari vs PBO for subgroup interactions based on a variety of baseline characteristics and selected comorbidities. **[Results]** Efficacy outcomes were significantly improved for Bari vs. PBO in the overall study population. Within each subgroup, efficacy outcomes favored Bari over PBO and were generally similar to the overall. Significant quantitative interactions were observed for Bari vs. PBO for BMI and race in ACR50 and DAS28-CRP≦3.2 ($p<0.1$); no significant interactions were observed for the other baseline characteristics including number of prior cDMARDs and comorbidities. No qualitative interactions were observed. **[Conclusions]** Significant quantitative interactions were observed for BMI and race in ACR50 and DAS28-CRP≦3.2, but Bari demonstrated a consistent efficacy, irrespective of baseline characteristics and comorbidity.

P2-107

Upadacitinib (ABT-494) in Patients with Active Rheumatoid Arthritis and Inadequate Response or Intolerance to Biological DMARDs: A Phase 3 Randomized, Placebo-Controlled, Double-Blind Study of a Selective JAK-1 Inhibitor

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Conflict of interest: Yes

[Object] Safety and efficacy of upadacitinib (UPA), an oral, selective JAK-1 inhibitor in rheumatoid arthritis (RA) pts with bDMARD-IR. [Methods] Pts received (2: 2: 1: 1) UPA15 or 30mg once daily or PBO for 12 wks followed by UPA15 or 30mg from Wk12 onwards. Primary endpoints (Wk12): proportion of pts with ACR20 and proportion with DAS28CRP≦3.2 (NRI). [Results] Of 498 treated pts, 451 (90.6%) and 419 (84.1%) completed weeks 12/24. Pts had established, severe, refractory disease at BL; 53% had ≧2 prior bDMARDs. At Wk12, more pts on UPA15 and 30 vs PBO met ACR20 (64.6% and 56.4% vs 28.4%, $p<.001$) and DAS28-CRP≦3.2 (43.3% and 42.4% vs 14.2%, $p<.001$), DAS28-CRP<2.6, CDAI≦10, SDAI≦11 and SDAI≦3.3. Responses were maintained through Wk24, and comparable for pts switched to UPA at Wk12. Up to Wk12, AE frequency was similar in PBO and UPA15, but higher for UPA30; from Wk12-24, AE frequency was similar for UPA arms, with more serious infections and HZ cases in UPA30. 5 malignancies were reported. PE was reported in 2 pts upto Wk12 and 4 more from Wk12-24, 1 with DVT. 2 deaths were reported. [Conclusions] Efficacy of UPA vs PBO was demonstrated in these bDMARD-IR pts. Safety was generally consistent with UPA Ph2/3 trials. More Ph3 data will allow benefit: risk to be comprehensively evaluated.

P2-108

A Phase 3 Randomized, Placebo-controlled, Double-Blind Study of Upadacitinib (ABT-494), a Selective JAK-1 Inhibitor, in Patients with Active Rheumatoid Arthritis with Inadequate Response to Conventional Synthetic DMARDs

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Conflict of interest: Yes

[Object] To assess safety and efficacy of upadacitinib (UPA), an oral, selective JAK-1 inhibitor in pts with active RA and inadequate response to csDMARDs. [Methods] Pts received (1:1:1) once-daily UPA at 15 or 30 mg, or PBO for 12 wks (P1). Primary endpoints were the percentage of pts achieving ACR20 and the percentage achieving DAS28-CRP LDA at Wk 12 (NRI). [Results] All 661 randomized pts were treated; 618 (93.5%) completed P1. At Wk 12, more pts on UPA 15 and 30 mg vs PBO ($p<.001$) achieved ACR20 (64% and 66% vs 36%), and DAS28-CRP LDA (48% and 48% vs 17%). Also, more pts ($p<.001$) on UPA vs PBO met ACR50 (38% and 43% vs 15%), ACR70 (21% and 27% vs 6%), CDAI LDA (40% and 42% vs 19%) DAS28-CRP<2.6 (31% and 28% vs 10%); pts on UPA vs PBO had improvements in DAS28-CRP, HAQ-DI, morning stiffness duration and FACIT-F ($p<.001$). AEs [125 (57%) and 118 (54%) vs 108 (49%)] and serious AEs [9 (4%) and 6 (3%) vs 5 (2%)] were numerically higher for UPA vs PBO. There were 4 cases of HZ/VZV infection (1 on PBO). Two malignancies and 1 adjudicated MACE were reported. There were no deaths, cases of TB or GI perforations. [Conclusions] UPA demonstrated efficacy at both doses vs PBO. Safety and tolerability were consistent with observations in the Ph 2 UPA studies.

P2-109

Efficacy and safety of secukinumab in Japanese patients with active ankylosing spondylitis (AS): 24-week results from an open-label, phase 3 study

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Conflict of interest: None

[Object] To assess the clinical efficacy, safety and tolerability of secukinumab (SEC) subcutaneous injections up to 52 weeks in Japanese patients with active AS. [Methods] Thirty Japanese patients with active AS fulfilling modified NY criteria, with a score ≧ 4 on BASDAI and ≧ 4 cm spinal pain score on a VAS despite current or previous treatment with NSAIDs and/or anti-TNF-α agents were included. Patients received open-label SEC 150 mg at week 0, 1, 2, 3, and 4, followed by treatment every 4 weeks. The primary outcome was ASAS20 response rate at week 16. Overall safety and tolerability were also assessed. Data up to the last patient's week 24 visit were analyzed. [Results] Twenty-eight subjects completed treatment up to week 24, and 2 discontinued. At week 16, ASAS20/40 and BASDAI50 response rates were 70.0%/46.7% and 36.6%, respectively. More than half of the subjects had an ASAS20 response at week 4. AE rate was 83.3%, and 3 SAEs were reported. The most frequent AE was viral upper respiratory tract infection (40%). [Conclusions] SEC treatment improved signs and symptoms of active AS in Japanese patients after 16 weeks of treatment, with a similar safety profile as seen in past SEC studies in AS, PsA, and psoriasis, demonstrating that SEC is a beneficial treatment option in AS.

P2-110

Intravenous murine adipose-derived stem cells inhibit lung inflammation and fibrosis of bleomycin-induced lung injury in a dose-dependent manner

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Conflict of interest: None

[Object] Interstitial pneumonia (IP) is a life-threatening pathological condition that causes respiratory failure when it progresses. Adipose-de-

rived stem cells (AdSCs) have recently been considered a useful treatment tool for autoimmune disease because of their anti-inflammatory and immunosuppressive effects. We investigated the therapeutic effect of intravenous AdSC transplantation in a mouse model of bleomycin-induced IP. [Results] AdSCs accumulated in the pulmonary interstitium and inhibited both inflammation and fibrosis in the lung, markedly improving the survival rate of mice with bleomycin-induced lung injury in a cell number-dependent manner. AdSCs inhibited the production of pro-inflammatory cytokines such as TNF-α and IL-12 in activated macrophages by inducing apoptosis. AdSCs inhibited the differentiation and proliferation of Th2-type mCD4+ T cells but promoted the differentiation and proliferation of regulatory T cells, suggesting that the phenotypic conversion of T cells may be one of the mechanisms for the anti-inflammatory effect of AdSCs on pulmonary fibrosis. [Conclusions] Intravenous AdSCs could be a promising treatment for patients with IP.

P2-111

Similar clinical efficacy of tofacitinib versus non TNF inhibitors for 12 months in active RA patients

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Conflict of interest: None

[Object] This study aims to compare the disease status of patients with active rheumatoid arthritis after treatment with tofacitinib or non-tumor necrosis factor (TNF) biologics. [Methods] The study included a total of 50 rheumatoid arthritis patients (18 males, 32 females; mean age 68.3±1.3 years). We prospectively and randomly enrolled 25 patients for treatment with tofacitinib (Tofa group: 10 males, 15 females; mean age 68.3±2.0 years) and 25 for treatment with non-TNF biologics (non-TNF group: 8 males, 17 females; mean age 68.3±1.7 years). Mean DAS-28CRP, CDAI, HAQ-DI, and MMP-3 values were recorded at baseline and at four, eight, and 12 months. [Results] There was a significant difference in the percent changes of disease activity score 28, C-reactive protein and Crohn's disease activity index at every time point versus baseline in both treatment groups. Health assessment questionnaire-disability index was also significantly different at every time point in both groups except for at four months in the non-TNF group. [Conclusions] Tofacitinib was well tolerated in active rheumatoid arthritis patients and exerted effects comparable to those of non-TNF biologics.

P2-112

Efficacy of Tofacitinib in routine care of patients with rheumatoid arthritis: 52 weeks result

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Conflict of interest: None

[Object] To investigate the efficacy of Tofacitinib in routine care of patients with rheumatoid arthritis at 52 weeks. [Subject] We performed a retrospective study of 21 patients who were treated with Tofacitinib for 52 weeks. Average disease duration was 17.2 years, Steinbrocker stage Classification, Stage 2:2 cases, stage 3 7 cases, stage 4 12 cases. [Estimate] We estimate for tenderness joint counts, swollen joint counts, CRP, Patients VAS, Dr VAS, DAS28 (CRP), SDAI, MMP-3, at baseline, 12 weeks, 24 weeks, and 52 weeks. [Results] We treated 11 patients by 5mg/day Tofacitinib, 9 patients by 10mg/day Tofacitinib. Average Ages were 74. 8.90% (21/21 cases) had treated with Biologics before. Average DAS28, SDAI, MMP-3 at baseline were 4.71, 23.3, 335.1. Average DAS28 (CRP), SDAI, MMP-3 were 2.55-2.01-1.84 (at 12 weeks-24 week-52 weeks), 9.90-6.21-4.44, 165.2-128.7. There were significantly improved from baseline beetween at 12 weeks, 24 weeks, 52 weeks. [Conclusions] We suggest that Tofacitinib is effective in routine care of patients with rheumatoid arthritis.

P2-113

The effect of tofacitinb or abatacept on bone metabolism and osteoclast regulator of rheumatoid arthritis

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Conflict of interest: None

Objectives: To clarify the mechanism of tofacitinib (TOF) or abatacept (ABT) for bone metabolism and bone remodeling regulator in rheumatoid arthritis (RA). **Methods:** 38 patients with active RA were started on treatment with TOF or ABT. Circulating levels of NTx, osteocalcin (OC), soluble RANKL (sRANKL) and osteoprotegerin (OPG) were examined by ELISA at the baseline and after 12 weeks. **Results:** In TOF group, average of NTx levels tend to decrease. However, these change were not significant. Average of OC levels at 12 weeks increased significantly from the baseline. Average of sRANKL, sRANKL/OPG levels at 12 weeks decreased significantly from the baseline. In ABT group, average of NTx levels at 12 weeks decreased significantly from the baseline. Average of OC levels at 12 weeks tend to increase. However, these change were not significant. Average of sRANKL, sRANKL/OPG levels at 12 weeks were not change compared with the baseline. In comparison of TOF group and ABT group, reduction rate of sRANKL and sRANKL/OPG at 12 weeks in TOF group was significantly greater than those in ABT group. **Conclusions:** These results indicate that TOF has improved the bone metabolism of RA via the control of RANKL and RANKL/OPG balance. Further study about the effect of bone formation by TOF is needed.

P2-114

A case report: a patient with rheumatoid arthritis who was prevented joint destruction and improved range of motion of the elbow by administration of Tofacitinib

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Conflict of interest: None

Background: We report a case of the patient with rheumatoid arthritis (RA) who was prevented joint destruction and improved range of motion of her left elbow by administration of tofacitinib. *Case:* The patient with RA was a 70 year-old Japanese woman. Her affected duration of RA was seven years. She had received salazosulfapyridine 1000 mg/day and methotrexate (MTX) 4 mg/week for RA. Because joint destruction of her left elbow had progressed, MTX was gradually increased. Elevation of liver enzyme was observed after increasing the dose of MTX till 8 mg/week. Ursodeoxycholic acid was added and MTX was decreased to 6 mg. Because arthritis of her left elbow was continued, tofacitinib 10 mg/day was administrated. Her symptoms have immediately improved after adding tofacitnib. The joint destruction of her left elbow have prevented in the X-ray findings and joint range of motion have improved fifteen months after that. *Conclusions*: Tofacitinib is one of JAK inhibitor approved for the treatment of RA. This case has been prevented joint destruction and improved range of motion of her left elbow due to tofacitinib.

P2-115

On the effect and safety of Tofacitinib for rheumatoid arthritis patients in our hospital

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Conflict of interest: None

[Object/Methods] 17RA patients that are treatment with TOF for more than 52 weeks in our hospital and, I was examined that, effectiveness (DAS28-ESR), survival rate, and side effects [Results] Patient background, age 53 to 88 years old, 5 males, 16 females, 12 with MTX combined, 9 with noncombination (4 mg to 10 mg in combination, 1 case with cessation, 1 case weight loss), steroid use The example was 8 cases and all were less than 5 mg. 8 cases of serologically positive (ACPA or RF) cases and 11 cases of BIO use cases (ETN 6 cases 3 cases GLM 3 cases ABT 1 case CZP 1 case). As an effect, it was 5 cases of good response, 9 cases of moderate response, 3 cases with no response at 52 weeks or more after administration in DAS 28 - ESR compared to before. One case of ineffective, one case of withdrawal, one case of JAK FREE, two cases as side effects, liver dysfunction in 3 cases, shingles in 3 cases, malignantoccurred in 2 cases, 14 out of 21 now continued [Conclusions] Although the outcome of TOF in our hospital was relatively good, serious side effects such as herpes zoster and malignant tumor also occurred and careful progress was observed in the use of TOF including complications I have to go.

P2-116

The efficacy of tofacitinib in elder patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To assess efficacy and safety of tofacitinib (TOF) in elder patients with rheumatoid arthritis (RA) in real world. [Methods] 6 patients with RA were initiated TOF in our institution from May 2016 to Oct 2017, and all of them were continued TOF over three months. TJC, SJC, patient VAS, CRP, DAS28 ESR, SDAI, reduction of csDMARDs and PSL dose, and safety were evaluated at the point of baseline and each month between 6th months. And we interviewed the reason of choosing TOF. [Results] Patients profiles; females 83 %, the mean age 72.8±5.3 years old, the mean disease duration 14.5±12.1 years, Stage3,4 50%, class3,4 50%, MTX combination cases 66%, PSL combination cases 66%, bio naive cases 33%, DAS28 ESR at the point of baseline. 2 patients were treated by TOF 5mg/d. Reduction of TJC, SJC, CRP, patient-VAS, DAS28 ESR (6.18±1.9→3.12±0.57), mean MTX dose (8.3±7.2→5.3±4.3mg), mean PSL dose (3.7±4.0→1.7±2.4mg) were observed at the point of 6th months. 4 patients achieved LDA at 6 months. 2 patients had to discontinue TOF because of adverse effect (liver dysfunction, headache). [Conclusions] The TOF treatment in elder patients with RA was useful in regard to the effectiveness, and reduction of MTX, PSL.

P2-117

Patient Oriented Control of RA with Tofacitinib

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Conflict of interest: None

[Object] Tofacitinib is the first oral Janus kinase inhibitor indicated for treatment of moderate to severe RA. Compare with other biologics, Tofacitinib needs no injections and will not make a secondary antibody. These make patients who live in remote locations from the hospital (especially like our Okhotsk area) to take Tofacitinib depend on their symptoms. [Methods] Since March 2015, twenty nine RA patients were prescribed Tofacitinib. Among them, people who live in minimum 30km away from the hospital and have minimum 6 months observation periods were sixteen patients (four men and twelve women). All of them were prescribed conventional DMARDs and instructed to take tofacitinib (5mg) depends on their RA symptoms. They were surveyed about severe adverse event (like malignancy and herpes zoster), disease activity (DAS28). [Results] The average age was 75 years old. The average distance between their house and the hospital was 48.8km. The average DAS28 (CRP4) was significantly improved from 4.6 to 2.1. The average mHAQ was also significantly improved from 1.1 to 0.6. There were no severe side effects during the survey periods. [Conclusions] The patient oriented use of tofacitinib is an effective way to control RA, especially patients who live in remote locations from the hospital.

P2-118

An Analysis of Tofacitinib Pharmacokinetics and Safety in Japanese and non-Japanese Patients with Rheumatoid Arthritis

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Conflict of interest: Yes

[Object] Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). We compared pharmacokinetics (PK) and PK-safety relationship of tofacitinib in Japanese and non-Japanese patients (pts) with RA. [Methods] Data included 4 Phase 2 studies of tofacitinib (monotherapy or with methotrexate [MTX]) in pts with RA: 2 in Japanese pts (A3921039, A3921040; N=360); 2 in non-Japanese pts (A3921025, A3921035; N=430). Pts were stratified by body weight (BW). Exposure metrics on tofacitinib concentration (C): Cmax, Cmin, C averaged over 12 h (Cavg), and area under C-time curve (AUC) at steady-state. For PK-safety analyses, relationship of PK parameters with incidence of serious adverse events (SAEs) and non-SAEs was analyzed by linear logistic regression. [Results] Mean Cmax, Cmin and AUC for tofacitinib 5 mg BID (monotherapy/with MTX): 60.4/64.2 vs 61.9/54.1 ng/mL, 4.4/3.7 vs 4.2/3.4 ng/mL and 262/262 vs 263/226 ng·h/mL in Japanese and non-Japanese pts, respectively. Japanese pts with BW ≦50 kg and >50 kg had similar exposure. Regression analysis curves for SAEs and non-SAEs were similar across the exposure range. [Conclusions] Japanese and non-Japanese pts with RA had similar tofacitinib exposure; SAE and non-SAE incidences as functions of Cavg were similar.

P2-119

Virus reactivation in patients with rheumatoid arthritis using tofacitinib

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Conflict of interest: None

[Object] We clarify the reactivation rate of varicella virus (VZV), hepatitis B virus (HBV), EB virus (EBV) and cytomegalovirus (CMV) under TOF for RA. [Methods] We measured VZVIgG, VZVIgM, high sensitivity HBs antigen, HBV-DNA, CMVIgG (EIA), CMVIgM (EIA), CMV antigenemer, EBV VCA IgG (EIA) and EBV VCA IgM (EIA) once every 3 months. Antigenemia positive, high sensitivity HBs antigen positive, IgG antibody raised by 4 times or more was defined as virus reactivation. [Results] 35 RA patients, women 77%, age 65 yrs, disease duration 10 yrs, 74% positive for CCP antibody, SDAI 9.5, corticosteroid (PSL) use rate 14%, mean PSL 2.2 mg/day, MTX usage 23%, mean dose 7.5 mg/week, TOF (average 8 mg/day) was administered on average for 12 months. Each virus reactivation rate was 2.9, 8.6, 25.5 and 0% for CMV, HBV, VZV and EBV, respectively. There were no cases where more than two types of virus reactivation came. As clinical symptoms CMV had fever, VZV showed all cases, eruption. No liver dysfunction was observed in HBV reactivation case. A significant difference (68.8 vs 29.7 $p < 0.05$) was observed in the CMV IgG value between the cases of HBV reactivation and no other virus reactivation cases. [Conclusions] Viral reactivation by TOF administration in RA is diverse and its rate is high (37.1%).

P2-120

Do we need to stop JAK inhibitor, when the patients suffer from Helpes zoster in patients with rheumatoid arthritis?

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Conflict of interest: None

[Object] We have experiened Herpes Zoster treated by JAK inhibitor in patients with rheuamtoid arthritis. At first we stopped it. However, after stopping JAK inhitor, Herpes Zoster got worsed immediately. Is it good to stop JAK inhibitor in patients with Herpes Zoster? [Methods] Retrospectively, we checked 5 cases (not stopping JAK inhibitor), and 3 cases (stopping JAK inhibitor). [Results] ALL not stopping JAK inhibitor cases were good couse. 2 stopping JAK inhibitor were not good course. [Conclusions] Do we need to discuss whether stopping JAK inhitors or not in RA patients with Herpes Zoster.

P2-121

Influence of reconstruction in ulnar drift upon wrist joint after metacarpophalangeal joint replacements

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Conflict of interest: None

[Object] Sometimes, the angle of the wrist joint in patients with rheumatoid arthritis patient after metacarpophalangeal joint replacement improved. In this study we compare pre- and post-operative the angles of wrist joints, and we investigated the radial deviation of the wrist joint. [Methods] We mesured the pre- and post-operative angle between metacarpal radius cortex in index finger and radial axis in in rheumatoid arthritis patient who underwent MCP artificial joint replacement from 2013 and April 2017, and measured the angle in 20 hands of healthy controls. We calculated the diferernce of the angle between the preoperative angle and the reference angle (preΔangle), and its between the postperative angle and the reference angle (post Δangle). The each angle were compared. Postoperative radiographs were peformed 6 months after operation. [Results] We evaluated 69 rheumatoid arthritis patients. The mean age was 63.57 years. The average of preΔangle was 7.13 degrees. The average of postΔangle was 3.32 degrees. Both of them showed a significant difference ($P < 0.05$). [Conclusions] In this study we found that the wrist joint angle was significantly improved by performing MCP joint replacements. Therefore, it is not necessary to carry out a wrist surgery prior to MCP joint replacement.

P2-122

Extensor tenolysis at the wrist during metacarpophangeal arthroplasty for rheumatoid arthritis

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Conflict of interest: None

[Objective] The aim of this study is to invstigate the patient's characteristics of who required additinal enxtensor tenolysis at the wrist during metacarpophangeal (MCP) arthroplasty for rheumatoid arthritis. [Methods] 66 hands in 51 patients who underwent arthroplasty for MCP joints were include in the current study. We investigated the rate of patients who required extensor tenolysis at the wrist. Then, the relationship between the presence of tenolysis (tenolysis (+) group/tenolysis (-) group), and the history of wrist surgery was examined. We also compared the clinical results between two groups with HAND20, DASH score, range of motion (ROM) of MCP joint. [Results] In 8 hands within 66 hands, additional extensor tenolysis at the wrist was required due to tendon adhesion. In 15 hands with the history of wrist surgeries, extensor tendon adhesion at the wrist was noted in 6 hands. The rate of cases who required the tenolysis was significantly difference higher in the cases with the history of wrist surgery ($p<0.01$). There was no significant in the improvement of HAND20, DASH score and ROM of MCP of MCP joint between two groups. [Conclusion] In cases with history of wrist surgery, extensor tenolysis at the wrist was required more frequently during MCP arthroplasty.

P2-123

Total arthrodesis for the severely deteriorated wrist in the patient with rheumatoid arthritis

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Conflict of interest: None

[Objectives] The wrist is one of the frequently affected joints in RA and the site where often destructive change tend to progress in RA. The aim of this study is to investigate the usefulness of total wrist arthrodesis for the severely deteriorated wrist. [Methods] Forty wrists in 34 RA patients underwent total wrist arthrodesis using Wrist Fusion Rod (WFR) at our hospital between January 2007 and June 2015. The mean age at surgery was 67 years, the mean disease duration was18 years, and the postoperative follow-up period was 4 (1 to 9) years. Clinical and X-ray evaluation were performed before and after surgery. [Results] The postoperative pain score was 11.5 (0 to 78) / 100. After surgery, DAS28-ESR (4), grip power and the DASH score improved significantly. As a complication, delayed wound healing occurred in 6 joints, breakage of the rod occurred in one joint, but there was no infection. In X-ray evaluation, alignment improved in most cases, and bony fusion was obtained at the radiocarpal joint. The level of satisfaction after surgery was 75 (median)/100. [Conclusions] Total wrist arthrodesis for the unstable and severely deteriorated wrist is an useful salvage surgery.

P2-124

Effect of wrist and fingers surgery on disease activity and drug therapy in patients with rheumatoid arthritis

Michiaki Suzuki[1], Ken Kumagai[1], Hyonmin Choe[1], Shunsuke Yamada[1], Shintaro Watanabe[1], Chika Ohsako[1], Akiko Nagaoka[1], Yuichi Mochida[2], Kengo Harigane[2], Kagayaki Sahara[2], Yutaka Inaba[1], Tomoyuki Saito[1]
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Conflict of interest: None

[Objectives] We evaluated factors affecting disease activity and drug therapy of upper limb surgery (wrist joint, fingers) in patients with rheumatoid arthritis (RA). [Method] Forty-two RA patients with severe joint destruction underwent upper limb surgery (wrist joint, fingers). The patients included 41 females and 1 male, with a mean age of 63.6 years at the time of surgery. Preoperative and postoperative RA disease activity was measured using the Disease Activity Score 28 (DAS28). We evaluated Stage, Class, duration, DAS28-CRP, operation, drug therapy in patients with RA. [Results] DAS28 was not significantly decreased from 2.8+/-1.0 preoperatively to 2.5+/-1.0 postoperatively. Biologic agent was increased from 38.1% preoperatively to 47.6% postoperatively. MTX / PSL was decreased from 73.8% / 50% preoperatively to 69% / 35.7% postoperatively. [Conclusion] This study suggested that preoperative and postoperative disease activity did not change in patients with RA underwent upper limb surgery (wrist joint, fingers).

P2-125

Wrist arthrodesis in rheumatoid arthritis using an LCP metaphyseal locking plate versus an AO wrist fusion plate

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Conflict of interest: None

[Object] While wrist arthrodesis using plates is an established treatment with well-documented successful union rate for severely destroyed wrists, plate-related complications have been a matter of great concern. [Methods] We retrospectively compared wrist arthrodesis using AO wrist fusion plates in nine and LCP metaphyseal plates in seven patients with rheumatoid arthritis. [Results] The mean follow-up was for 58 months in the AO wrist fusion plate group and 39 months in the LCP metaphyseal plate group. Bone union at the arthrodesis site was achieved in all cases of both groups. The comparison of the original position of the fusion on the immediate postoperative radiographs and the position on the most recent follow-up radiographs demonstrated good stability in both groups. Plate-related complications occurred in four cases, and none, respectively. Complications were composed of one case for pain over the plate, one for wound dehiscence and infection, one for extensor tendon adhesion, and one for fracture. [Conclusions] Wrist arthrodesis using LCP metaphyseal plates was a favorable method for rheumatoid arthritis patients with comparable stability and lower risk of plate-related complications than the AO wrist fusion plate.

P2-126

Nvestigation on the improvement patterns of finger extension range after surgical reconstruction of extensor tendon of rheumatoid patients

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Conflict of interest: None

[Object] The patterns of postoperative improvement after extensor tendon reconstruction depends of individual difference. The purpose of this study was to investigate the improvement modalities. [Methods] We examined retrospectively the medical records of RA patients who underwent surgical operation of the wrist and extensor tendon reconstruction for extensor tendon rupture, and compared the improvement mode of the finger extension range with the background factor. [Results] 60 RA patients with 64 hands were enrolled. The median rehabilitation period was 123.5 days. On average, 45.9 (0-141.0) days until the beginning of improvement tendency of the metacarpophalangeal joint extension of fingers undergoing extensor tendon reconstruction, average 92.4 (42.0-169.0) days until reaching the plateau. [Conclusions] It may take a period of several months until the improvement of finger extension become stable, therefore patient's sufficient understanding is important in postoperative rehabilitation. There was also a case of up to 141 days before extension began to recover, therefore it can be said that it is important to continue posterior therapy for a sufficient period even if the rate of improvement is slow.

P2-127

A case requiring multi-site surgery for residual wrist and thumb deformities after remission of rheumatoid arthritis (RA)

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Conflict of interest: None

[Object] Even after clinical remission of rheumatoid arthritis (RA) with treatment, some patients still have impaired activities of daily living due to residual joint disorders and deformities. We now report a patient with residual wrist and thumb deformities despite Disease Activity Score (DAS) remission who subsequently had a successful outcome after multi-site surgery performed in several steps. **[Case]** A 64-year-old man who was a woodblock artist had bilateral wrist and thumb deformities. He developed RA in 2007 and began treatment with biological drugs in 2012. Initial examination showed flexion contractures of the wrists and marked deformities of the thumbs, with a C-reactive protein (CRP) of 0.05 and DAS 28 (3CRP) of 1.84. Total arthrodesis of both wrists in two stages was performed in 2014. Left thumb CM joint arthroplasty and MP joint arthrodesis were performed in 2015 and in 2016, right thumb IP joint arthrodesis was performed. Currently, in 2017, daily activities such as gripping, grasping and etc have improved **[Conclusions]** Control of RA progression has dramatically improved with biological drug therapy. However, in patients with impaired ADLs due to residual joint deformities, appropriately timed and performed surgical therapy can improve quality of daily living.

P2-128

The influence of foot surgery for postoperative disease activity in rheumatoid arthritis

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Conflict of interest: None

[Object] Influences by foot surgeries for postoperative disease activity (DAS28-CRP; DAS) and drug therapy in rheumatoid arthritis (RA) were analyzed. [Methods] From 2006 to 2016, 150 RA cases who underwent foot surgeries were reviewed. The doses of methotrexate (MTX) and glucocorticoid (GC), and changes of DAS between before and one year after surgery were compared. Changes of DAS were also analyzed in cases who underwent foot and other joint surgery. The analyses of DAS were performed in 39 cases whose DAS were completely obtained. [Results] The mean age at surgery was 66.7 years old (42~81). The mean rate of administration of MTX and GC were 59% and 41%, respectively. The mean dose were 6.5 (2~14) and 3.4 mg/week (1~7.5), respectively. There was no difference of mean doses of MTX and GC between before and after surgery. Also, mean DAS showed no difference between before (2.97) and after surgery (3.02). There were 16 cases of isolated foot surgery and 23 cases of foot and other joint surgeries. Neither cases showed difference in DAS between observation periods. [Conclusions] We found no difference of DAS in cases of foot surgeries. This may reflect that foot surgery tended to perform for improving pain and function in small and inactive joint arthritis.

P2-129

Analysis of wound healing after forefoot surgery in patients with Rheumatoid arthritis

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Conflict of interest: None

[Object] We analyzed risk factors causing delayed wound healing in RA patients who underwent forefoot surgeries. [Methods] We investigated 50 feet operative procedures from 37 RA patients (1male and 36 female, a mean age of 61 years, range 31 to 78 years) underwent forefoot surgeries from 2010 to 2016. We examined duration of disease, use of steroid, methotrexate and biological agent, BMI, JSSF scale before operation, HV angle, M1M2 angle, operation methods, operative time, tourniquet time, number of skin incisions and pinning. We defined delayed wound healing as wound that were needed care after removing sutures. [Results] Of the 50 feet, delayed wound healing was recorded in 11 feet (22%). JSSF-Hallux score (delayed group, 49.8±8.1, healing group, 58.9±12.1, $p<0.05$) and JSSF-Lessor score (delayed group 37.6±15.7, healing group 51.4±16.2, $p<0.05$) before operation in delayed healing group were significantly lower than those of healing group. We recognized significant differences especially in function in JSSF-Hallux score and pain in JSSF-Lessor score between the two groups. [Conclusions] We could suggest that taking care of wound might be important for RA patients that shows lower score of JSSF-scale before operation.

P2-130

Distal osteotomy for Hallux valgus using absorbable screw

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Conflict of interest: None

[Object] In recent years osteotomy with joint preservation for forefoot deformity of rheumatoid arthritis has been increasing. We investigated cases of hallux valgus osteotomy using an absorbable screw. [Methods] All cases Women, rheumatoid arthritis 3 cases 4 toes, hallux valgus 1case 2 toes. Average age was 69 years old at the surgery. Follow-up period was 8-14 months. At the same time lesser toe metatarsal shortening osteotomy was done at 5 feet. Distal metatarsal osteotomy was done and moved the distal bone fragment outward. Insert HA containing PLLA screw (Osteotrans Plus) from the inside of the proximal bone fragment toward the distal bone fragment. Insert Osteotrans pin 1.5 mm from the distal bone fragment end into the proximal bone fragment. The screw head was removed with a ryuuel. After the operation, The load of the forefoot was set at 6 weeks after the operation. [Results] Bone union was obtained in all cases. The average HV angle was 42 degrees before the operation, 12 degrees at the final observation. Movement of distal bone fragments exceeding 3 degrees was not measured in AP and oblique radiography. One case of postoperative wound necrosis was seen but cured. There were no problems caused by the fixation of the absorbing screw.

P2-131

Clinical outcomes of shortenig osteotomy of partial lesser toe 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 forefoot surgery for RA patients who were divided into two groups according to the surgical procedures; all resection group: resection osteotomy of lesser toe, partial resection group: shortening osteotomy of partial lesser toe. [Methods] 21feet of 18 RA patients (all resection group; 12 feet 10 RA patients, partial resection group; 9 feet 8 RA patients). HVA, M1/2 angle, M1/5 angle, clinical outcomes using SAFE-Q were examined. [Results] In partial resection group, HVA, M1/2 angle, M1/5 angle decreased significantly at last follow-up, but in all resection group, M1/5 angle decreased not significantly. SAFE-Q improved significantly in both group, but not improved significantly between all resection group and partial resection group. [Conclusions] SAFE-Q of Shortening osteotomoy of partial lesser toe not improved significantly in comparison to resection osteotomy of lesser toe.

P2-132

The Association of Hindfoot Valgus/Varus Alignment with Metatarsus Primus Elevatus in Rheumatoid Arthritis Patients

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Conflict of interest: None

[Object] To clarify the association of hindfoot valgus/varus alignment with metatarsus primus elevatus in rheumatoid arthritis patients. [Methods] A retrospective study was performed of standing AP and lateral radiographs of 53 patients (78 feet; average age 66 years) who underwent toeplasties in our hospital. The elevation of the first metatarsal bone in relation to the second metatarsal was measured as MPE. The shape of posterior talocalcaneal joint line was classified as one of two types: flat (type F) and round. When the shape of the posterior talocalcaneal joint line was classified as type F, the foot was defined as hindfoot varus deformity. [Results] Median MPE was 1.7 mm (the first- third quantile: 0-5.4 mm). Comparative study was performed between the group with MPE>5 mm (N=19 feet) and that with MPE<2 mm (N=40 feet). In the group with MPE>5 mm, nine out of 19 feet (47.4 %) were classified as type F, whereas in the group with MPE<2 mm, three out of 40 (7.5 %) were classified as type F. [Conclusions] There is a significant relationship of hindfoot varus deformity with metatarsus primus elevatus in rheumatoid arthritis patients.

P2-133

A case of rheumatoid arthritis with severe destruction of the ankle complicated with Charcot arthropathy

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Conflict of interest: None

[Case] A 40 years-old female. Nine years ago, her bilateral wrists, ankles, and knees got swollen, and she had been treated with glucocorticoids and NSAIDs. Radiographs of her left ankle showed severe dislocation with an old fracture of the medial malleolus, valgus deformity, lateral shift of the calcaneus, and collapse of the talus. Although she had no abnormalities in glucose tolerance or spinal cord, abnormal peripheral nerve function was detected predominantly in her left leg. Based on these observations, we diagnosed her as RA complicated with Charcot arthropathy. We started her treatment with MTX and glucocorticoids, then added infliximab 3 months later. One year after IFX administration, we undertook arthrodesis of her left ankle using a nail with fins and autologous bone graft. As of 10 months after surgery, she can walk using a walker without pain. [Discussion] There have been a few reports that severe joint destruction associated with RA may cause Charcot arthropathy. Before planning surgeries for weight-bearing joints with severe bone destruction or deformity associated with RA, surgeons should note that they might be complicated with Charcot arthropathy and examine carefully if there are abnormalities in glucose tolerance, spinal cord or peripheral nerve functions.

P2-134

The assessment of whole lower limb alignment using HC line in the treatment of foot and ankle deformity: a case report

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Conflict of interest: Yes

[Background] We report on our experience with a patient of juvenile rheumatoid arthritis (JRA) who had a different clinical course on the left and right ankle after bilateral subtalar arthrodesis. [Case Presentation] A 38 years old woman who diagnosed as JRA when she was 3 years old. She had a progress of ankle and foot deformities after 20 years old and underwent bilateral subtalar arthrodesis 9 years ago. However, after initial surgery she had progress of ankle deformity only in her left side. Although there were severe clubfoot deformities in both sides before the initial surgery, there was no significant differences in not only inversion deformity but also the varus hindfoot alignment between both sides in X-ray. Then her bilateral weight bearing axes were evaluated using Hip Calcaneal line (HC line). The right HC line was detected at the lateral part of ankle due to the valgus knee deformity by JRA, on the other hand the left HC line continuously passed through the medial part of ankle after initial surgery. [Conclusions] The progression of deformity only in the left ankle was seemed to be occurred by the different stress concentration between both ankles. The whole lower limb alignment using HC line should be assessed in the initial treatment of foot and ankle deformity.

P2-135

Resection of the proximal interphalangeal joint for reconstructing dorsally dislocated metatarsophalangeal joint of the lesser toe

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Conflict of interest: None

Resection arthroplasty has been performed to reconstruct forefoot deformities of rheumatoid arthritis (RA) for a long time. In these days, joint preserving surgeries to shorten metatarsal bone has also become common procedure in Japan. We report another surgical procedure and its benefits. Resection of the proximal interphalangeal (PIP) joint was performed in 3 feet of 2 patients to reconstruct dorsally dislocated metatarsophalangeal (MTP) joint as reported by van der Heide HJ et al. Longitudinal dorsal incision from PIP to MTP joint is made. MTP joint capsule is released. Then, resection of the distal side of proximal phalanx is performed but extensor tendon is preserved. MTP joint is repositioned and transfixed intramedullary by K-wire. K-wire was removed after 3 weeks. This procedure is not only easy to perform but also less complications. Especially, this procedure might have advantage for the one or two dorsally dislocated feet.

P2-136

Disease activity in patients with rheumatoid arthritis after surgery of the upper and lower extremities

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Conflict of interest: None

[Objectives] We evaluated effects of surgery on disease activity of rheumatoid arthritis (RA) in each surgical site. [Method] Total 208 RA patients who underwent joint surgery including synovectomy, arthroplasty, arthrodesis and joint replacement were retrospectively reviewed. The patients were classified into 42 cases of hand, 20 of elbow, 23 of hip, 84 of knee, and 39 of foot. Age, disease duration, pre- and post-operative DAS28, and change of DAS 28 (ΔDAS28) were compared among surgical sites. [Results] The mean age at the time of surgery was 63.6 years in hand, 68.4 years in elbow, 68.0 years in hip, 68.1 years in knee, and 66.2 years in foot (NS). The mean disease duration was 15.2 years in hand, 23.6 years in elbow, 14.7 years in hip, 15.7 years in knee, and 22.7 years in foot ($P<0.05$). Preoperative DAS28-CRP was 2.8 in hand, 3.6 in elbow, 3.2 in hip, 4.2 in knee, and 22.7 in foot ($P<0.05$). The mean ΔDAS28 was -0.31 in hand, -0.23 in elbow, -0.43 in hip, -0.57 in knee, and -0.08 in foot ($P<0.05$). [Conclusion] This study suggested that effects of surgery on RA disease activity depended on surgical site.

P2-137

A case of polyarthritis with progressive large joints destruction and needs to joint reconstruction surgery

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Conflict of interest: None

This case is 78 years old, women. A chief complaint was both knee-joints pain which was conservatively treated. The osteolytic lesion was observed in the lateral femoral condyle of the right. The walking ability was restricted severely due to both knee joints pain. At the X-ray, we recognized joint space narrowing with bone erosion in both knee joints and 4 x 5 cm osteolytic lesion in the lateral condylar of the right. The pathological diagnosis was nonspecific inflammations and no malignancy. RA could not be confirmed. However, considering clinical findings as RA, MTX and TNF inhibitor was started, but the joint destruction were progressed and the remarkable ADL restriction persisted. TNF inhibitor was ineffective and the joint reconstruction surgery was performed in right knee and left hip. Although ADL improved markedly after the joint reconstruction surgeries, new joint destruction appeared on the right elbow, and MTX, IL-6 inhibitor was started. The joint symptoms improved dramatically, the right elbow was able to preserve the joint. In this case, the joint destruction progressed rapidly at the large joints. By administration of MTX and IL-6 inhibitor, joint symptoms have been well controlled. I reported a case was difficulty in the diagnosis and the treatment.

P2-138

Clinical consideration of the using total elbow arthroplasty in 3 RA cases for the functional reconstruction post elbow fracture

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Conflict of interest: None

[Object] We considered clinical problems to use total elbow arthroplasty (TEA) in 3 RA cases for the functional reconstruction post obsolete elbow fracture. [Methods] We used constrained type TEA in 2 cases and surface replaced type TEA in 1 case. [Results] Constrained type TEA with iliac bone autograft was performed for one mutilated obsolete elbow fracture case. The pedicle flap for complication of skin necrosis on olecranon was needed postoperatively. The range of motion (ROM) was 30-135°. Another case, the low profile constrained type TEA was performed with osteosynthesis using absorbable screw and wiring. The hyper skin tension was observed so we shifted the joint line 10 mm above. The skin circulation disorder was observed, but we avoided skin necrosis with extension elbow position. The ROM was 20-140°. The last case was an ankylosing elbow deformity after supracondylar fracture. We planned corrective osteotomy using 3D bone model. We performed surface replaced type TEA with osteosynthesis using absorbable screw and wiring. The ROM was 40-140°. [Conclusions] When we perform TEA for the RA patient who had obsolete elbow fracture, the preoperative planning such as the selection of low profile TEA system and surgical technique to avoid hyper skin tension is important.

P2-139

Impacts of Total Elbow Arthroplasty on Disease Activity and Functional disability in Rheumatoid Arthritis treated with Biologics

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Conflict of interest: None

[Object] We examine impacts of Total Elbow Arthroplasty (TEA) on postoperative disease activity, HAQ and Patient-Rated Elbow Evaluation (PREE) in RA patients using biologics. [Methods] In RA patients using biologics, 24 joints including 14 ETN, 5 TCZ, 2 ADA, 2 IFX and 1 ABT for which TEA was performed from 2006 to 2014 were included. Disease activity was assessed by CDAI and functional disorder by HAQ and PREE before and after surgery. [Results] Mean age and disease duration was 63.8 years old and 24.6 years. CDAI was significantly improved from 7.8 to 4.5 in LDA group and 15.5 to 7.7 in MDA group respectively. HAQ was significantly improved from 2.0 to 0.6 in LDA group and 2.0 to 0.4 in MDA group respectively. PREE was significantly improved from 35.6 to 8.0 in LDA group and 36.3 to 12.4 in MDA group respectively. Improvement in HAQ was achieved in function items not only for upper limb but also lower limb. [Conclusions] With its availability to achieve better supportive property, TEA achieved improvement in upper limb function. Further, TEA was useful for achieving lower limb function since elbow joint is a weight bearing joint in RA patients. Combination of medical and surgical therapy has been proved to be possible to achieve even higher ADL.

P2-140

Clinical outcome of the linked elbow prosthesis (PROSNAP) for the rheumatoid elbows

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Conflict of interest: None

[Object] We investigated the mid-term clinical results of total elbow arthroplasty (TEA) using the linked elbow prosthesis (PROSNAP) for the rheumatoid elbows. [Patients and Methods] Thirty-three elbows in 31 rheumatoid arthritis patients were investigated. The mean follow-up period was 42.5 (range 12-109) months. The clinical condition was assessed according to range of motion (ROM), Japanese Orthopaedic Association-Japan Elbow Society Elbow Function Score (JOA-JES score), and Mayo Elbow Performance score (MEPS). [Results] The mean preoperative ROM in extension and flexion were -31.9 degrees and 106.9 degrees, respectively. The mean preoperative JOA-JES score and MEPS were 46.3 points and 48.5 points, respectively. The mean postoperative ROM in extension and flexion were -30.6 degrees and 141.5 degrees, respectively. The mean postoperative JOA-JES score and MEPS were 87.5 points and 96.4 points, respectively. Complications were noted in 6 elbows (18.2%). Two elbows (6.0%) required revision surgery, one is for infection and one is for polyethylene wear. [Conclusions] Although the clinical results of PROSNAP for the rheumatoid elbows were satisfactory, two elbows (6.0%) required revision surgery.

P2-141

Peripheral Helper T cells in Systemic Lupus Erythematosus

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Conflict of interest: None

[Object] To assess “peripheral helper” T (T_{PH}) cells in patients with systemic lupus erythematosus (SLE) and determine their relationship to other subset of cells and to disease activity. [Methods] Peripheral blood mononuclear cells were obtained from patients with SLE and healthy individuals as controls, and were analyzed by flow cytometry. We defined T_{PH} cells as memory $CD4^+$ T cells expressing PD-1^{hi} and lacking CXCR5. The frequency and activated status of T_{PH} cells were compared with those of other immune cells including B cell subsets, and the disease activity. [Results] The proportion of T_{PH} cells was increased in SLE patients than healthy controls. The proportion of activated T_{PH} cells was also elevated in SLE patients and correlated with disease activity. The frequency of T_{PH} cells correlated with that of plasmablasts, and activated T_{PH} cells correlated with activated switched memory B cells. The frequencies of activated T_{PH1} ($CXCR3^+CCR6^-T_{PH}$) cells and T_{PH2} ($CXCR3^-CCR6^-T_{PH}$) cells were higher in SLE patients with active disease. [Conclusions] As activated status of T_{PH} cells was associated with disease activity in SLE, this subset might play an important role in lupus pathogenesis.

P2-142

Interferon-alpha production by plasmacytoid dendritic cells is enhanced and associated with increased TLR7 retention in the lysosomes of these cells in systemic lupus erythematous

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Conflict of interest: None

[Object] Interferon-α (IFN-α) plays an important role in the pathogenesis of systemic lupus erythematosus (SLE). However a Toll-like receptor (TLR) 9 agonist induced IFN-α production is not increased in plasmacytoid dendritic cells (pDCs) in SLE. TLR7 agonists also activate pDCs to produce IFN-α, and TLR7 has been shown to be involved in the progression of autoimmune responses in murine lupus models. In this study, we investigated the IFN-α-producing capacity of pDCs from SLE patients after stimulation with a TLR7 agonist. [Methods] Peripheral blood mononuclear cells (PBMCs) were stimulated with a TLR7 agonist, and IFN-α production by pDCs was examined by intracellular cytokine staining and flow cytometry. Localization of TLR7 in cellular compartments in pDCs was investigated by confocal microscopy. [Results] The IFN-α producing capacity of pDCs was increased when stimulated with a TLR7 agonist in SLE compared to in HC. The TLR7 agonist-induced IFN-α producing capacity of lupus pDCs was correlated with disease activity. TLR7 localization was increased in lysosome compartments in pDCs from SLE patients. [Conclusions] The enhanced IFN-α production by pDCs stimulated with a TLR7 agonist was associated with increased TLR7 retention in lysosomes of pDCs in SLE.

P2-143

Anti-DNA antibodies enhance incorporation of DNA into live cells, which may activate the natural immunity pathways in SLE

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Conflict of interest: None

[Object] Since two decades ago when Alarcón-Segovia published their observation, anti-DNA antibodies have been known to be internalized by live cells. It has been reported recently that internalization of anti-DNA antibodies resulted in secretion of inflammatory cytokines, but the precise mechanisms are not well elucidated. This study is aimed to make clear the mechanism of these phenomena which may be relevant to lupus pathophysiology. [Methods] THP-1 or EA.hy926 cells were incubated for 1-2 hours with mouse IgG monoclonal anti-dsDNA antibody 2C10 and/or Alexa 488-labeled 2 kbp dsDNA. After washing, fixation, and permiabilization, cells were analyzed by fluorescent microscopy and flow cytometry. [Results] 2C10, but not normal mouse IgG, was internalized by the cells. The ratio of 2C10-incorporating cells was not significantly affected by the addition of DNA. On the other hand, fluorescence-labeled DNA solely was not internalized, but it was internalized in the presence of 2C10 in an antibody-dose dependent manner. [Conclusions] Plasma from SLE contain higher levels of DNA than healthy control. Current results show that DNA can be facilitated to enter live cells by anti-DNA antibodies. Internalized DNA may possibly stimulate the cells to produce inflammatory cytokines.

P2-144

Antibodies to AHNAK1 is a novel autoantibodies specifically recognized in patients with systemic lupus erythematosus

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Conflict of interest: None

T cells of systemic lupus erythematosus exhibit several activation signaling anomalies. Calcium signaling is essential for the proper function of immune cells. Recent studies have shown that AHNAK1 is important for efficient calcium signaling in T cells through its ability to properly localize calcium channels at the plasma membrane and cytoplasm. Therefore, we assumed that autoimmune response to AHNAK1 occurs in SLE as antibodies to AHNAK1 potentially alter the nature of calcium signaling through binding of AHNAK1 resulting in pathogenesis of SLE. Patient’s sera consisting of SLE, PM/DM, SSc, SS, MCTD, RA, and normal healthy controls (NHCs) were collected and used for the present study. Immunoreactivity against AHNAK1 antigens was evaluated by

ELISA in these sera. The level to anti-AHNAK1 antibodies was significantly elevated in SLE patients compared to both NHCs and other diseases. In clinical profile, the frequency of lymphopenia was significantly higher in SLE patients with anti-AHNAK1 antibodies. In the present study, we found that anti-AHNAK1 antibodies were specifically recognized in SLE. Alteration of calcium signaling through binding of the antibodies to AHNAK1 may play an important role for pathogenesis of SLE.

P2-145

Analysis of the oxidative stress and the antioxidant power in patients with systemic lupus erythematosus

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Conflict of interest: None

[Object] ROS is associated with autoimmune disease. We weighed the oxidative stress and the antioxidant in patients with SLE. [Methods] We measured d-ROMs and BAP in SLE patients sera before and after treatment and normal sera with FREE made in Diacron. [Conclusions] The disease activity decreased before and after therapy (SLEDAI: before 17.7±8.5, after 4.6±3.8), and in d-ROMs, an average of 357.6±112.3U. CARR, BAP were an average of 1873.33±636.8μM in before. In d-ROMs, an average of 430.05±216.4U.CARR, BAP were 3450.94±1217.3μM after. The change was not found in before and after therapy in d-ROMs and significantly increased in BAP. As for the antioxidant properties, the group significantly increased after treatment for a group before treatment. d-ROMs before and after therapy and BAP before therapy more significantly than a healthy subject showed high level in patients with SLE. [Examination] The oxidative stress in SLE patients before or after treatment was higher than normal control. The antioxidant power and antioxidant properties were higher after treatment than before. We concluded that SLE patients were exposed to oxidative stress constantly, and the disease control related to antioxidant power and antioxidant properties with treatment.

P2-146

The regulatory role of Allergin-1 in autoantibody production

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Conflict of interest: Yes

[Object] 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-1KO) mice were treated with dead thymocytes. The titer of anti-dsDNA and anti-Histone antibodies in serum was measured by ELISA. 2) After dead thymocytes injection, the deposition of IgG and C3 on glomerulus was analyzed by immunofluorescent staining. 3) The expression of Allergin-1 on peritoneal macrophages was analyzed by flowcytometry (FCM). 4) Peritoneal macrophages from WT and Allergin-1KO mice were co-cultured with fluorogenic reagent or dead thymocytes. The phagocytic activities in macrophages were examined by FCM. **[Results]** 1) The titer of anti-dsDNA and anti-Histone antibodies was significantly higher in Allergin-1KO mice compared with WT mice. 2) The deposition of IgG and C3 was not significantly difference between WT and Allergin-1KO mice. 3) Allergin-1 was expressed on peritoneal macrophages. 4) The phagocytic activities were significantly lower in Allergin-1KOmacrophages than that in WT macrophages. **[Conclusions]** Allergin-1 might suppress autoantibodies production through the regulation of phagocytosis in macrophages.

P2-147

Clinical usage of mycophenolate mofetil in patients with systemic lupus erythematosus

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Conflict of interest: None

[Object] We investigated the current usage of mycophenolate mofetil (MMF) in our patients with systemic lupus erythematosus (SLE). [Methods] We reviewed retrospectively the clinical records of SLE patients administered with MMF from April 2008 to October 2017 in our department. [Results] 39 cases were included, the average age at the begining of MMF use was 38.2 years and the mean duration of disease was 131.5 months. 32 were lupus nephritis (LN), the others were neuropsychiatric lupus, pulmonary hypertension, hemolytic anemia and skin lesion. Among 32 LNs, 28 used MMF for remission induction and 4 used for maintenance therapy. Renal biopsy was performed at 81.3%. Prednisolone (PSL) was used in all cases, the initial dose was 31.5 mg. The dose of PSL at the final observation was 8.6 mg (observation period: 19.8 months). Steroid pulse therapy was performed at 59.0%. Multi-target therapy at 23.1%. In LN cases, complete remission was 62.5%, partial remission 25.0%. The mortality rate was 5.1%, but there was no death related directly to MMF. Infection was the most common adverse event. The discontinuation rate due to adverse events was 12.8%. [Conclusions] Although adverse events of MMF had many infections, the continuation rate was good, suggesting efficacy and safety of MMF.

P2-148

Current status of treatment and management status of SLE patients of our institute

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Conflict of interest: Yes

[Object] We aim to know current status of new SLE treatments introduction and management status of our SLE patients. [Methods] We reviewed clinical data concerning treatment and management satus of our SLE out patients in September 2018. [Results] Total patients are 346 (33 males, average age 47.8). Corticosteroid, Tacrolimus, MMF, Azathioprine, Hydoxy chloroquine are prescribed for 93%, 57%, 19%, 24%, 8% of our patients. Patients treated with corticosteroid alone are 14%. Those with plus one immunosuppressant are 42%. Those with plus two or more immunosuppressants are 38%. Average of Anti ds-DNA antibody titers, complement C3, creatinine of patients are 10.9 U/ml, 91.8 mg/dl, 0.83 mg/dl. The patient ratios of with high Anti ds-DNA antibody, with low C3 and with high Cr>1.5 are 19%, 3%, 3%. [Conclusions] Among immunosuppressants, we preferentially prescribed Tacrolimus. We prescribed two or more immunosuppressants for 38% of our patients. We achieve good managemnt status.

P2-149

A study on reasons for abandoning pregnancy in SLE patients: from LUNA registry

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Conflict of interest: None

In recent years, due to advances in treatment and accumulation of information, SLE patients became an possible to combine life events such as treatment and pregnancy. On the other hand, there are cases where SLE patients abandon their pregnancies, but there is little information on the reasons. [Methods] Research design is cross-sectional study. The subject was a female SLE patient meeting ACR criteria registered in the registry (LUNA) under construction between Showa University and Okaya-

ma University. 1: Existence of experience abandoning pregnancy due to SLE, and 2: questionnaire survey on reasons for abandonment of pregnancy. The questionnaire items are the following seven items. [Results] Among the 309 female SLE patients who were registered, 192 people answered the questionnaire (median age 43 years old). 16.7% (32/192 people) answered that they had given up on pregnancy due to SLE. [Conclusions] It was less than 20% who gave up pregnancy for SLE. It is important to provide an environment that can consult about pregnancy and to provide sufficient information on the effects of SLE and therapeutic drugs on pregnancy.

P2-150

Efficacy and safety of hydroxychloroquine in patients with systemic lupus erythematosus in our hospital

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Conflict of interest: None

[Objectives] To evaluate the efficacy and safety of hydroxychloroquine (HCQ) in Japanese patients with systemic lupus erythematosus (SLE) in clinical practice. [Methods] We retrospectively collected and analyzed medical records and laboratory data for 56 SLE patients from January 2016 to September 2017. [Results] Medication persistence rate was 94.6%. Cutaneous lesions and arthralgia were improved in 69.6% and 35% of patients, respectively. Administration of HCQ for over 6 months significantly reduced predonisolone (PSL) dose (9.2±7.1mg/day to 6.6±3.3mg/day; $p<0.05$) and SLEDAI score (5.1±3.2 to 2.7±2.6; $p<0.05$), while there was no significant difference in anti ds-DNA antibody titers, complement levels, and blood cell counts. There were no patients with increased SLEDAI score. HCQ was discontinued in 4 cases because of visual degradation in 1 and drug eruption in 3, although 1 eruption case was successfully desensitized. Gastrointestinal symptoms and headaches were more frequently observed than in the past reports (12.5%, 7.1%). [Conclusions] HCQ was well tolerated and may contribute to dose reduction of PSL and improvement of disease activity in addition to eruptions and arthralgia. We need to recognize gastrointestinal symptoms and headaches as frequent adverse effects.

P2-151

Efficacy of Hydroxychloroquine in 63 Japanese patients with Systemic lupus erythematosus

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Conflict of interest: None

[Objectives] The aim of this study is to investigate clinical features in stable systemic lupus erythematosus (SLE) patients who can reduce immunosuppressants after hydroxychloroquine (HCQ) is administrated. [Methods] We retrospectively studied 63 low disease activity patients with SLE who were added HCQ at our institution between October 2015 and July 2017. Patients were divided into 4 groups according to their medication; (1) steroid monotherapy, (2) antimetabolites (mycophenolate mofetil, mizoribine or azathioprine) and calcineurin inhibitors (tacrolimus or cyclosporin) add on steroid therapy, (3) calcineurin inhibitors (CNI) add on steroid therapy, and (4) antimetabolites add on steroid therapy. [Results] Previous immunosuppressants could be reduced within 3 months after adding HCQ in 41 patients, but not in 22. Steroid was administrated with a single agent in 20 patients, antimetabolites and CNI add on steroid therapy in 19, CNI add on steroid therapy in 18, antimetabolites add on steroid therapy in 6. The proportion of patients in whom previous immunosuppressants could be reduced were 75%,74%, 44%, 67%, respectively. [Conclusions] HCQ could be more effective in SLE patients treated with steroid monotherapy or in combination with antimetabolites than in combination with CNI.

P2-152

Analysis of clinical features of systemic lupus erythematosus associated with the amount of prednisolone

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Conflict of interest: None

[Object] We evaluated clinical features of systemic lupus erythematosus (SLE) associated with the amount of prednisolone (PSL). [Methods] 79 cases of SLE divided into three groups, PSL 0mg (A), PSL≦5mg (B) or PSL>5mg (C), from April to July, 2016. [Results] The rates of NPSLE, infection and strengthening of the immune suppression therapy within one year were significantly high in the order of A<B<C at trend analysis. How to use the immune suppression drugs and the rates of lupus nephritis (LN) and osteoporosis were no significant difference. Otherwise, the rate of vertebral bone fracture was higher in B and C than A. In C group, the amount of WBC, lymphocytes, IgG and IgM were significantly low. [Conclusions] These data indicated that however PSL was useful in high activity of SLE, for example NPSLE, no use of PSL did not cause flare up. Furthermore, the rate of infection and vertebral bone fracture increased if PSL was used even a little amount. These suggested that PSL should be decreased gradually and discontinued, in especially LN, then changed another immune suppression drug in terms of side effect.

P2-153

Hydroxychloroquine therapy for patients with systemic lupus erythematosus

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Conflict of interest: None

[Object] We investigated the effectiveness and safety of hydroxychloroquine (HCQ) therapy in patients with systemic lupus erythematosus (SLE). [Methods] We retrospectively analyzed backgrounds and laboratory data for SLE patients with HCQ in our hospital from April 2017. Disease activity was assessed at baseline and after 1 month. [Results] Of 42 patients enrolled, mean age at HCQ administration was 38 [15-72] years old, 37 were females, the median disease duration was 6 years and the median HCQ duration was 96 [21-215] days. Five patients had adverse events (rash 1, diarrhea 4) and 2 patients stopped HCQ. One patient died due to SLE. Of 21 patients, HCQ therapy was started in the maintenance period. One was blood cell disorder, one was nephropathy, six were arthritis, and two were eruption. Dose of prednisolone was 10 [5-22.5] mg/day, platelet was 24.9 [10.2-35.6] $\times 10^4/\mu l$, C3 was 86.5 [62-120] mg/dl, anti-ds-DNA antibody was 7.5 [0.0-83.5] IU/ml, urinary protein/creatinine ratio was 0.04 [0.024 - 0.649] and SLEDAI-2K was 2 [0-6] (median). We found that C3 was significantly elevated at baseline to 1 month in the patients with low C3 at administration (74.7 to 78.9, $p=0.049$). [Conclusions] Add on HCQ therapy increased C3 in a short period in patients with SLE maintenance treatment.

P2-154

What the approval of mycophenolate mofetil (MMF) and hydroxychloroquine sulfate (HCQ) broughtto the SLE patients-analysis of 20 cases in our hospital-

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Conflict of interest: None

[Object] MMF and HCQ were approved as drugs for SLE and LN in 2015. We investigate how this has changed the treatment for SLE. [Meth-

ods] A total of 20 patients diagnosed as SLE and treated in our department between 2012 and 2017 were enrolled and we investigated their pathogenesis and treatment. [Results] 20 patients were all women and the average age at onset was 37.05 years. The cases required of hospitalization were nine and the cases with pregnancy were two. Five cases with renal disorders were all performed of renal biopsy. There were two cases of class IV G (A) and one each case of IV G (A/C), IV G (A/C) + V. About treatment, there were 5 cases of single steroid therapy, 9 cases of massive steroid i.v. therapy. As combination drug, there were 11 cases of tacrolimus, 5 cases of HCQ, 3 cases of MMF, and one each case of azathioprine, mizoribine, and cyclophosphamide. The average SLEDAIs of pre- and aftertreatment were 13.75 (6-28), 8.2 (2-22), respectively. [Conclusions] SLE and LN are prevalent among young women. Preservation of fertility and risk reduction during the course of pregnancy are required in the treatment. Combining approved drugs and existing ones according to disease condition and lifestyle made it possible to obtain therapeutic effect more safely and more efficiently.

P2-155

The efficacy of mycophenolate mofetil in Japanese patients with systemic lupus erythematosus

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Conflict of interest: None

[Object] Although mycophenolate mofetil (MMF) has recently been approved for lupus nephritis in Japan, there are few reports which evaluating the effect of MMF in Japanese patients. We therefore conducted a retrospective clinical study to assess the efficacy of MMF in Japanese patients with systemic lupus erythematosus (SLE). [Methods] Twenty patients (mean age 39.1 ± 9.1 years, 14 females) with SLE who received MMF were included in this study. We assessed the therapeutic effects of MMF at 1, 3, and 6 months after starting treatment. We collected thirteen patients took tacrolimus and thirteen patients received intravenous cyclophosphamide to compare the efficacy with MMF. [Results] Median serum levels of anti-double stranded DNA antibody titer decreased from 17.5 IU/mL to ≦12 IU/mL, median SLE Disease Activity Index decreased from 12 to 4, median daily prednisolone dosage decreased from 19.0 mg to 10.0 mg. Median urine protein level decreased from 2.15 g/gCr to 0.7 g/gCr after 6 months in 12 patients with lupus nephritis. There was no significant difference in therapeutic efficacy among the three therapies. [Conclusions] MMF is effective to Japanese patients with SLE.

P2-156

The efficacy of Hydroxychloroquine add-on in patients with Systemic Lupus Erythematosus during maintenance phase

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Conflict of interest: None

[Object] To evaluate the efficacy of Hydroxychloroquine (HCQ) add-on in patients with Systemic Lupus Erythematosus (SLE) during maintenance phase. [Methods] The laboratory data, SLEDAI, prednisolone (PSL) dose and adverse effect were evaluated in 16 SLE patients taking HCQ. [Results] 16 patients, 14 females, were included. The average age was 42±13 years. The median disease duration was 6[1-26] years. The average dose of PSL was 9±2.8 mg/day. The median of the treatment periods by HCQ was 9.5[2-17] months. Before HCQ administration, low complement C3 level (37.5%) and increased anti-DNA antibody (31.3%), lymphocytopenia (<1000/μL) (43.8%), thrombocytopenia (<20×10^4/μL) (25%), SLEDAI ≧ 2 (56.3%) were observed. C3 level (mg/dL) before HCQ administration, 3 months after, 6 months after were 52[40-76], 62[42-92], 61.5[42-91], and anti-DNA antibody (IU/mL) were 16[7.5-140], 10[2.5-110], 5[3-74], lymphocyte (/μL) were 599±166, 769±442, 899±684, platelet (×10^4/μL) were 11.6[5.4-18.8], 15.2[6-20.4], 14.2[7-20.3], SLEDAI were 6[2-13], 2[0-8], 2[0-8] respectively. The dose of PSL were reduced in 4 patients 6 months after HCQ administration. [Conclusions] HCQ might have beneficial effects on laboratory data and steroid-sparing in patients with SLE during maintenance phase.

P2-157

Usefulness of hydroxychloroquine in patients with SLE

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Conflict of interest: None

[Object] We evaluate the progress of the SLE patient receiving hydroxychloroquine (HCQ) serologically and examine further effective use. [Methods] We examined 63 SLE patients receiving HCQ from December 2015 in our hospital.13 patients with average values of C3 and C4 before HCQ administration were both below the reference value were extracted. We examined the transition of C3 and C4 at 3 months after administration and at the the last observation day. 2 cases without data at 3 months after were excluded. [Results] At 3 months after, both C3 and C4 were elevated in 7 out of 11 cases, and only one case normalized both C3 and C4. At the last observation day, 3 cases normalized both C3 and C4. There were 5 cases in which neither C3 nor C4 were normalized from administration to the last day. All 5 cases were used 2 or more drugs, and more than 5 years from onset to administration HCQ, but other than that, no features were observed. There was no case in which both C3 and C4 decreased at the the last observation day. [Conclusions] In this study, we could not find a feature in 5 cases where neither C3 nor C4 were normalized at the time of the last observation, but because there is a possibility that the short observation period may have an effect, it is also necessary to continue observation.

P2-158

A clinical study on efficacy and safety of hydroxychloroquine for systemic lupus erythematosus

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Conflict of interest: None

[Object/Methods] Since hydroxychloroquine (HCQ) was approved in Japan, there have been some reports about the drug efficacy and safety without sufficient date so far. We evaluated the patient background, efficacy, and adverse events of 65 systemic lupus erythematosus (SLE) patient with the HCQ at our department. [Results] All of 65 cases were for SLE and the patients were 6 males and 59 females with average age of 37 years old. The median disease duration was 6 years. The reasons for HCQ administration were skin rash and arthritis as approximately 50% and 30% respectively. The ratio for stable SLE patients was 22%. Adverse events appeared in 8 out of 65 cases, of which 6 cases had drug eruption, but no eye disorder was recognized in 8 cases. It was recognized that the complement had been increased in C3 and CH50 level within 6 months. There was one case for the exacerbation of SLE. [Conclusions] It is reported that HCQ indicated high efficacy for skin lesion in some cases in Japan, and the efficacy was also confirmed at our department as well. Because of increase in complement serologically, it was considered that the drug may possibly tend to suppress overall SLE activity. In future, we will continue the research prospectively and deliver a report with the clinical examination.

P2-159

The association between periodontitis and the disease activity of systemic lupus erythematosus: a cross-sectional study

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Conflict of interest: None

[Objectives] To assess the association between periodontitis and the disease activity of SLE. [Methods] The subjects were SLE patients who were under 65-years-old. Periodontitis was evaluated using pocket of depth, attachment loss and divided into four categories. The Main outcome was SLEDAI. The secondary outcome was the complement and anti-dsDNA antibody level. In the main analysis, a multiple regression analysis was conducted to assess the association between periodontitis and the disease activity of SLE with adjustment for age, sex, current smoking status, current PSL dose, the maximum dose of past PSL treatment and current immunosuppressant therapy. [Results] 83 participants were eligible. The prevalence of periodontitis was 62.6% in moderate periodontitis, 8.4% in severe periodontitis. With reference to non-periodontitis, the regression coefficients [95%CI] of moderate periodontitis and severe periodontitis for SLEDAI were -0.76 [26.4 to 127.7] and 4.5 [-3.4 to 6.49]. In the secondary analysis, with reference to non-periodontitis, the regression coefficients [95%CI] of severe periodontitis for anti-dsDNA antibody was 77.1 [26.4-127.7]. [Conclusions] There was not statistically association between periodontitis and the disease activity of SLE.

P2-160

Examination of pregnancy outcome with tacrolimus usage in systemic lupus erythematosus

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Conflict of interest: None

[Object] To examine the pregnancy outcome with tacrolimus (TAC) usage in systemic lupus erythematosus (SLE) patients. [Method] We studied 40 SLE patients who accounted for 54 deliveries over an 8-year period from 2008 to 2016. We retrospectively analyzed the pregnancy outcomes of SLE patients and its prognostic factors with or without TAC treatment. Analyses of covariance with adjustments for the propensity score were used to compare the patients' backgrounds between TAC users and non-TAC users. [Results]: Fifteen of 54 (27.8%) cases were treated with TAC, and they tended to have a higher dose of prednisolone, hypocomplementemia, lower estimated glomerular filtration rate, past history of lupus nephritis and complication with anti-phospholipid syndrome. In the adjusted background of TAC users, the risks of, low fatal body weight, non-reassuring fetal status (NRFS), and preterm birth did not increase compared to non-TAC users. However, gestational diabetes and thrombocytopenia were extracted as predictive risk factors for lower fetal body weight, and hypertension was extracted as a predictive risk factor for NRFS. [Conclusions]: TAC users had no statistically significant difference in risks contributing to outcomes compared to non-TAC users.

P2-161

Efficacy and Safety of Hydroxychloroquine in Japanese Systemic Lupus Erythematosus Patients with Maintenance Therapy

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Conflict of interest: None

[Object] To clarify efficacy and safety of hydroxychloroquine (HCQ) in Japanese systemic lupus erythematosus (SLE) patients with maintenance therapy. [Methods] Retrospective observational study was conducted. Twenty-two patients were enrolled. Described were age, sex, initial HCQ dose and administration period, comparison of prednisolone dose and laboratory data at the HCQ start date and at 6 months after HCQ start date, concomitant immunosuppressive drugs, and the number of patients withdrawing from HCQ and causes for withdrawal. Wilcoxon matched-pairs signed rank test was employed to compare the prednisolone dose and laboratory data recorded at HCQ start date and at 6 months after HCQ start date. [Results] Patients in this study consist of 21 female patients and 1 male patient. Median of age was 42 years old. Median of HCQ administration period was 198 days. With 6 months HCQ administration, prednisolon doses were significantly reduced (P=0.035), and titers of serum anti-double strand DNA antibodies also decreased significantly (P=0.024). Four patients ceased HCQ due to eruptipon, diarrhea and fever. [Conclusions] HCQ might be used concomitantly to reduce prednisolone dose safely without recurrence in Japanese SLE patients with maintenance therapy.

P2-162

Clinical features of male patients with systemic lupus erythematosus

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Conflict of interest: None

[Object] Systemic lupus erythematosus (SLE) is an autoimmune disease that causes various symptoms. Favorable age ranges from 20 to 40 years and the ratio of male to female is 1:10. The difference between clinical features of male SLE and female SLE has been pointed out than before, but details are not clear. We examine the characteristics of male SLE cases in our facility. [Methods] During 2011 to 2017, 41 patients (male 9, female 32) who met the ACR (American College of Rheumatology) criteria in 1997 newly diagnosed SLE and treated at Department of Rheumatology and Collagen Diseases in Shinonoi General Hospital. We compared retrospectively clinical symptoms, examination results, treatments for each group. [Results] Of the 41 patients, we can see skin symptoms (39%), nephropathy (20%), serositis (16%), and neuropathy (5%) as organ disorders. The age at onset tended to be higher in male at 52.3 ± 19.0 years old and female 42.6 ± 19.6 years old. There were no statistically significant differences in clinical features between them. But fever, lymphadenopathy, pleuritis tended to be higher in men, and nephropathy more common in female. There were no nephropathy in male group. [Conclusions] We report a certain tendency in male SLE.

P2-163

Analysis of SLE patients treated by Hydroxychloroquine

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Conflict of interest: Yes

[Background] Hydroxychloroquine is in the process of accumulation of uses in Japan. [Object Methods] We analyzed the efficacy and safety of Hydroxychloroquine to our SLE patients, who were prescribed it within 6 months after launch in Japan. [Results] Ten cases (nine female), average age 38.5±8.1 years old, average body weight 49.9±6.7kg, average ideal body weight 47.5±4.8kg. Of them, five patients were with Lupus nephritis. One had severe diarrhea and stopped the use, but nine of them kept using it. Some patients succeeded in decreasing the dose of prednisolone. [Conclusions] Hydroxychloroquine seem effective and safe to our SLE patients.

P2-164

Assessment of Health Related Quality of Life by the Three-component Model of SF-36 in Japanese Patients with Systemic Lupus Erythematosus: A Cross-sectional Study

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Conflict of interest: None

[Object] We previously reported the reliability of the 2-component model of SF-36 in Japanese patients with systemic lupus erythematosus (SLE). We aimed to cross-sectionally investigate the health-related quality of life (HRQoL) in Japanese patients with SLE by the 3-component model, which has newly developed for Japanese. **[Methods]** Japanese patients with SLE (n = 393) completed the SF-36 and other related demographic questionnaires, and physicians simultaneously completed the SLE Disease Activity Index 2000 (SLEDAI-2K) and the SLICC Damage Index (SDI). **[Results]** The mean age, SLEDAI-2K score, and SDI score were 44.7 years, 2.5, and 0.6, respectively. The mean physical, mental, and role component summary (PCS, MCS, and RCS) scores of the SF-36 in the SLE patients were 45.7, 47.8, and 47.1 respectively, which were significantly lower than the age- and sex-matched national norm score, 50. The PCS scores were inversely collated with age and the SDI scores (r = -0.41 and -0.39), but not with the SLEDAI-2K scores. **[Conclusions]** HRQoL measured by the SF-36 was reduced in Japanese patients with SLE. Similar to our previous results by the 2-component model, the PCS scores were inversely collated with age and the SDI scores by the 3-component model.

P2-165

The usefulness of tacrolimus to remission induction therapy of lupus nephritis in daily clinical practice

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Conflict of interest: None

[Object] To assess the usefulness of tacrolimus (TAC) in remission induction therapy of lupus nephritis (LN) in daily clinical practice. [Methods] We selected the patients with LN treated for remission induction at Tsukuba University hospital from Apr. 2007 to Sep. 2017, and divided them into 3 groups; prednisolone (PSL) + TAC (n=20), PSL + TAC + mycophenolate mofetil (MMF) (n=5), and PSL + cyclophosphamide pulse (IVCY) (n=12). We retrospectively compared their 1) characteristics at intervention (clinical presentation, SLEDAI, and renal pathology), 2) treatment course (PSL dose, urine findings, anti-DNA antibody (a-DNA), complement, and lymphocyte), and 3) incidence of infection up to 6 months from the start of therapy. [Results] 1) There was no difference in the patients' characteristics. 2) PSL was reduced equally among 3 groups, and the urine findings, a-DNA, and complement were equally improved. In PSL + IVCY group, lymphocyte tended to decrease compared to PSL + TAC group. 3) There was no difference in the incidence of infection among 3 groups. In cases with infection, lymphocyte tended to decrease compared to the cases without infection. [Conclusions] We confirmed that the usefulness of TAC in remission induction therapy of LN was comparable to IVCY in daily clinical practice.

P2-166

Investigation of hydroxychloroquine (HCQ) therapy for Systemic lupus erythematosus (SLE) in our hospital

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Conflict of interest: None

[Objectives] To clarity the effect of HCQ therapy in patients with SLE, we performed this retrospective study. [Methods] 39 patients with SLE who fulfilled SLICC criteria and received an initial HCQ therapy in our hospital from January to June 2017 were selected for this study. Data were collected retrospectively from medical records and analyzed descriptively. [Conclusion] The results suggest that HCQ could decrease serum anti-DNA levels in SLE patients, in addition to steroids dose-sparing effect. [Results] Eligible patients were 21-62 years old, including 4 males and 35 females. The range of dosage of PSL was 1 to 60 mg in all patients. 6 of 39 patients that were treated with PSL doses above 20 mg or increasing of other immunosuppressants at baseline were excluded from the analysis.2 of 39 patients discontinued HCQ due to skin symptoms of drug allergy or the elevation of serum creatinine levels within the observation period. The average serum levels of anti-DNA antibodies (anti-DNA) at initial HCQ therapy were 13.51±3.28 U/ml (mean±standard error of mean). Serum levels of anti-DNA at month 3 were siginificantly lower than those at baseline (13.51±3.28 U/ml vs 10.85±2.80 U/ml, p=0.0316). Moreover, the dosage of PSL at month 3 was significantly lower than that at baseline.

P2-167

Hydroxychloroquine monotherapy on systemic lupus erythematosus without organ-threatening disease

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Conflict of interest: None

[Objectives] To evaluate the usefulness of hydroxychloroquine (HCQ) monotherapy on systemic lupus erythematosus (SLE) without organ-threatening disease. [Methods] We enrolled 13 patients with SLE treated with HCQ monotherapy who visited our hospital from September 2015 to September 2017. Their medical records were reviewed. [Results] A case with additional administration of 20mg prednisolone within 2 weeks because of preuritis, and a case with discontinuation of HCQ within 2 weeks because of adverse events were excluded. 2 were male and 9 were female, and mean age was 41.9 years old. After started HCQ monotherapy, all of 7 patients presented with arthralgia were improved, 6 out of 8 patients who presented with skin symptom experienced an improvement, 2 patients experienced an improvement of hypocomplementemia, and 2 patients experienced an improvement of anti-ds DNA antibody titer. [Discussion] This report showed efficacy of HCQ monotherapy. HCQ monotherapy could be an option for treatment of SLE without organ-threatening disease.

P2-168

A clinical profile of 9 patients with elderly-onset systemic lupus erythematosus

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Conflict of interest: None

OBJECTIVE & METHODS: In previous reports, it is known that elderly-onset systemic lupus erythematosus (SLE) has a different clinical profile from ordinary SLE. To determine the clinical features, we have retrospectively examined 9 patients with SLE developed over age of 70 years who were hospitalized or admitted to our department in the past 5 years. RESULTS: 3 men and 6 women. The onset-age was 72 to 87 years. We have 3 cases with skin erythema, 7 cases with arthritis. 4 cases with cytopenia, 7 cases with anti-DNA antibody positive. 5 cases have serositis, only 2 cases combined lupus nephritis. 8 patients received steroids, 4 with immunosuppressive drugs and 2 with hydroxychloroquine. The initial treatments were successful in most cases. Ischemic heart disease was involved in one case, malignancy was in another case. We had 2 cases of death, dying of prostate cancer and bacterial pneumonia respectively. CONCLUSIONS: In our cases of elderly-onset SLE, complications of serositis occurred frequently and nephritis was a little. The treatment response was good. Clinical features different from ordinary SLE were presented. It is expected that treatment strategies will change in the future due to addition of new drugs for SLE. We here report our cases including literature considerations.

P2-169

Effect of additional hydroxychloroquine on stable SLE patients

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Conflict of interest: None

[Object] Hydroxychloroquine sulfate (HCQ) was also approved in Japan in September 2015. There are still few reports on efficacy and safety in clinical practice, and the effect of decreasing the maintenance steroid dose by starting administration of HCQ in overseas where it is administered from the first time. We examined that to stable SLE patients. [Methods] We enrolled 36 patients of SLE who had been fixed for 3 months or more in steroid and immunosuppressive maintenance therapy. PSL maintenance dose, anti-DNA antibody titer, Dr, VAS and SLEDAI were evaluated at 12, 24 and 52 weeks after HCQ started. [Results] The patient background at baseline is 36.8 ± 9.5 years old, 92% female, mean disease duration 11.6 ± 8.2 years. The average value at baseline and after 24 weeks were 9.5±4.3,8.2±4.5mg / day for PSL maintenance dose, 35±39, 25±32IU / ml for anti-DNA antibody titer (RIA), 0.8±0.4, 0.5±0.3 for Dr, VAS, 6.3±5.1, 3.3±2.3 for SLEDAI. Dr, VAS and SLEDAI decreased with a significant difference. (P value=0.003, 0.004) [Conclusions] The improvement effect of SLEDAI was also confirmed by the initiation of combined use of HCQ in SLE patients during steroid and immunosuppressant maintenance therapy. It is expected that further reduction of maintenance steroid dose.

P2-170

A survey on adverse events at the start of hydroxychloroquine administration

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Conflict of interest: None

[Object] We investigated the current condition of HCQ treatment for allowing a pharmacist as an expert to provide the appropriate information in such a circumstance. [Methods] From 40 SLE cases with HCQ administration, the study targeted the total 35 cases (8 patients with discontinued HCQ administration due to adverse events and 27 cases with continued HCQ administration). With reference to the medical records, the study retrospectively investigated the adverse events and the patient background at the start of the administration while statistical analysis made a comparison between 2 groups. [Results] The reasons for HCQ introduction among the patients were skin disorder, low complement, arthritic pain, and renal disorder/desire of pregnancy. The incidence of adverse event was 22.9% with 6 cases for suspicious drug-induced rash and 2 cases for suspicious blood disorder as the reasons for drug discontinuation. We found a significant difference between the discontinuation group and the continuation group as average ideal weight and average applied dose of HCQ per day respectively. [Conclusions] As the actual condition of clinical care with HCQ at our hospital, approximately 20% of the patients had side effects with skin rash as occurred most frequently.

P2-171

Clinical picture of late-onset systemic lupus erythematousus in Japanese patients

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Conflict of interest: None

[Introduction] Systemic lupus erythematosus is a multi systemic autoimmune rheumatic disease that often occurs in women of child bearing age. It can affect any age, and 4-20% of SLE patients are above the age of 50 late-onset SLE. Recent studies suggested that young onset SLE had more common systemic manifestations including nephritis, neuropsychiatric, and hematologic involvement and a more fulminant disease course than late onset SLE. [Object] We retrospectively studied the clinical characteristics and prognosis of a Japanese SLE population to review the behavior of late onset patients whose onset of disease, defined as the initial manifestation of SLE, occurred after the age of 50 years. [Methods] From September 1997 to August 2017, we investigated 77 SLE patients from an inception cohort of our hospital, we assess clinical, laboratory, and histologic findings and outcomes in patients with SLE. [Results] The incidences of lupus nephritis, as well as the requirements of immunosuppressive therapies were similar in the two groups. [Conclusions] In this study, late onset lupus nephritis patients did not belong to a benign subgroup of the lupus nephritis population, and it was found that intensive therapy of late onset patients potentially increased the risk of adverse events.

P2-172

Study on the effect of hydroxychloroquine (HCQ) on the incidence of diabetes / dyslipidemia in SLE patients who had received high-dose glucocorticoid (GC) therapy -From LOOPS registry-

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Conflict of interest: None

Objectives: We examined the effect of combined use of HCQ on the onset of diabetes/dyslipidemia in SLE patients who received high-dose GC therapy. Methods: We compared the cases in which newly developed diabetes or dyslipidemia occurred in one year after high-dose GC therapy in 82 SLE patients who were hospitalized in our department before and after August 2015 when we could use HCQ, and be categorized as HCQ users versus nonusers at the time of intoroduction of GC. Results: The HCQ nonusers/users was 60/22 cases, and it was 87/86% in female, 44.1/42.1 years of age, 127/167 months of disease duration, SLEDAI 16.7/18.7, BILAG 16.7/18.1, BMI 21.1/20.0, HbA1c 5.59/5.59% and there was no difference in the background. Disease activity improved significantly in both groups after 1 year. after 1 year PSL equivalent of 7.5 mg/day or less was 45%/61% in the HCQ nonuser/user group, and the HCQ-user group was maintained at significantly lower doses.4 cases /1 case were new in the HCQ nonuser / user group for the new onset of diabetes and the new onset of dyslipidemia was 8 cases /1 case, and the onset of dyslipidemia tended to be slightly less in the HCQ user group. Conclusion: It was suggested that HCQ could also suppress the onset of dyslipidemia, especially in SLE patients who need high dose GC therapy.

P2-173

Will the pregnancy-related events of SLE patients affect the medium-term course after delivery?

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Conflict of interest: None

[Object] In PROMISSE study in 2015 on pregnancy with SLE, it has been reported that adverse pregnancy outcomes (APO) including fetal or neonatal death, birth before 36 weeks and small-for-gestational age neonate, occurred 19%. However, in SLE patients who gave birth at our hospital from March 2010 to September 2016, 16 of 39 cases had APO. In addition, there were 8 cases requiring additional treatment of SLE during pregnancy. The purpose of this study is to investigate the medium-term course after delivery of SLE patients and the influence of pregnancy-related events. [Methods] We investigated the clinical course of 39 SLE patients who gave birth at our hospital from March 2010 to September 2016 and analyzed its relation with pregnancy-related events. [Results] From delivery to October 2017, 69% of patients had continued visiting our hospital and the follow-up period was an average of 42[5-88] months. In the APO group, the rate of hypocomplementemia at the time of survey was

significantly high. In the patients who required additional treatment of SLE during pregnancy, the rate of immunosuppressant administration was significantly high. [Conclusions] In our study, pregnancy-related events in SLE patients did not have a significant effect on the medium-term course after delivery.

P2-174

Actual use experience of mycophenolate mofetil for systemic lupus erythematosus

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Conflict of interest: None

[Object] Standard treatment of systemic lupus erythematosus (SLE) is consisted of corticosteroids and immunosuppressive agents. However, some patients do not reach remission either with insufficient response or adverse effects of these agents. Recent studies have shown that mycophenolate mofetil (MMF) has equivalent efficacy and less side effects to intravenous cyclophosphamide for the treatment of lupus nephritis. Actual use of MMF in our hospital was studied. [Methods] Medical records of 25 patients with SLE who received MMF in our hospital from September 2013 to August 2016 were retrospectively reviewed. [Results] 19 patients were female and 6 were male. Mean age was 39±11 year-old. Mean duration of SLE was 7.9±6.7 years. Mean maintenance dose of MMF was 1.75 g/day and all patients received corticosteroids. The mean administration period of MMF was 341 days. Renal involvement was observed in 17 patients (10 patients received biopsy). Use of MMF decreased SLEDAI and urinary protein. One patient discontinued MMF due to nausea. Three patients discontinued MMF due to plan for pregnancy. [Conclusions] It was suggested that MMF is effective and relatively safe for patients who would like to keep the pregnancy capabilities.

P2-175

Association of TET (ten eleven translocation) gene polymorphism with systemic sclerosis (SSc) in Japanese population

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Conflict of interest: None

[Object] Methylation of cytosine residues in genomic DNA has an important role in epigenetic changes in gene expression. TET protein is involved in the de-methylation of DNA. SSc is characterized by fibrosis and the hypoxia state of the peripheral organization. It is reported that the TET1 mRNA of the SSc fibroblasts is more decreased than healthy controls (HC) in hypoxic condition. In the genome-wide-related analysis of Japanese SSc, the *TET1* gene was related to the onset of disease, and we examined the relationship between the *TET* gene and the Japanese SSc pathology. [Methods] 303 Japanese SSc patients and 431 HC were recruited in this study. Three SNPs, *rs755622*, *rs4852324*, *rs6705628* on the TET gene were genotyped using Taqman assay. [Results] The three SNPs of *TET* gene were not significant differences between Japanese SSc and HC, but it showed significant difference between *rs755622* and anti-RNP antibodies, nail fold bleeding (NFB), pitting scar, pulmonary hypertension (PH), *rs485232* and anti-centromere antibodies, skin ulcers, PH, *rs6705628* and NFB ($p<0.05$). [Conclusions] It is thought that the oxygen condition could affect mutations in *TET* genes. The high expression of the *TET* gene is predicted to recover the condition resulting from hypoxia and may be a new treatment for SSc.

P2-176

Quantitative analysis of peripheral vascular bed in patients with systemic sclerosis by using photoacoustic imaging technology: the second report

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Conflict of interest: None

[Object] The aim of this study is to evaluate the usefulness of photoacoustic imaging (PAI) for quantitative analysis of peripheral vascular bed in patients with systemic sclerosis (SSc). Peripheral circulatory disorder is a one of the major complication of SSc and indicates the involvement of internal organs. Previous studies revealed that nail-fold capillaroscopy and thermography are useful visualization methods, but quantitative analysis is still difficult. PAI is a novel technique that uses the photoacoustic effect. Using PAI, we can noninvasively obtain an image of the microvessels in the fingers. [Methods] Nine SSc patients and three healthy controls (HC) were enrolled in the study. The volume of the vascular bed was measured bilaterally at proximal and distal sites of the 2nd to 5th fingers using PAI. [Results] The volume of the digital vascular bed at 37 sites of SSc patients and at 21 sites of HC could be obtained. All SSc patients showed a significantly decreased digital vascular bed volume as compared with HC. [Conclusions] PAI may be a useful method for evaluating vascular bed volume of SSc patients. More data on subjects with clinical signs and comparison with other modalities will provide the information to determine the prognosis of peripheral ischemic damage.

P2-177

Mitigating effect to Raynaud's phenomenon by warming the wrist joint using a disposable hand warmer

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Conflict of interest: Yes

[Object] Raynaud's phenomenon is common in systemic sclerosis, but the effect of drug treatment is not sufficient. Dipping hands in hot water, wearing gloves, and griping hand warmer are usually used to prevent or to release Raynaud's phenomenon, but these make problems in daily work. It would be convenient if Raynaud's phenomenon could prevent without covering fingers. However, it has not been demonstrated whether preventive effects can be obtained by heating parts other than fingers. Here, we examined the effect of the wrist joint warming with disposable hand warmer. [Methods] After the obtaining the permission of the ethical committee of Osaka University Hospital and informed consents, ten patients with systemic sclerosis used hand warmer specialized for wrist joints named Maki-poka. They repeated using and not using Maki-poka in weekly units, and noted their subjective evaluation. [Results] A subjective score in the week of wearing a hand warmer on the wrist joint was observed to show a decreasing tendency compared to the non-wearing period (mean 2.3 vs 3.9), but it did not reach a statistically significant difference. [Conclusions] The effect of mitigating Raynaud's phenomenon by warming of the wrist joint is required to be verified with an expanded scale.

P2-178

Analysis of Long term outcome of pulmonary hypertension associated with connective tissue disease

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Conflict of interest: None

[Object] To analyze the long term outcome of pulmonary hypertension associated with connective tissue disease. [Methods] We assessed 30 cases of CTD-PH diagnosed by right heart catheterization (RHC) or echocardiography. Pulmonary hypertension (PH) associated with left-heart disease was excluded. [Results] The median of age and gender ratio (female) were 70 years old and 90.3%. There were 17 SSC cases, 6 SLE

cases, 2 MCTD cases, 3 PM/DM cases, 1 RA case, 2 APS cases. Twenty-three cases were diagnosed by RHC, 7 cases were by echocardiogram. Seventeen of 30 cases were complicated interstitial pneumonia (IP). At the time of diagnosis as PH, the median of mPAP, TR-PG, %VC, and %DLCO were 29mmHg, 50.6mmHg, 78.6%, and 30.8% respectively. Vasodilator of pulmonary artery was used in 27 cases, 11 cases were treated by monotherapy, 14 cases were by two drugs, 2 cases were by three drugs. Six cases were died, and the caouse of death were IP (n=2), SLE (n=1), Liver failure (n=1), PH (n=1), heart failure (n=1). Survival time was 1220days (median). Five-year survival rate by all the causes of death was 68.2%, and by PH was 92.3%. [Conclusions] The prognosis of CTD-PH can be involved in factors other than PH, adequate management of connective tissue disease and complications is necessary.

P2-179

Use of bosentan for PGE1 resistant digital ulcers related to systemic sclerosis and mixed connective tissue disease

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Conflict of interest: None

[Object] Ischemic digital ulcers (DUs) are a common complication of systemic sclerosis (SSc) and mixed connective tissue disease (MCTD). This study aimed to characterize patients with SSc and MCTD ongoing DU resistant to prostaglandin E1 (PGE1) therapy treated with bosentan. [Methods] We tried to treat DU patients by PGE1 for 4 weeks firstly, then if we did not achieve improvement of DU, treated with bosentan. [Results] The study included 8 patients, 1 diffuse cutaneous SSc (dcSSc), 4 limited limited cutaneous SSc (lcSSC), and 3 mixed connective tissue disease (MCTD). 1 patient with dcSSC withdrew from treatment because of congestive heart failure. In other 7 patients, 5 patients showed cure of DUs, 2 patients showed improvement of DUs. 2 patients showed anemia during treatment, 1 patient withdrew from treatment, the other could continue treatment by decrease bosentan dose. [Conclusions] The therapy with bosentan was useful in patients with PGE1 resistant DUs of lcSSC or MCTD. In patients with dcSSC the bosentan effect was still unclear.

P2-180

Clinical features of systemic sclerosis patients with arthritis

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Conflict of interest: None

[Object] SSc is an autoimmune disease characterized by vascular injury, tissue fibrosis, scleroderma and interstitial pneumonia (IP). Some SSc patients have arthritis. This study clarifies the features of such patients. [Methods] We reviewed medical records of 52 SSc outpatients from 2013-2017. [Results] Of 13 patients with arthritis. 6 were complicated with RA, 3 with SLE, one with SjS. Mean age of SSc onset, gender ratio, clinical phenotype did not differ between patients with/without arthritis. Although positive rates of ANA, anti-Scl70, anti-centromere, anti-RNA polymerase III Ab did not differ between ± arthritis, positive rates of RF, ACPA, anti RNP Ab in patients with arthritis were significantly higher (76.9% vs 25.6%, 53.9% vs 2.6%, 30.8% vs 5.1%). IP was seen in all patients with arthritis and in 74.4% without arthritis. 9 patients had not been treated by GC or immunosuppressant (IS) before the arthritis onset. In arthritis, 5 patients were treated by GC alone, 2 by a combination of MTX and anti-TNF, 3 by a combination of other ISs. Skin scores were improved in 2 patients treated with anti-TNF. [Conclusions] SSc patients with both IP and positive RF/ACPA/ anti-RNP in serum tend to have arthritis. Anti-TNF is a medication for arthritis and sclerodermatitis.

P2-181

The study of Alkaline phosphatase isozyme (ALPISO) in the patients with systemic sclerosis (SSC)

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Conflict of interest: None

(Object) Generally, alkaline phosphatase isozyme (ALPISO) is used to examine the abnormality of liver function especially induced by obstructive mechanism. By chance, I found the elevation of ALPISO1 in almost half of examined patients with SSC whose liver functions were normal. In this study, I investigated the reason why ALPISO1 was elevated in the patients with SSC. (Methods) Thirty SSC patients whose average age was 65 years old, average duration was 14 years and 28 females were enrolled in this study and examined the ALPISO at the same time other blood clinical index. (Results) ALPISO1 was positive in sixteen patients (53%) and in which patients rheumatoid factor, erythrocyte sedimentation rate, BNP, KL6 were slightly higher than ALPISO1 negative patients (14 cases) although no significant deference was found. In ALPISO1 positive patients, 2 patients were complicated with MCTD. In negative group, 4 patients complicated another collagen diseases two were rheumatoid arthritis and two were Sjogren syndrome. (Conclusions) In almost half of SSC patients, ALPISO1 was positive. Although the reason why ALPISO1 is elevated in SSC is unclear, it is meaningful to investigate the mechanism.

P2-182

Clinical significance of anti-RNA polymerase III antibodies in our hospital patients with systemic sclerosis

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Conflict of interest: None

[Object] Anti-RNA polymerase III (RNAPIII) antibodies are specifically detected in sera from patients with systemic sclerosis (SSc). It is known that these antibodies are associated with diffuse cutaneous SSc (dcSSc) and renal crisis. Recently, these antibodies are also related with cancer. In this study, we investigated clinical significance of anti-RNAPIII antibodies in patients with SSc. [Methods] The study comprised 26 SSc patients who had anti-RNAPIII antibodies and clinical manifestations were investigated. Anti-RNAPIII antibodies were measured by enzyme-linked immunosorbent assay and anti-nuclear antibodies (ANA) were screened by indirect immunofluorescent. [Results] In these 26 patients,15 were dcSSc and 11 were limited cutaneous SSc. The average age was 65.5 years and 18 were female. All patients were positive for ANA and nucleolar pattern were shown in 4 patients. In anti-RNAPIII antibodies positive patients, 2 had anti-centromere antibodies, but no patient were positive for anti-topoI. Twenty three of all patients showed Raynaud's phenomenon, 21 were complicated with Interstitial pneumonia and 3 were diagnosed with renal crisis and cancer. [Conclusions] Anti-RNAPIII antibodies were associated with dcSSc and renal crisis, and frequently found in SSc patients who had a cancer.

P2-183

Clinical features of anti-centromere antibody positive limited cutaneous systemic scleroderma

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Conflict of interest: None

[Object] Anti-centromere antibody positive limited cutaneous systemic scleroderma (lcSSc) progresses chronically and complicates severe organ dysfunction and merges many other autoimmune diseases. Clinical features of centromere antibody positive lcSSc are examined. [Methods] 75 patients who had hospitalized in our outpatient clinic from 2012 to 2017 were enrolled. We assess their clinical characteristics and data. [Results] Female were 69 (92%). Mean age was 68 years old. The duration between onset of Raynaud phenomenon and first visit was 10.5 year. Clinical characteristics; Incidence of Raynaud phenomenon and sclero-

dactylia were 76 and 89.3%. Organ damages; interstitial pneumonia, pulmonary hypertension, PBC, Sjogren syndrome, Hashimoto's disease, SLE were 30.6%, 32%, 46.7%, 57.3%, 30.6% and 8%%, respectively. Incidence of antibodies; anti-SS-A Ab was 46.7%, anti-TPOAb/anti-TG Ab was 25.3%, M2 Ab was 32%, anti-dsDNA Ab was 8%, and anti-RNPAb was 8%. [Conclusions] Anti-centromere antibody positive lcSSc is a disease which predominantly occurs in females, and complicates interstitial pneumonia, pulmonary hypertension, primary biliary cirrhosis, Sjogren's syndrome, Hashimoto's disease at extremely high rates. SLE was thought to merge at a relatively high rate.

P2-184

Investigation of clinical practice of scleroderma in our hospital

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Conflict of interest: None

[Object] We examined the scleroderma practice situation to determine patients background, complications, a treatment regimen, an outcome of scleroderma in our hospital. [Methods] We investigated complications of scleroderma and an outcome in scleroderma and the patients with the name of disease in an electronic chart in retrospective by March, 2017 from April, 2012. [Results] We intended for 81 scleroderma (male 16 female 65 average age 56.2±14.7 years old). It was eight morphoea, systemic type scleroderma 73, scleroderma kidney five, intractable cutaneous ulcer ten, 18 interstitial pneumonia home oxygen therapy induction case one of those, pulmonary hypertension five. Fatal case one case with the interstitial pneumonia, a fatal case with the malabsorption syndrome with intestinal fibrosis were one patient. Without organ complications, the thing which became the annual periodical follow from half a year was 53 cases. The symptomatic treatment for organ complications was provided about the treatment primarily, and use of steroid case 12 cases, the IVCY enforcement case were only one patients. [Conclusions] About the scleroderma case in our hospital, disease background, complications varied every case, but higher than half were mild cases and were only follow for a fixed period.

P2-185

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 classification criteria for systemic autoimmune rheumatic diseases and their overlap syndrome. [Methods] A total of 952 patients with systemic autoimmune rheumatic diseases are included in this study. The following criteria were used: 1997 revised ACR criteria and 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, the criteria by Bohan and Peter (definite or probable) and 2017 EULAR/ACR criteria for PM/DM. [Results] A total of 103 and 118 patients fulfilled old and new SLE criteria, respectively. Similarly, 35 (old) and 47 (new) patients met SSc criteria, 297 (old) and 389 (new) patients met RA criteria, and 12 (PM) /7 (DM) and 11 (PM)/12 (DM) patients met old and new criteria. Twenty-three and 37 patients were identified as overlap syndrome by the old and the new criteria sets, and the number reduced to 7 (old; 4 SLE-SSc and 3 SLE-PM) and 10 (new; 7 SLE-SSc and 3 SLE-PM) when patients with RA-overlap were excluded. [Conclusion] Although the revised classification criteria showed an improved sensitivity, the handling of RA-overlap syndrome was a critical challenge. In addition, SLE-SSc overlap syndrome has been still predominant except for RA-overlap.

P2-186

Two Cases of Anti-Topoisomerase I-Positive Systemic Sclerosis Where Rheumatoid Arthritis Appeared First

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Conflict of interest: None

[Case 1] A 66-year-old woman was developed rheumatoid arthritis (RA) in 200X-15. The patient achieved remission with methotrexate (MTX) and etanercept (ETN). In June 200X, arthritis was exacerbated and interstitial pneumonia (IP) was appeared, and the drug was switched from MTX to tacrolimus. In August 200X, acrosclerosis was appeared and the presence of anti-topoisomerase I (topoI) antibody was observed, and the patient was diagnosed as having systemic sclerosis (SSc). The patient received intermittent high-dose intravenous cyclophosphamide (IVCY) and switched to tocilizumab from ETN. [Case 2] A 68-year-old woman was developed RA in 201Y-8. Remission was achieved with bucillamine. In 201Y-2, Raynaud's phenomenon, and acrosclerosis were appeared and the presence of anti-topoI antibody was detected, and the patient was diagnosed as having SSc. In 201Y, IP was appeared, and the patient received moderate doses of prednisolone and IVCY. [Discussion and Conclusion] Most reports concerning the combination of RA and SSc describe the arthritis-like symptoms in SSc as "arthritis of SSc" or "concomitant onset of RA." In the present two cases, a typical feature of RA was developed before anti-topoI antibody-positive SSc. Here, we report our findings as we think these cases to be valuable.

P2-187

Immune mediated necrotizing myopathy associated with antimitochondrial antibody-positive primary biliary cholangitis and systemic sclerosis

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Conflict of interest: None

[Case] 69-year-old man was diagnosed with primary biliary cholangitis (PBC) by increased hepatobiliary enzymes and antimitochondrial antibody (AMA). He also developed sclerema from fingers to forearm, and diagnosed with systemic sclerosis (SSc). Creatinine kinase (CK) was increased to 2800 IU/L, although there were no muscle weakness, muscle grasping pain, or myositis-specific autoantibody. T2 weighted image of MRI showed high intensity in the right serratus anterior muscle. Biopsy of the serratus anterior muscle showed numerous muscle necrosis fibers and regenerating fibers without infiltration of inflammatory cells. Anti-HMGCR antibody and anti-SRP antibody were negative. He was also diagnosed with immune-mediated necrotizing myopathy (IMNM) associated with AMA. Corticosteroid, tacrolimus and intravenous immunoglobulin were administered, and CK level was decreased. [Clinical Significance] In addition to anti-HMGCR antibody and anti-SRP antibody, AMA was detected in 10% of IMNM patients. We report a rare case of IMNM associated with AMA-positive PBC and SSc. We should take care of IMNM in AMA-positive patients.

P2-188

Diffuse alveolar hemorrhage with thrombotic microangiopathy in a systemic sclerosis patient with high titer positive anti-RNA-Polymerase III Antibody

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Conflict of interest: None

A 63-year-old woman was admitted due to hemoptysis and diagnosed with diffuse alveolar hemorrhage (DAH) by chest CT and BALF. Her Chest CT findings was shown diffuse grand grass appearance without chronic interstitial lung disease (ILD). Systemic sclerosis (SSc) as an underling disorder was recognized with high titer of anti-RNA polymerase III antibody (RNAPIII) 1340 (Index). M-PSL pulse was administered for DAH, but after day 3 admission, she developed TMA with decreased platelet count and haptoglobin (< 10 mg/dl) without renal dysfunction and hypertension. Because of progressive respiratory failure by DAH, plasma exchange (PE) by FFP was started, and she was managed under mechanical ventilation with respiratory care. PE was continued at day4, 5, 7 and respiratory failure was improved and she could withdrawal oxygen therapy. ADAMTS-13 activity was decreased of 18.5 % and inhibitor was negative at admission. TMA state was improved with increased platelet and ADAMTS-13 activity at day 50. Chest CT findings has been also revealed disappearance of DAH without suggestive chronic ILD related with SSc. Although the pathogenesis of anti-RNAPIII antibody is unclear, there is a possibility that PE and PSL were effective for TMA and DAH by decreased level of anti-RNAPIII antibody.

P2-189

Digital gangrene after a transradial cardiac catheterization in a patient with limited cutaneous systemic sclerosis

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Conflict of interest: None

[Introduction] It is uncertain whether transradial catheterization (TRC) is suitable for patients with Raynaud's phenomenon (RP). [Case] A 62-year-old female patient with about 40 years history of RP presented to us with digital gangrene. Her systemic sclerosis (SSc) related antibodies were negative. Skin thickening of the fingers are distal to MCP joint. The 2013 classification criteria for SSc by ACR/EULAR confirmed the diagnosis of limited cutaneous SSc. Administering beraprost hadn't controlled recurrent skin ulcer. After she took a TRC for the evaluation of her aortic valve stenosis, her finger's color was gradually worse. After 2 weeks, her right 2nd finger was necrosis. After 6 months, an abscess adjacent to this appeared. MRI suggested osteomyelitis in the finger. CTA revealed the occlusion of the radial artery (RA) and her finger's ischemia. Administering tadalafil improved the blood supply to fingers. The amputation of the finger was performed, because leaving it unoperated is high risk for the infection. The postoperative course is uneventful. RP has disappeared. [Discussion] Some articles reported fingers of patients with RP were ischemic after some kinds of examinations via RA. [Conclusion] We don't recommend any examinations via RA including TRC to patients with RP.

P2-190

Efficacy of tocilizumab (TCZ) in systemic sclerosis with rapidly progressing of skin sclerosis: A case report

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Conflict of interest: None

A 52-year-old male noticed redness and swelling in his both fingers since X-1 in December. Later, he witnessed tension on the abdomen skin, and the pigmentation on his forearms. Since no abnormal findings were reported in his blood test, it was followed up with symptomatic treatment. Since X in July, he presented tension on the skin of the right forearm, both thighs front, chest, feet soles, and cheeks, and complained of anterior chest pain. Hence, he was admitted to our hospital where we diagnosed him with skin sclerosis. The skin biopsy revealed hyperkeratosis on the epidermal basal side, and we observed increased thickening of the dermis. Accordingly, the patient was diagnosed with scleroderma. His skin sclerosis was recognized in the right forearm, front of thighs, chest wall, abdomen, and both cheeks. In addition, the skin hardening progressed rapidly. Thus, we administered TCZ at 162 mg every 2 weeks, under the combination of steroid therapy. These therapies stopped the progression of skin sclerosis, and his skin exhibited gradual softening. After 13 months of TCZ therapy, mRTSS decreased from 19 to 11, and the total z-score of Vesmeter hardness was decreased from 159 to 33. We considered that this case highlights the efficacy of TCZ treatment in skin sclerosis.

P2-191

Coexistence of anti-Scl-70 antibody and anticentromere antibody (ACA) in systemic scleroderma: Case series and review of the literature

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Conflict of interest: None

The occurrence of anti-Scl-70 antibody and ACA is considered to be mutually exclusive. We report two rare cases of systemic scleroderma (SSc) of the coincidence of these two antibodies. <Case 1> 62 year old Japanese woman who suffered Raynaud phenomenon was diagnosed as SSc at an office 10 years ago. She presented to our hospital with fingertip ulcer and arthralgia. She had infected fingertip ulcer and skin involvement on forearms. Anti-Scl-70 antibody and ACA were positive. We treated her with bosentan and Beraprost Sodium (PBS), and her clinical symptoms became stable. <Case 2> 66 year old Japanese woman developed Raynaud phenomenon 4 years ago. She visited a clinic with fingertip ulcer and was diagnosed as SSc by coexistence of anti-Scl-70 antibody and ACA in January last year. Her fingertip ulcer was cured with bosentan and PBS. She developed bronchial pneumonia and dosed antibiotic therapy in January, but her symptoms didn't recover. Then, she referred to our hospital in February. She got a follow-up examination for her good general conditions and cured spontaneously. At first visit her mRSS was 10, later mRSS increased 18 and interstitial pneumonia was developed in September next year. We administered steroid and intravenous pulse cyclophosphamide, and her symptoms improved.

P2-192

A case of scleroderma renal crisis with intimal thickening and necrotic arteritis in the renal interlobular artery

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Conflict of interest: None

[Case] A woman in her 70s, who had 9-year history of systemic sclerosis (anti-RNA polymerase III antibody), was previously treated with methylprednisolone (mPSL) and intravenous cyclophosphamide (IVCY) for her skin involvement. Her dosage of mPSL had been reduced to 8 mg/day. On admission, she had been febrile for 4 months, and her CRP levels increased to 9.40 mg/dl, and her eGFR decreased to 21.7 mL/min/1.73 m^2. Her urine protein was 1+, and her urine sediment was normal. Although plasma renin activity was higher than normal, her blood pressure remained normal. Her renal biopsy revealed fibrinoid necrosis and inflammatory cell infiltrations in the interlobular artery walls, which suggested necrotizing arteritis. However, intimal thickening of the interlobular artery was the most prominent finding, and ultimately all these findings were considered as the features of scleroderma renal crisis (SRC). There were no other features of systemic vasculitis, and her ANCA was negative. Infection was unlikely. Her dosage of mPSL was increased to 16 mg/day, and 3 courses of IVCY were administered. She became afebrile, her CRP levels decreased to normal range, and her eGFR increased to 31.2. **[Clinical significance]** This case would contrib-

ute to the elucidation of the pathomechanisms of SRC.

P2-193

Improvement of NVC findings in a patient complicated with microscopic polyangitis in scleroderma

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Conflict of interest: None

[Object] Capillary microscope (NVC) is to observe the capillary of the nail and is the tool which diagnoses systemic scleroderma (SSc). Because we compare the NVC views in before and after treatment and evaluated an effect of the treatment, we report it to a case of SSc complicated with microscopic polyangitis (MPA). [Case] An 82-year-old woman. She contracted a disease in SSc and interstitial pneumonia (IP). She was hard to breathe and hemoptysis. We recognized a new frosted glass using CT. MPO-ANCA rose with> 500 U/ml significantly before. We recognized an intratracheal hemoid secretion with a bronchoscope. We had a diagnosis of the alveolus bleeding that merged MPA in SSc. We gave steroid pulse therapy, cyclophosphamide therapy and accepted improvement of the chest shadow in the CT. It was the capillary expansion and the meandering before the treatment. However, after the treatment, the capillary expansion and the meandering decreased with the improvement of the symptom. [Conclusions] We can evaluate the microcirculation of the whole body by evaluating the capillary image of the nail wall using NVC. NVC is used at the time of diagnoses such as SSc mainly at present. However, it is expected in future that NVC becomes useful for the treatment evaluation of various lesions.

P2-194

Successful treatment of membranous nephropathy in a patient with mixed connective tissue disease by combination therapy with tacrolimus and intravenous cyclophosphamide

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Conflict of interest: None

A 61-year-old woman was admitted to our hospital complaining of lower extremities edema. She was diagnosed with mixed connective tissue disease (MCTD) at the age of 39 years old. She developed nephrotic syndrome at the age of 60, and renal biopsy revealed the association of membranous nephropathy (MN). Oral prednisolone (PSL) 30mg and mizoribine (MZB) 100mg daily were initiated, but failed to achieve remission. Switching MZB to tacrolimus (TAC) 3mg daily decreased urine protein/creatinine ratio (UPCR) to 2.0-4.0 g/gCr, but persistent proteinuria remained. Because she developed severe edema of her lower extremities and became unable to walk, intravenous cyclophosphamide (IVCY) was added expecting immediate improvement. UPCR was reduced to 0.5-2.0 g/gCr and walking difficulty was significantly ameliorated following IVCY. TAC + IVCY combination therapy was continued and PSL was tapered. Efficacy of TAC + mycophenolate mofetil combination therapy for lupus nephritis (LN) has been well documented. Since Asian LN patients have much higher response rate to CY than black or white patients, IVCY could be a beneficial treatment for the LN. Although no standard therapy has been established at this point, TAC + IVCY could be a beneficial therapeutic option for MN associated with MCTD.

P2-195

Early intervention of corticosteroid improved a patient with connective tissue disease-associated pulmonary arterial hypertension (CTD-PAH) without therapeutic drug for PAH

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Conflict of interest: None

[Abstract] A 24-year-old woman was referred from nearby doctor for management of suspected connective tissue disease-associated pulmonary arterial hypertension (CTD-PAH). Because of high fever and severe malaise, she admitted nearby doctor. Her TRPG was 64.3mmHg and respiratory blood pressure fluctuations of inferior vena cava were not observed. Antibiotics and hydrocortisone improved her fever and malaise. She had autoantibodies. Subsequently she transferred to our hospital. Her TRPG decreased to 34mmHg by hydrocortisone, but still respiratory blood pressure fluctuations of was not observed. Because of PAH, Raynaud phenomenon, U1-RNP antibody, interstitial pneumonia, pleurisy, she had a diagnosis of Mixed Connective Tissue Disease and she was given 25mg of prednisolone (PRD). Mean pulmonary artery pressure was 21mmHg by right heart catheter. After 11 day after hospitalization, her TRPG decreased to 29mmHg. Her PAH was improved without using drug for PAH. After 21 day after hospitalization, she left the hospital with azathioprine and PRD was reduced. Subsequently TRPG decreased 25mmHg at 42 day, 19mmHg at 134 day. Our case demonstrated that early innervation of PRD improved CTD-PAH without therapeutic drug for PAH.

P2-196

A case of mixed connective tissue disease successfully treated for hemophagocytic syndrome with HLH-2004 chemo-immunotherapy including etoposide, dexamethasone and cyclosporine A

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Conflict of interest: None

[Case] A 49 year-old woman. 9 years ago, she was diagnosed as MCTD and received therapy with steroid and azathioprine. Due to fever and thrombocytopenia, she was hospitalized. She received increased steroid therapy, and she left the hospital with 35mg of prednisolone (PSL). After PSL was tapered to 12.5mg, she felt a loss of appetite, headache and dysphagia. Then, her fever and nausea occurred, and she was hospitalized again. She was diagnosed as disseminated intravascular coagulation (DIC) and received steroid pulse therapy and transfusion therapy, but the disease was not improved. Infections including viruses were negative. Phagocytosis were recognized in the bone marrow and she was diagnosed as HPS. In accordance with HLH 2004, she received chemo-immunotherapy with etoposide, dexamethasone, cyclosporine A and her disease got well controlled. [Clinical significance] I experienced a case of HPS during the course of MCTD. Although steroid pulse therapy didn't respond, the disease control was obtained by chemo-immunotherapy according to HLH 2004. It is thought that the same protocol is effective in the case that improvement cannot be obtained only by PSL treatment. So, we report details of this case with some literature review.

P2-197

A Case of Anti-RNP Antibody-positive Aseptic Meningitis with Few Findings Suggesting MCTD and SLE

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Conflict of interest: None

A 16-year-old female. Three months prior to visiting the hospital the patient experienced a fever of 39°C and above for a period of one week. On the second day of hospitalization, her consciousness level (CL) decreased and as a result, she underwent a cerebrospinal fluid (CSF) examination which showed increased cell count. She subsequently underwent testing for anti-RNP antibody in serum and CSF. The results indicated IL-

6: 2680 pg/mg in CSF. She was screened for primary diseases with the possibility of meningitis with MCTD and SLE. Although she met the diagnostic criteria for SLE, she was negative for anti-DNA antibody and no findings characteristic of MCTD or SLE. Steroid semi-pulse therapy of mPSL 500 mg/day was started on the fourth day. Although, her CL improved, since diplopia due to sixth nerve palsy remained, Second course of steroid semi-pulse therapy was begun on the 18th day. This was a case of aseptic meningitis onset that was positive for anti-RNP antibody in both serum and CSF, but that had few findings suggested MCTD or SLE. Although the symptoms presented by the case may have been prodromal symptoms of MCTD and SLE, the pathophysiology was also suggestive of autoimmune-mediated encephalopathy, which has become focused on, in recent years, in the field of neurology.

P2-198

Case reports of scleroderma and MCTD combined to dyspnea by examination and lifting of BNP

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Conflict of interest: None

[Case one] Seventy nine years old male [Present illness] The patient existed diffuse scleroderma in X-six. He was conveyed to ER by dyspnea. On chest CT, increase of left pleural effusion and shadow of upper lung presented compared to the last time. [Progression] We concluded he was combined cardiac failure to diffuse scleroderma. On guideline ETS/ERS twenty fifteen, possibility of pulmonary hypertension was intermediate. In the case, the possibility that pulmonary hypertension combined to diffuse scleroderma was high. [Case two] Seventy six years old female [Present illness] The patient existed fever, malaise, asitia in X-eight. She was suspected polymyositis. We started twenty-mg of PSL. In X-three, she grew sclerosis of finger, ulser of the end of finger. So we suspected scleroderma and added CyA. At the last time, we diagnosed MCTD and started MTX. In X, she grew shortness of breath by the exercise. [Progression] On guideline ETS/ERS twenty fifteen, the possibility of pulmonary hypertension was high. In the case, the possibility that pulmonary hypertension combined to MCTD was high. [Clinical significance] We report the data of patient who goes to our hospital, together with the above two case. We consider the case that combined pulmonary hypertension to scleroderma and MCTD.

P2-199

A case of MCTD with RA and Graves' Disease, complicated with severe adverse effects to pleural drugs

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Conflict of interest: None

Case: A female patient in her fifties, came to our hospital because of history of hematemesis due to a rupture of esophageal varices. Ultrasonic examination in previous hospital showed hepatic cirrhosis and ascites. The etiology of haptic cirrhosis was thought to be drug-induced. The culprit drug was MTX. She had long history of MCTD from 1992. Active CCP/RF positive polyarthritis and hyperthyroidism both newly developed at the year of 2009. SASP and MMI were prescribed to both two autoimmune diseases, but neutropenia with high grade fever appeared. SASP and MMI were discontinued, and altered to MTX. And longstanding use of MTX was supposed to cause severe hepatic damage to this patient. Conclusion: This case showed that there were individuals who react to some specific drugs too much. We should pay much attention to interaction between drugs and patients on thinking about pathogenesis of diseases.

P2-200

A case of MCTD pulmonary arterial hypertension successfully treated with steroid pulse, cyclophosphamide and riociguat

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Conflict of interest: None

The patient was forty years old woman. Two year before the admission, she visited our hospital with the chief complaint of puffy fingers and arthralgia. Anti-RNP antibody was high and she was diagnosed with MCTD. She had no signs of pulmonary hypertension with cardiac ultrasonography. One year before the admission, she was pregnant and felt skin sclerosis. She also felt dyspnea. At the year of admission, she delivered the child in January. After then, the dyspnea was getting worse. Skin sclerosis was extended to the both forearms, face and body when she visited our hospital in April. TRPG was 64 mmHg with no left ventricular failure in May. No ILD or CTEPH was detected with chest CT. Right heart catheterization underwent on June and mPAP was 43 mmHg. PCWP was 15 mmHg. So she was diagnosed with CTD-PAH (WHO class II) and admitted to our hospital on June. Steroid pulse and intravenous cyclophosphamide was admitted. Also, treatment with beraprost and riociguat was admitted and TRPG decreased to 33 mmHg before the discharge. Here we report the rare case of MCTD successfully treated with steroid pulse, cyclophosphamide and riociguat.

P2-201

A Case of Juvenile Dermatomyositis of Anti-MDA-5 Antibody-Positive without Complications by Interstitial Pneumonia to Date

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Conflict of interest: None

(Case) A six years old boy has displayed symptoms such as malaise, swelling of fingers, and low were observed on dorsal digital. The blood test revealed elevated aldolase levels and anti-MDA-5 antibody-positive result. The value of creatinine kinase was normal. Hyperkeratosis was observed in the dermatopathology tissue, liquefaction degeneration was observed in dermoepidermal junction, and lymphocytic infiltrate and mucin deposition were observed in the upper dermis. A finding in concord with piriformis myositis was visible on MRI. In these results, he was diagnosed with dermatomyositis. After two courses of steroid pulse therapy, the symptom has been relieved. Pneumonia has not been shown during eighteen months from the onset to the present. (Discussion) There are less cases in pediatrics and no conclusion has been made about the relationship between anti-MDA-5 antibody and ILD even though it was reported that anti-MDA-5 antibody was correlated with interstitial lung disease (ILD) in pediatrics. In my case, I consider that it would be necessary to carefully observe the course about ILD.

P2-202

The Two Cases with the Skin Findings Which was Critical for Estimating the Positive Anti-MDA-5 Antibody Value

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Conflict of interest: None

[Objectives] We report the two cases with the skin findings which was critical for estimating the positive anti-MDA-5 antibody. [Case1] A 62-year-old woman with a exertional dyspnea. Anti-ARS antibody was positive, and we had treated her for interstitial lung disease (ILD) associated with anti synthetase syndrome with prednisolone (PSL), tacrolimus, and azathioprine. After 24 months, mechanic's hands and an ulcerative rash were appeared in the palmar side of her fingers. Anti-MDA-5 anti-

body, highly suspected this syndrome, was proved to be positive. [Case2] A 41-year-old man with a fever and a red rash. Anti-MDA-5 antibody was positive, and we had treated him for dermatomyositis (DM) and ILD with PSL and cyclosporine. PSL had been tapered, and discontinued after 6 years. Anti-MDA-5 antibody was proved to be negative after 8 years. When he had been treated with tacrolimus 0.5mg only, mechanic's hands and a rash in the palm and the flexor of the elbow were appeared. He didn't have other symptoms of DM and ILD, but anti-MDA-5 antibody was proved to be positive. [Conclusions] The relation between anti-MDA-5 antibody and long-term outcome of DM is unclear. This antibody should be measured when patients have characteristic skin lesions, even without rapidly progressive ILD.

P2-203

Successful treatment using rituximab in a patient with refractory polymyositis complicated by scleroderma renal crisis

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Conflict of interest: Yes

Corticosteroids are the first-line treatment for patients with inflammatory myopathies. Myositis can be a clinical feature of scleroderma (polymyositis-scleroderma overlap syndrome), and treatment of this syndrome is a challenge for clinicians because moderate to high doses of corticosteroids are considered a risk factor for development of acute kidney injury in affected patients. We report here the case of a 56-year-old woman with scleroderma who developed polymyositis and was successfully treated with rituximab. Initial treatment of the polymyositis with prednisolone 40 mg/day was rapidly tapered to 2.5 mg/day due to development of scleroderma renal crisis, for which 4 weekly infusions of rituximab (500 mg; off-label) were given. She responded well to rituximab in addition to prednisolone 2.5 mg/day. Clinical significance: Rituximab may improve inflammatory myopathies, even in cases where high-dose corticosteroids should be avoided due to complications. Rituximab should be considered as a treatment option in cases of refractory polymyositis.

P2-204

A case of anti-ARS antibody-positive polymyositis associated with anti-TNF therapy for rheumatoid arthritis

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Conflict of interest: None

[Case] A 76-year-old woman, who had rheumatoid arthritis (RA) with interstitial pneumonia (IP), was maintained remission by tacrolimus combined with etanercept (ETN) therapy since 2008. Her CPK level initially increased on January 2017. Then, her IP on chest CT exacerbated with increased serum KL-6 level. Positive level of anti-ARS antibody was revealed, and she was admitted to our hospital. The electromyogram from her extremities showed myogenic pattern and muscular MRI demonstrated edematous chages indicating inflammatory myopathy. Therefore, we diagnosed with polymyositis (PM). Discontinuation of ETN led to slight improvement of CPK level, however, oral prednisolone (PSL) 30mg daily was initiated because of exacerbated IP. PSL therapy and discontinuation of ETN normalized CPK level and improved PM findings on MRI. Furthermore, IP on chest CT was also improved. [Conclusion] The present case suggests the possibility of anti-TNF agent-induced PM because the patient developed PM during ETN therapy and discontinuation of ETN led to slight improvement of CPK level. Several cases of new onset and exacerbation of PM during anti-TNF therapies are rarely reported, and we should remind to consider new onset of polymyositis associated with anti-TNF therapy for rheumatic diseases.

P2-205

A case of anti-HMGCR antibody-associated myopathy without history of taking statins

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Conflict of interest: None

A 58-year old woman admitted to our department because of general fatigue, inferior limb pain, and elevated serum CPK. Two month before administration, she visited her family doctor due to the same compliant, and the elevation of serum CPK (approximately 1500 U/L) was pointed out. On admission, physical examination revealed mild weakness of the neck flexor, wrist flexor and extensor. She had no skin rash and anti-ARS antibody was negative. EMG and muscle contrast MR images indicated no noteworthy findings. Pathological analysis of the left biceps muscle revealed fiber size variation, necrotic and regenerated fibers with minimal lymphocytic infiltration into the muscle fibers. Although serum anti-SSA antibodies were positive, she had no sicca and pathological findings of the lip didn't fulfill the classification criteria of Sjögren syndrome. Serum anti-HMGCR antibodies were detected in her serum, and she was diagnosed as anti-HMGCR antibody-associated myopathy. After 50mg/day of prednisolone, in combination with tacrolimus, were started, her serum CPK was decreased and significant improvement of muscle weakness was observed. We report this case with a literature review.

P2-206

A case of anti-ARS antibody positive dermatomyositis complicated with pericardial effusion

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Conflict of interest: None

Case: We report the case of a 76-year-old woman diagnosed as dermatomyositis (DM) with positive for anti-ARS antibody and complication of pericardial effusion. She was aware of dyspnea on exertion 5 years before, and suffered from skin roughness from July X. In May X, chest X-ray revealed abnormal lung shadow with cardiac dilatation. Gottron's sign, Gottron papules, proximal muscle weakness and grasping pain of muscles were observed. CK 416 IU/L, aldolase 15.4 U/L, CRP 0.83 mg/dl, positive for anti-ARS and anti-SS-A antibodies were reveled. The CT scan showed interstitial pneumonia and massive pericardial effusion. Though heart wall motion was normal, pulmonary hypertension (TR PG 48 mmHg) was suggested by cardiac echo. She was diagnosed as DM and treated with PSL 50 mg/kg (1 mg/kg/day), and her cutaneous lesions were improved with normalized laboratory data and pericardial effusions were decreased with improvement of pulmonary hypertension. **Clinical significance:** Symptomatic myocardial complications with DM was reported as 10-30%, including heart failure, arrhythmia, myocarditis and coronary artery disease. pleural effusion and pericardial effusion have also been reported. Thus, we want to highlight the need for consideration of DM as one of the important differential diagnoses.

P2-207

The differences of anti-Jo-1 antibody positive or negative in anti-ARS antibody syndrome

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Conflict of interest: None

[Object] We compared the patients who has anti-Jo-1 antibody to who has not (Jo-1 (+) / Jo-1 (-)), in the anti-ARS antibody syndrome (ASS). [Methods] 7 patients visited our hospital from Apr. 2016 to Nov. 2017 with ASS. Respiratory function test (RFT), Chest X-ray, CT were performed, and LDH and KL-6 were measured. The chest CT images were classified on ATS/ERS 2013 IIPs classification. CY500mg/day was used once a week, PSL was used as post-therapy. [Results] 1 was PM and

6 were DM. All has IP. Jo-1 (+) was 3. 1 in Jo-1 (-) died during this period. RFT results in 6 survivors were improved. But no significant difference was observed between the 2 groups (Jo-1 (+)/Jo-1 (-)). After treatment, serum LDH and KL-6 levels reduced, but no significant difference was observed in 2 groups. At Chest CT images, 3/3 in Jo-1 (+) and 2/4 in Jo-1 (-) have irregular infiltration shadows under the pleura. 1/3 in Jo-1 (+) and 4/4 in Jo-1 (-) has the reticular or line shadow under the pleura. After treatment, the interstitial shadow get better in Jo-1 (+). But, there was no change in Jo-1 (-). [Conclusions] Although ASS complicates IP, there are differences in image, and the Jo-1 (+) group has better therapeutic response on the image. On the other hand, there was no significant difference in RFT or serologic result.

P2-208

A case of overlapping anti-PL7 antibody-positive polymyositis and scleroderma

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Conflict of interest: None

[Case] A 72-year-old man was diagnosed with organized pneumonia 7 years prior, and was treated with prednisolone (PSL). One year prior to the current presentation, he was found to be positive for anti-aminoacyl tRNA antibody and tacrolimus (TAC) was added to PSL. However, in the 6 months prior to the current admission, he developed decreased appetite, weight loss, fever, shoulder and upper arm myalgias, elevation of creatine phosphokinase (CPK), lower leg dermal sclerosis, and a new pleuropericardial effusion. His symptoms worsened, and he was referred to our hospital. On examination, anti-PL7 antibody testing was positive and skin biopsy revealed thickening of the dermis with accumulation of collagen fibers. We diagnosed anti-PL7 antibody-positive polymyositis (PM) with overlapping scleroderma (Scl). We started intravenous immunoglobulin (IVIG), followed by high-dose intravenous cyclophosphamide (IVCY), and methylprednisolone (mPSL) 60 mg/day, with subsequent improvement in his symptoms. [Clinical significance] Cases of anti-PL7 antibody-positive PM overlapping with Scl have been reported in Japan. The present case was significant for the clinical course in which PM and Scl worsened during therapy with PSL and TAC, while multidrug therapy with IVIG, IVCY, and mPSL was effective.

P2-209

A case of anti-3-hydroxy-3-methylglutaryl-coenzyme A reductase antibody-positive necrotizing myopathy to be distinguished from dermatomyositis diagnosed after the appearance of erythema and elevated levels of serum CK

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Conflict of interest: None

[Background] Recent studies have shown anti-3-hydroxy-3-methylglutaryl coenzyme A reductase (anti-HMGCR) antibody is a useful marker to diagnose necrotizing immune-mediated myopathy. [Case report] A 46-year-old man underwent resection of gastric cancer and chemotherapy, and had an elevated serum CK level. Although it reached 4000 IU/L and high levels of serum hepatic enzymes were detected, he had no symptoms or medical treatment. The level of serum CK decreased after the chemotherapy was finished, but erythema emerged in his back which the skin biopsy suggested dermatomyositis. Although laboratory test did not detect anti-ARS antibody and none of typical skin objects such as Gottron's sign or heliotrope rash was detected, he suffered slight femoral muscle weakness. The MRI study showed contrast effect in the right biceps femoris muscle and following pathological studies suggested necrotizing myopathy, which led us to detect serum anti-HMGCR antibody. As an initial therapy, oral PSL 60mg/day was administered and both the level of serum CK and muscle fatigue ameliorated. [Conclusion] We should screen for anti-HMGCR antibody when we treat patients with necrotizing myopathy detected by skin biopsy or who suffered malignant tumor with atypical symptoms of dermatomyositis.

P2-210

Inflammatory myopathy associated with anti-mitochondrial antibody presenting with eosinophilia and acute onset dropped head

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Conflict of interest: None

A 60-year-old man undergoing hemodialysis was referred to our hospital because of a 2-week-history of eosinophilia and elevation of serum creatine kinase (CK). His muscle strength was preserved and there was no evidence of cardiac involvement. His eosinophilia was thought to be idiopathic. Then, posterior cervical pain and dropped head emerged. Magnetic resonance imaging and positron-emission tomography-computed tomography showed the abnormality in posterior cervical muscles. The muscle biopsy was performed and revealed immune-mediated necrotizing myopathy. Anti-signal recognition particle antibody and anti-3-hydroxyl-3-methylglutaryl-coenzyme A reductase antibody were negative and anti-mitochondrial antibody (AMA) was positive. He was diagnosed with inflammatory myopathy associated with AMA. He was treated with prednisolone (PSL) 60 mg/day. Tapered PSL, his disease sustains remission. Inflammatory myopathy associated with AMA tends to affect to paraspinal muscles. The reported cases with lordotic posture or dropped head showed chronic course. In inflammatory myopathy with dropped head, we should consider about inflammatory myopathy associated with AMA. In addition, there are few reports that eosinophilia is coincident with inflammatory myopathy associated with AMA.

P2-211

Immune-mediated necrotizing myopathy followed by resectable multiple cancer

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Conflict of interest: None

[Clinical Case] A 65-year-old male. 6 months before admission, abdominal and back muscle pain occurred, and CK elevation persisted after statin discontinuation. He had no muscle weakness or rash. MRI indicated inflammation of erector spinae muscle and triceps, and EMG showed myopathic changes. Anti-ARS antibody, ANA and whole-body CT were negative. Muscle biopsy showed necrosis and regenerating fibers without inflammation, and Necrotizing myopathy was diagnosed. Prednisolone (1mg/kg/day) induced remission, but relapse occurred while tapering. Prostate cancer was found because of elevated PSA and resected, but CK elavation persisted. 2 years after diagnosis, CT showed incidental thymus cancer and was resected. [Discussion] Immune-mediated necrotizing myopathy (iNM) is one of the inflammatory myopathies classified by pathological descriptions. INM has subtypes of anti-SRP antibody+, anti-HMGCR antibody+ and seronegative. A prospective cohort study with 119 iNM has reported that 12-21% cases got single but multiple cancer within three years. INM and Polymyositis are similar in clinical features, but different in the frequency of cancer. It is important to identify pathological features and antibodies for diagnosis. When iNM is refractory or easy to relapse, cancer screening is crucial.

P2-212

A case of refractory polymyositis with anti-SRP and anti-Ku antibodies

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Conflict of interest: None

[Case] A 50 year-old female presented with Raynaud's phenomenon and slight fever for a few years was diagnosed with Sjögren's syndrome and mild interstitial pneumonia one year before hospitalization. Meanwhile, CK was 174 U/L at this time, but it gradually increased, and muscle weakness of limb proximal muscles and swallowing difficulty occurred 2 weeks before hospitalization and rose CK 3551 U/L on hospitalization. A needle EMG and a muscle biopsy revealed the specific findings, so she was diagnosed with polymyositis without scleroderma. Although treatment was started with azathioprine after steroids and tacrolimus, the effect was insufficient, so immunoglobulin intravenous therapy was performed. After that, muscular strength and CK gradually improved. Both anti-SRP antibody and anti-Ku antibody were strongly positive. **[Clinical Significance]** Although anti-SRP antibody is reported that associated with necrotizing myopathy and anti-Ku antibody is reported that associated with systemic sclerosis-myositis overlap syndrome, this case didn't apply to any case. On the other hand, anti-SRP antibody is reported that associated with refractory myopathy. Overlapping of myositis-specific antibodies is rare, but it seems to be meaningful to accumulate and investigate such cases.

P2-213

A case of anti-PL-12 antibody-associated fasciitis in which the initial symptoms were myalgia and a fever

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Conflict of interest: None

(Case) A 33-year-old female developed a fever and myalgia in May 2017. She was admitted to our hospital for a possible diagnosis of autoimmune disease due to positivity of serum anti-nuclear antibody and mild interstitial pneumonia in June 2017. A physical examination revealed a fever and myalgia of the dorsal part of the thigh. Blood tests showed positivity for anti-PL-12 antibody, a normal creatine kinase level, and elevated aldolase and CRP levels. As the myalgia was suspected to be due to inflammatory myopathy, we performed magnetic resonance imaging (MRI) of the thigh, and fascial involvement was observed around the dorsal muscles of the thigh. The histopathological findings on an en bloc biopsy of the biceps femoris showed fasciitis without myositis, so we diagnosed her with anti-PL-12 antibody-associated fasciitis. Prednisolone and tacrolimus improved her fasciitis symptoms. **(Clinical significance)** We recently reported that myalgia in patients with inflammatory myopathy is attributable to fasciitis rather than myositis. In patients with suspected inflammatory myopathy who present with myalgia but no muscle weakness, if fasciitis is histopathologically detected instead of myositis, the fasciitis is likely to contribute to myalgia and should be treated.

P2-214

A case of dermatomyositis complicated with remarkable pleural effusion in her right thoracic cavity

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Conflict of interest: None

<Case> A 67-year-old woman was admitted to our hospital because of recurrence of dermatomyositis and pleural effusion. Four years before, she was diagnosed with dermatomyositis complicated with interstitial pneumonitis. She has shown frequent recurrence despite combined therapy using glucocorticoid (GC), immunosuppressant, and intra-venous immune-globulin administration. One month prior to admission, she showed raising creatine phosphokinase (CK) along with tapering of GC, and followed foot edema, muscle weakness and dyspnea. She showed high concentration of serum CK and remarkable pleural effusion. High dosage of GC was applied her to treat relapsing dermatomyositis and serum CK declined quickly, but the pleural effusion did not improved. The day 78 from admission, lymphangiography was performed to identify the site of effusion leaking, then suggested to be due to efflux from the thoracic duct. After this examination, pleural effusion gradually decreased, and she was discharged on day 112. <Discussion> Pleural effusions are rarely shown in the patients with dermatomyositis. Previous reports suggested the relationship between pleural effusion and dermatomyositis but the mechanism has not been clear. We will discuss the mechanism assumed by the results of our experienced case.

P2-215

Recovery from Acute Respiratory Failure with BIPAP in a Patient with Necrotizing Myopathy

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Conflict of interest: None

59 year-old woman receiving rosuvastatin since 2011, demonstrated abnormally high muscle enzyme (CK) level in August, and CK level still rose after statin discontinuance (2712 IU/L). She realized shoulder heaviness and neck dropping in October, and was administered to our hospital in November, 2016. We diagnosed as Statin-associated necrotizing myopathy (SANM), for anti-HMGCR Ab was positive and muscle biopsy showed muscle-cell necrosis and regeneration lacking lymphocyte infiltration, and induced 1000 mg steroid pulse, 30 mg predonisone (PSL). The CK level once dropped but recurred with hypoxemia and hypercapnia as the PSL dose decrease, indicating acute respiratory failure. We induced non-invasive positive pressure ventilation (NPPV) with steroid pulse, intravenous immunoglobulin (IVIG), 30 mg PSL and 3 mg tacrolimus, and both CK level and her symptoms improved, which enabled ending NPPV on day 28, discharge on day 45, and decreasing PSL dose to 12.5 mg. SANM is a rare autoimmune disease with symmetrical weakness, muscle enzyme elevation caused by statin treatment. The therapeutic strategy is not established yet, and our report provides combination of PSL, immunosuppressants and IVIG with NPPV may provide new insights for remission induction in patients with respiratory failure.

P2-216

Cardiac Involvement in Juvenile-Onset Polymyositis with anti-Ku antibody: A Case Report

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Conflict of interest: None

A 16-year-old woman who developed myalgia and progressive weakness in weeks was admitted to our hospital because of CK elevation. Blood test showed skeletal muscles and myocardial injuries. MRI and EKG results matched inflammatory myopathy. We diagnosed as polymyositis and initiated treatment with 1 mg/kg/day prednisolone after muscle biopsy. The CK level declined to a slight degree but kept at high level. As a failure response to glucocorticoids, methotrexate and intravenous immune globulin were administered, but no improvement. Muscle biopsy showed immune-mediated necrotizing myopathy. By test for specific autoantibodies, polymyositis with anti-Ku antibody was diagnosed. High-level biochemical markers of myocardial injury suggested cardiac involvement, no evidence in echocardiography and MRI, intravenous cyclophosphamide (IVCY) was administered. Both skeletal muscles and myocardial injuries started improved after 3-time IVCY. Clinical and serological improvement was achieved in 6-time IVCY. Statistically, the prevalence of asymptomatic cardiac involvement is rare (3-6%) and polymyositis with anti-Ku antibody show good response to corticosteroid. We report a case of corticosteroid refractory anti-Ku-positive polymyositis with asymptomatic cardiac involvement improved with IVCY.

P2-217

A case of anti-MDA5 antibody-positive dermatomyositis complicated by hemophagocytosis syndrome followed by acute interstitial pneumonia during the treatment

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Conflict of interest: None

A 72-year-old woman with sustained fever, generalized malaise, andskin rash since 2month before visited our hospital. There were heliotrope rash, Gottron's sign, skin ulcers, and eproximally-dominant muscle weakness. Blood test revealed elevated myogenic enzyme, and needle electromyogram showed a myogenic change. Thus, the patient was diagnosed as having dermatomyositis. Because she had thrombocytopenia, bone marrow examination was performed and comlication of hemophagocytic syndrome was diagnosed, and 1mg/kg of prednisolone was begun. Later serum anti-MDA5 antibody was reported to be positive and tacrolimus was added. Her condition improved, and she was discharged without dyspnea. However, 2weeks later, she visited our hospital again because of dyspnea. Serum ferritin levels were elevated to 4952 ng/ml, and chest HRCT revealed invasive shadows around the bronchial vascular bundle and peripheg of both the lungs. So methyl predonisolone pulse therapy was started on the first day of re-hospitalization, but her condition rapidly exacerbated, and she died. This study presents a case with hemophagocytic syndrome that was complicated in whom rapidly progressive interstitial pneumonia developed during the treatment. We present the findings of the autopsy and review of previous reports.

P2-218

Transient dermatomyositis-like condition developed in elderly women with atopic history and statin internal history: a case report

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Conflict of interest: None

A 70-year-old woman. She has had Lipitor's oral history over 10 years ago but had been canceled 2 months ago. An eruption appeared on the front of the neck after the upper respiratory symptoms, but it was thought that the history of atopic dermatitis had deteriorated. Immediately afterwards, muscle weakness dominated by extremity proximal muscles appeared, and myalgia and myogenic enzyme elevation were observed. Because of the enlargement of the skin rash, we performed a biopsy of the right upper arm and did not contradict dermatomyositis. In the needle electromyogram, resting discharge and myogenic change of right biceps brachii muscle and right sternocleidomastoid muscle were observed. In the muscle biopsy tissue of the bipod muscle of the left upper arm, it did not contradict as myositis. All autoantibodies specific to myositis were negative as far as they were examined. Muscle symptoms and rashes improved promptly only with rest. <Discussion> We suspected autoimmune mediated necrotizing myopathy or pharmacologic myopathy due to statin, but the timing of statin therapy and discontinuation did not match. Dermatomyositis was suspected from tissue results, but naturally lightened at an early stage.

P2-219

Successful treatment with tofacitinib for anti-MDA5 antibody-positive dermatomyositis with interstitial pneumonia complicated with rheumatoid arthritis

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Conflict of interest: None

A 40-year-old female presented to our hospital with an initial complaint of fatigue, polyarthritis, rash, and dyspnea. She had heliotrope eyelids, Gottron's papules. Laboratory tests showed elevated muscle enzymes and inflammatory response. Chest CT revealed ground-glass opacity in the all lobes and pericardial effusion. Ultrasonography revealed active synovitis. She was diagnosed with RA and DM-IP. Anti-MDA5 antibody was positive, ferritin level was 433.7 ng/mL, KL-6 level was 1222 U/mL, and AaDO2 was 61.4 torr. Because of rapidly progressive IP, she was treated with predonisolone (PSL), cyclosporine, and intravenous cyclophosphamide. IP improved just after initially treatment, but the efficacy was gradually poor throughout the treatment course. And, she was still suffered from polyarthritis. Informed consent was obtained from patient and family, we additionally administered tofacitinib (TOFA) 10mg/day. After induction of TOFA in approximately one week, both polyarthritis and IP remarkably improved. After the dose of PSL was decreased, the disease activity was completely controlled. It is publicized that TOFA has an excellent effect for RA, TOFA may be effective treatment of anti-MDA5 antibody-positive DM-IP. We report with some literature review.

P2-220

A useful case of FDG-PET for evaluation of pulmonary involvement comorbid with anti-MDA5 antibody positive dermatomyositis

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Conflict of interest: None

Case presentations The patient was 70-year-old woman. She presented with 2-month history of skin eruption, 3-week history of proximal muscle weakness, and the grip tenderness of muscle. In addition, her laboratory data showed elevation of CK, aldolase, and CRP. These features were consistent with a diagnosis of dermatomyositis. Autoantibody testing for myositis-specific antibody revealed that she had anti-MDA5 antibody. Because she had past history of endometrial cancer, FDG-PET was performed. Positive uptake was observed in muscles of the shoulder and the right lower lobe of lung. Since rapidly progressive interstitial lung disease was expected, we initiated aggressive immunosuppressive therapy with corticosteroids, cyclophosphamide, and cyclosporine A. Two months later, she improved skin eruption, muscle symptoms, and malaise so she discharged the hospital. Though, the fibrotic change was progressed in the right lower lobe of lung, where the uptake of FDG was observed. This case indicated that a positive lung uptake on FDG-PET was concerned with pulmonary involvement in anti-MDA5 antibody positive dermatomyositis from early period.

P2-221

A case of eosinophilic granulomatosis with polyangitis (EGPA) presenting severe lower leg pain, successfully treated by early administration of intravenous immune globulin (IVIG)

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Conflict of interest: None

[Case] A 60-year-old lady with bronchial asthma was referred to our hospital. 7 weeks before, she began having subfever. 6 weeks before, sharp pain appeared in the posterior side of both lower legs, while palsy of lower legs developed gradually. 3 weeks before, she could hardly walk. On admission, she had myasthenia in right arm and legs. She felt pain in legs and palsy of hands and legs. Hypoesthesia was at left leg. Leukocytosis (26650/μl) with hypereosinophilia (11113/μl) and elevated CRP (3.97mg/dl) led the diagnosis of EGPA according to the Japanese

criteria. 45mg of PSL were started, resulting prompt amelioration of eosinophilia, palsy and pain were persistent. 30 days after starting PSL, IVIg (15000mg,5days) was started. Only a week later, pain disappeared. Myasthenia and palsy were improved. Now, she can walk without equipment, taking 5mg of PSL. The palsy remains only in the planta pedis. [Discussion] IVIg is indicated for steroid resistant neuropathy of EGPA. However, the optimal timing of administration has not been determined. The timing varies widely from several weeks to several years in the literature. In our case, early IVIg was highly effective. Early IVIg following steroid might improve the prognosis of neuropathy in EGPA.

P2-222

A case of eosinophilic granulomatosis with polyangiitis complicated with jejunocolic fistula

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Conflict of interest: None

A 48-year-old man had fever and stomachache. His primary care physician found eosinophilia, so he was admitted to a hospital near his home. On this admission, his symptoms worsened and numbness in his lower limbs developed. After the treatment of intravenous methylprednisolone 250mg per day, his symptoms improved. However, contrast CT shows no enhancement in a section of his transverse colon, so he was transferred to our hospital. After this admission, he was diagnosed as eosinophilic granulomatosis with polyangiitis (EGPA) by the findings; eosinophilia, allergic rhinitis, and polyneuritis, and so treated with steroid and intravenous cyclophosphamide (IVCY). As these treatment had normalized his symptoms, he was treated continuously with IVCY per month, oral prednisolone (PSL) with gradual reduction, and intravenous immunoglobulin. However, at 150 days after first admission, an abdominal pain developed, when the dose of PSL was reduced, 20mg per day. Abdominal contrast CT, colonoscope, and contrast enema suggested 6cm stenosis of transverse colon and jejunocolic fistula. And so he underwent transverse colectomy and jejunectomy. Cases of EGPA with intestinal perforation were often reported, but the case of EGPA with intestinal fistula is very rare and instructive.

P2-223

Case study of a patient with eosinophilic granulomatosis with polyangiitis combined with phrenic nerve palsy

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Conflict of interest: None

[Patient] 33-yo male [Clinical course] The patient started to have muscle weakness and hypoesthesia in the four extremities, respiratory distress in the supine position was observed middle of March in 2017, and hospitalized at the end of March. Patient's eosinophil count was about 30,000. ANCA was negative. The patient was suspected to have heart failure due to orthopnea; however, an echo examination showed that heart function was normal. Chest X-rays showed elevation of the diaphragm on both sides; thus, we suspected phrenic palsy on both sides. A nerve conduction velocity test in the extremities showed findings consistent with mononeuritis multiplex. Furthermore, the phrenic nerve conduction test confirmed findings consistent with bilateral phrenic nerve disorder. We diagnosed the patient with EGPA with phrenic nerve paralysis, and started to administer PSL and Cyclophosphamide IV. The patient's various neurological symptoms and orthopnea due to phrenic nerve paralysis improved during hospitalization. [Conclusion] We treated a patient who had EGPA with phrenic nerve palsy, as well as orthopnea. EGPA is rarely associated with phrenic nerve palsy; however, if the patient exhibits orthopedic respiratory symptoms, it is necessary to take phrenic nerve palsy into consideration.

P2-224

A case of eosinophilic granulomatosis with polyangiitis developed shortly after administration of anti-interleukin 5 antibody mepolizumab

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Conflict of interest: None

A 56 years old man was admitted to our hospital because of peripheral neuropathy and hypereosinophilia (15,000/μl). He was diagnosed as having bronchial asthma two years ago and had been treated with inhaled glucocorticoid plus long-acting β2-agonists and an oral leukotriene antagonist. Seven months before admission, frequency of acute exacerbation of asthma had increased to once a month. Twenty-six days before admission, he started to receive 100mg of subcutaneous mepolizumab. Five days after injection of mepolizumab, he started to notice numbness of the bilateral feet, subsequently numbness and tingling sensation had worsened, extended proximally, and expanded to his fingers. Then, he was diagnosed as having mononeuritis multiplex and eosinophilic granulomatosis with polyangitis (EGPA), which was successfully treated with high-dose glucocorticoids and intravenous intermittent cyclophosphamide. Mepolizumab has been under development as novel biologic agent for the treatment of EGPA. Our patient developed full blown EGPA from forme fruste shortly after administration of mepolizumab, which has never been reported previously.

P2-225

A case of refractory eosinophilic granulomatosis with polyangiitis successfully treated with rituximab

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Conflict of interest: None

A 51-year-old male was admitted to our hospital with progressive numbness in both upper and lower limbs and difficulty walking. His physical findings revealed high grade fever, palpable purpura, sensory abnormality in all limbs and muscle weakness of lower limbs. The diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA) was made based on adult onset bronchial asthma, sinusitis, mononeuritis multiplex proven by nerve conduction studies, eosinophilia and positive MPO-ANCA. He also had myositis of lower extremities and multiple lacunar infarction. Treatment with high dose corticosteroids (GCs) including of intravenous methylprednisolone pulse therapy and intravenous cyclophosphamide (IVCY) prevented the deterioration of his findings. However, IVCY was discontinued in 3 additional courses due to the elevation of AST and ALT level. Azathioprine was also difficult to continue because of stomatitis. Subsequently, he presented fever again and his peripheral eosinophil counts and CRP level were elevated. Rituximab was administered as alternative therapy, then his eosinophil count normalized. After rituximab therapy, intravenous immunoglobulin therapy and mycophenolate mofetil were added. Then his symptoms gradually improved, and GCs dosage were successfully reduced.

P2-226

A case of immunodeficiency-associated lymphoproliferative disorders developed during Takayasu arteritis treatment

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Conflict of interest: None

[Background]Immunodeficiency-associated Lymphoproliferative Disorders (ILPD) is developed following abnormal immune response due to immunosuppressive therapy for transplantation and autoimmune dis-

eases. Case of ILPD developed in a patient with Takayasu arteritis (TAK) has never reported. **[Case]**A 41-year-old woman who had been diagnosed as ulcerative colitis and TAK at the ages of 19 and 30, respectively treated with 5 mg of prednisolone (PSL) and 100 mg of azathioprine (AZA). However, colonoscopy for screening incidentally showed mucosal lesion in the rectum without clinical symptoms at the age of 41, and histological analysis showed infiltration with CD20 (+), CD3 (-), CD5 (-), CD10 (-), EBER-ISH (+) atypical lymphocytes in this lesion, demonstrating EBV-associated B-cell lymphoma. We diagnosed as extranodal B-cell lymphoma associated with immunosuppressive therapy, treated with Rituximab (RTX) after withdrawal of AZA. With combination of RTX and PSL therapy, the patient achieved remission without relapse of ILPD and TAK. **[Discussion]**Since a therapeutic strategy for TAK with concurrent development of ILPD has not been established, our present case provides evidence that RTX in combination with PSL may be effective in patients with aortitis and ILPD.

P2-227

Two cases of refractory Takayasu aortitis in which tocilizumab was effective

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Conflict of interest: None

The first case is a 19 - year - old woman. She was diagnosed with Crohn's disease in March, X-4. She had fever in January of X - 3. MRA examination revealed aortic arch triple branch vessel wall thickening, left subclavian artery stenosis. She was diagnosed as Takayasu arteritis. She began treatment with steroid pulse therapy, prednisolone (PSL) 45 mg, antiplatelet agent. She was added methotrexate (MTX) 10 mg / week in February and changed to cyclosporine (CyA) 200 mg from April, inflammatory findings remained. Started with Tocilizumab (TCZ) 8 mg / kg / month from March X. After treatment started, subjective symptoms were improved. The second case is a 23 year old female. She had fever at February X-4. Vascular wall thickening of the aortic arch 3 branch, bilateral common carotid artery, right subclavian artery showed lumenal high stenosis with contrast CT. She began therapy with PSL 50 mg, antiplatelet agent. MTX 10 mg / week, X-2 year CyA 150 mg was added, but vasculitis remained. She started at TCZ 8 mg / kg / month since July. After starting, subjective symptoms were improved. TCZ was effective for Takayasu arteritis which was difficult to treat 2 cases. In the evaluation of activity, PTX-3 and MMP-3 showed a decrease with activity.

P2-228

A case of Takayasu arteritis with comorbid posterior reversible leukoencephalopathy syndrome responsive to tocilizumab

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Conflict of interest: None

A 23-year-old female presented with fever, chest pain, and syncope. She had no significant medical history. In July, the patient developed a sustained fever in the evening, and experienced loss of appetite and weight loss (-7 kg/month). At the beginning of August, the patient fainted after taking a bath, and was hospitalized the same day. The patient was transferred to our department in mid-October. A definite diagnosis of Takayasu arteritis was made, the patient was started on prednisolone (PSL) (40 mg/day), and the patient was discharged at the beginning of September. The patient visited our department at the end of September with a complaint of a sudden pain in the back of the neck. Emergency MRI was performed as the patient had seizures. Although areas of high fluid attenuated inversion recovery (FLAIR) intensity were noted on head MRI in the bilateral medial parietal lobes, cortex of the medial occipital lobe, posterior reversible encephalopathy syndrome (PRES) was suspected. The symptoms improved after blood pressure control and administration of TCZ. Areas of high FLAIR intensity became unclear on the MRI performed one week later and the patient was discharged in mid-October. We report a case of Takayasu arteritis with comorbid PRES in which TCZ was effective.

P2-229

Rates and risk factors of relapse in Takayasu arteritis

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Conflict of interest: None

[Object] Takayasu arteritis (TAK) is one of the large vessel vasculitis which affects the aorta and its major branches, and patients sometimes experience relapse. The aim of this study is to investigate rates and risk factors of relapse in TAK patients. [Methods] 102 patients satisfying the ACR 1990 criteria in our hospital during 1990 to 2015 were enrolled to this study. Relapse was defined according to Kerr's criteria, at least 2 of the following; 1) systemic symptoms, 2) elevation of inflammatory markers, 3) vascular lesion or ischemic symptoms, or 4) change in imaging. [Results] The mean age of patients was 35.3 and 92 patients were female. 96 patients received glucocorticoid and 58 patients (56.8%) experienced relapse. The mean dose of initial prednisolone (PSL) was 36.4±16.0 mg/day and that at relapse was 10.4±7.2 mg/day. PSL was tapered by 2.3 mg /month in average. The mean period until relapse was 44.5 months. Relapse was more frequent in younger patients (30.7 vs 41.2), and in antinuclear antibody (ANA)-negative patients (89.6% vs 63.6%, $p<0.01$). [Conclusions] In our cohort, relapse was observed in 56.8% of TAK patients. Younger onset and lower ANA titer are risk factors for relapse, and appropriate therapy in those patients needs to be established.

P2-230

Three cases of Takayasu arteritis which remained undiagnosed for a prolonged period of time with preceding ulcerative colitis

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Conflict of interest: None

Takayasu arteritis (TA) is a rare systemic vasculitis that is characterized by granulomatous inflammation of the aorta, its major branches, and pulmonary artery. There are some characteristic symptoms of TA including arterial bruit and decreased or absent pulse, but the most of symptoms are nonspecific. Patients with active TA show elevated levels of inflammatory reaction, but the laboratory findings of TA are also nonspecific. Since TA shares some genetic determinants with ulcerative colitis (UC), a prevalent inflammatory bowel disease, there are many case reports of UC patients complicated with TA. Recently, we experienced 3 cases of TA patients who have preceding UC and need several months or years to be diagnosed with TA. We report these 3 cases with some literature review to discuss the difficulty of the diagnosis of concomitant TA in UC patients.

P2-231

Long term survival with surgically treated Takayasu arteritis without immunosuppressive therapy; an autopsy case report

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Conflict of interest: Yes

A 68-year old woman was hospitalized for high blood pressure (220 mmHg). Physical investigation revealed blood pressure difference between upper and lower limbs, and abdominal murmur. Blood examination

showed no inflammation. Enhanced CT revealed calcification and coarctation in the entire circumference throughout the thoracoabdominal aorta. Angiography revealed conspicuous coarctation at Th11/Th12 with significant blood pressure difference. Diagnosis of atypical coarctation by Takayasu arteritis (TA) was made. As she refused antihypertensive medication, thoracoabdominal aortic bypass grafting and celiac and superior mesenteric artery reconstruction were performed. After the operation, her blood pressure was controlled well. TA did not recur without immunosuppressive therapy for 23 years. She died at age 92 years of chronic heart failure. Microscopic findings of autopsy revealed fibrotic thickening and calcification of the intima, rupture of the medial elastic fibers, fibrous thickening of adventitia and feeding vessels in the diseased aorta. They were consistent with the scarring stage of TA. Other large vessels showed no vasculitis. Few long-term autopsy cases of TA with surgical treatment without immunosuppressive therapy have reported.

P2-232

A case of Takayasu's arteritis had rapidly increasing aneurysm and preceded surgery treatment than medications

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Conflict of interest: None

<Background> Takayasu's arteritis (TA) sometimes causes vasodilation or aneurysm. Surgical treatment is generally performed after control of inflammation with medical treatment. Here we report a case of TA with an rapidly increasing aneurysm had priority the surgical treatment than medical treatment. <Case> A 19-year-old woman visited our hospital because of hoarseness from three weeks ago. X-ray showed enlargement of the aorta shadow, and computed tomography (CT) revealed the expanded ascending aorta and two large aneurysms. X-ray of health examination she took 10 months ago was no abnormality. TA was suspected from the images and elevated levels of C-reactive protein. Because the risk of rupture of the aneurysm was high, she underwent an artificial blood vessel replacement surgery. Various specific autoantibodies and infections were negative, and inflammatory cells were found in the aortic wall in pathological findings. Therefore she was diagnosed as TA. She was administered by 30 mg prednisolone, and added tacrolimus. Though the dose of prednisolone was gradually decreased, she has not experienced any relapse. <Clinical Significance> This case was rare of TA which had rapidly increasing aneurysm and was preceded surgery treatment than medications.

P2-233

The case of confirmed Takayasu arteritis occurred 2 years after occurrence of nodular erythema

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Conflict of interest: None

Introduction: Takayasu arteritis (TAK) is nonspecific in initial symptoms and there is no specific autoantibody, so confirmed diagnosis is difficult. We report the case of TAK diagnosed confirmly two years after initial visit. **Case:** The 25-years-old woman. 3 years ago, she visited A hospital and found a nodular erythema on the left foot instep. 2 years ago, she represented redness of the left ankle, incompatibility of the left abdomen and erythema nodosa of the lower thigh. C-reactive protein (CRP) was 12.1 mg/dL and all autoantibodies were negative. Despite the use of prednisolone (PSL) and colchicine, she repeatedly relapsed. One day, she represented chest discomfort and visited our hospital. Contrast computed tomography revealed aortic wall thickening from thoracic to descending aorta and we diagnosed TAK. Treatment with PSL 50 mg/day was started, and CRP was negative on day 7. The therapy continues with PSL 15 mg/day + azathioprine 50 mg/day now. **Consideration:** In this case, the aortic wall thickening occurred only in the thoracoabdominal aorta, so she represented atypical symptoms in TAK such as nodular erythema on the legs. About from 6 to 19% of TAK is reported to have nodular erythema. **Conclusion:** When we encounter young women with nodular erythema, we should suspect of TAK.

P2-234

Arthritis in a patient with Takayasu arteritis

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Conflict of interest: Yes

Background: Takayasu arteritis is an idiopathic large vessel vasculitis affecting the aorta and its major branches. Although systemic symptoms, such as malaise, weight loss and fever, are common in the early stages of this disease, joint manifestations are rarely seen. Case: We report the case of a woman in her 40s, who complained of arthritis of left knee and left ankle. Both rheumatoid factor and anti-cyclic citrullinated peptide antibody were negative. Treatment with low dose prednisolone and methotrexate resulted in improvement of polyarthritis. Six months later, however, she presented with chest and back pain, with an elevation of serum C-reactive protein levels. Enhanced computed tomography demonstrated significantly wall thickness in the brachiocephalic trunk, left common carotid artery and descending aorta. She was diagnosed with Takayasu arteritis. Clinical significance: We should keep Takayasu arteritis in mind for patients with seronegative undifferentiated arthritis.

P2-235

Exacerbation of aortitis syndrome due to discontinuing tocilizumab

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Conflict of interest: None

A 25-year-old man. He was diagnosed as Aortitis syndrome two years ago. He had been treated by the administration of steroid and methotrexate, but controlled not good. He was initiated Tocilizumab therapy, but he was affected acute tonsillitis 18 day after. He could not swallow anything with sore throat, then he was admitted with antibiotics and discontinued tocilizumab and methotrexate. Pain during swallowing did not improve, cough appeared on day 32 of the disease and blood sputum appeared on the 35th day. He underwent chest MRI scan and be made the diagnosis coarctation and occlusion left pulmonary artery caused by exacerbation of aortitis syndrome. Discontinuing tocilizumab soon after the initiation of tocilizumab therapy may exacerbate aortitis syndrome.

P2-236

Three cases of methotrexate-related lymphoproliferative disorder that developed during the treatment of chronic progressive neuro-Behçet's disease

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Conflict of interest: None

[Object] We report our experience with 3 patients who developed methotrexate-related lymphoproliferative disorder (MTX-LPD) during the treatment of chronic progressive neuro-Behçet's disease (CPNB). [Case] Case 1: a 47-year-old man who had developed CPNB when he was 28 years old. He began treatment with MTX at 32 years of age, and IFX was added at the 35 years of age. At 45 years of age, he developed a refractory cutaneous ulcer in his right lower extremity that was diagnosed as MTX-LPD, based on skin biopsy results. Case 2: a 43-year-old man who had developed CPNB when he was 28 years old. He began to receive MTX at 28 years of age. Since he developed fever and multiple cervical adenopathy at 42 years of age, he was diagnosed as having MTX-LPD, based on the results of lymph node biopsy. Case 3: a 43-year-

old man who had developed CPNB when he was 31 years old. He began treatment with MTX at 31 years of age, and IFX was added in the same year. At 43 years of age, MTX-LPD was suspected due to multiple cervical adenopathy and increase of soluble interleukin-2 receptor and thymidine kinase. [Conclusions] Although MTX is one of the effective drugs for CPNB, careful attention should be paid to the development of MTX-LPD during its administration.

P2-237

HLA-B7 crossreactive antigens with Behcet disease patient in Japanese and long-term outcomes

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Conflict of interest: None

[Object] It was reported that B7crossreactive antigens was related with ankylosing spondylitis. Uveitis and arthritis in are symptoms of reactive arthritis and ankylosing spondylitis, similar to Behcet Disease (BD). We investigated whether B7crossreactive antigens are newer genetic factors associated with BD by long-term observation. [Methods] The samples were obtained from a total of 46 Japanese BD patients. HLA-A and -B typing were done by a PCR-SSOP-Luminex method. [Results] HLA-B51-positive patients were 30.4% and HLA-A26-positive patients were 19.6% of BD patients. 78% patients with BD were positive about HLA-B7crossreactive antigens, except for HLA-B51-positive patients and HLA-A26-positive patients. Only four patients (8.6%) were negative of either factor (HLA-B51, A26 and B7crossreactive antigens). 53.8% of B7crossreactive antigens-positive patients had arthritis without spondylitis. They did not satisfied classification criteria of ankylosing spondylitis, psoriatic arthritis and Crohn's disease during 9.36 years as average observation period. [Conclusions] Most BD patients are related to HLA-B51, A26 and B7 crossreactive antigens in Japanese. The BD patients with the B7crossreactive antigens may not have B27 associated diseases.

P2-238

Efficacy of TNF inhibitors on Behcet's disease

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Conflict of interest: None

[Object] Behcet's disease is an intractable disease that affects many organs. The aim of this study is to assess clinical characteristics of patients with Behcet's disease who were treated with TNF inhibitors (infliximab, IFX; adalimumab, ADA). [Methods] 197 patients with Behcet's disease in Tohoku University hospital during January 2007 to June 2017 were enrolled to this study. Clinical characteristics, continuation rate, efficacy and complications of TNF inhibitors were retrospectively evaluated. [Results] Among 197 patients with Behcet's disease, 63 patients were treated with TNF inhibitors. We could get 58 cases treatment dates that could follow for over 1 year (IFX 47, ADA 6, IFX and ADA 5). TNF inhibitors were used more frequently in male (60%), in patients with eye lesion (69%) or special types (24 cases). Special types included 11 intestinal, 9 vascular, 3 intestinal and vascular, and 1neurological lesion. Continuation rate for 1 year was 86%. TNF inhibitors had steroid sparing effect particularly in patients without eye lesions. Notably, improvement of oral ulcer or arthritis was observed without any significant adverse effect. [Conclusions] TNF inhibitors were well tolerated and had steroid sparing effect in patients with Behcet's disease.

P2-239

The Behçet's disease (BD) criteria of international criteria for BD (ICBD) is much better than that of the international study group (ISG) for the Japanese BD patients fulfilled Japanese criteria

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Conflict of interest: None

[Object] To analyze the gradation of clinical features of Behçet's disease (BD) and the difference using international criteria for BD. [Methods] We enrolled our 264 BD patients diagnosed BD using Japanese BD criteria. We divided our patients to 4 groups with 5-year period: 49 BD patients arrived and started following until 2000; 70, '01-'05; 77, '06-'10; 69, '11-'15, and compared symptoms among them. We then analyzed the escape rate of our patients when we evaluated between ISG and ICBD, and compared each rate. [Results] The characteristics of our 264 BD patients were as described below: oral aphthous, 100.0%; genital ulcers, 78.0%; ocular lesions, 39.0%; skin lesions, 93.2%; arthritis, 1.0%; pogitive pathergy tests, 2.7%; intestinal lesions, 26.9%; neural lesions, 8.7%; vascular lesions, 8.3%; epididymitis, 4.2%; male, 28.4%; positive HLA-B51, 32.6%. The ocular and intestinal lesions decreased in our study: p-value, 0.02 and 0.03, respectively. The escape rate of our BD patients using ISG and ICBD were 12.9% and 23.4%, respectively, then, ICBD may be useful criteria for Japanese BD patient ($p<0.01$). [Conclusions] The ocular and the intestinal lesions decreased in our BD patients. Used as a diagnosing criteria, ICBD was more useful than ISG for Japanese.

P2-240

Ten years observation of Infliximab in treatment for uveitis of Behcet disease

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Conflict of interest: None

[Object] To assess the clinical course during 10 years in patients with uveitis of Behçet disease (BD) treated with Infliximab (IFX). [Methods] Observational research in daily clinical settings at the Osaka University Hospital. [Results] Thirty patients (21 Males and 9 Females) were treated with IFX in the treatment for uveitis of BD. The median age at the administration was 45 years [interquartile range: 36, 45], and the median duration from the onset of BD was 72 months [36, 118]. The median period of continuation of IFX was 2622 days (maximum: 3893 days), and the continuation rates were 86% at 1 year, 82% at 3 year, 74% at 5 year and 74% at 10 year. Seven serious adverse events occurred (2 bacterial pneumonias, gastrointestinal perforation, renal artery aneurysm, heart failure, infusion reaction and psoriasis). Seven patients resulted blind in both eyes although the treatment. The visual prognosis was strongly associated with disease duration and visual acuity at the administration of IFX. The cutoff values for predicting poor visual prognosis are 52 months of disease duration and 0.22 of visual acuity with 90% of sensitivity. [Conclusions] Disease duration and conserved visual acuity should be mostly noted in the treatment for uveitis of BD with IFX.

P2-241

Successful treatment with infliximab in a patient with Behçet's disease with extensive inferior vena cava thrombosis

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Conflict of interest: None

Inferior vena cava thrombosis associated with Behçet's disease is a rare and lethal complication in Japan. It is firstly treated with steroids and immunosuppressive agents, but often refractory to that therapy. We describe here successful treatment with infliximab in a patient with Behçet's disease with extensive inferior vena cava thrombosis. A 26-year-old man developed fever, oral aphthae, genital ulcers, arthritis and right back pain. Enhanced computed tomography revealed continuous thrombus from the

right renal vein to the inferior vena cava. He was diagnosed with Behcet's disease. The thrombus was extensive to iliac vein. He was started on prednisolone (PSL 30 mg/day), methotrexate, colchicine and infliximab. Computed tomography showed to stop extending thrombosis. No severe adverse events occurred during the clinical course. PSL is sparing to 5mg/day. Infliximab may be first-line therapy in sever venous thrombosis in Behçet's disease.

P2-242

Acute neuro-Behcet's disease presenting with longitudinal extensive transverse myelitis in a patient receiving infliximab

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Conflict of interest: None

[Case] A 67-year-old woman, who has been followed with a diagnosis of complete Behcet's disease at age 60 and has been administered infliximab (IFX 7.5 mg/kg, q8w) for five years was admitted to our hospital with right-side-dominant limb weakness, superficial sensory disturbance, and bladder dysfunction. The cranial MRI had no abnormal finding and the spinal MRI revealed a longitudinal extensive spinal cord lesion extending from the medulla oblongata to Th2. Cerebrospinal fluid (CSF) analysis demonstrated 205 cells/mm^3 (94% polymorphs), protein 252 mg/dL, IgG-index 0.87, and IL-6 13064 pg/mL. CSF myelin basic protein, IgG oligoclonal banding, and anti-aquaporin 4 antibody were negative. We diagnosed acute neuro-Behcet's disease (NBD) with longitudinal extensive transverse myelitis. Treatment with three courses of methylprednisolone pulse therapy combined with oral corticosteroid and methotrexate improved limb weakness. The spinal cord lesion observed in spinal MRI showed prominent improvement at 70 days after the start of treatment. [Conclusions] In patients with NBD, the frequency of myelitis is 8-14%. In case neurological symptoms develop in BD patients receiving IFX, acute NBD with myelitis needs to be included in differential diagnosis.

P2-243

A case of incomplete Behcet's disease with esophageal ulcer during low-dose prednisolone administration due to repeated oral ulcers

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Conflict of interest: None

A 35-year-old man was introduced to our hospital because of repeated oral ulcers, high fever and cervical lymphadenopathy during low-dose prednisolone (PSL) administration. Biopsied specimens of oral ulcers and cervical lymph node revealed nonspecific inflammatory findings. He was not diagnosed with Behcet's disease in spite of HLA-B51 positivity. He was treated with PSL (10mg/day) and the symptoms improved immediately. Four years later, he had esophageal discomfort. Endoscopic examination of the upper gastrointestinal tract revealed a punched-out ulcer in the middle esophagus. Biopsied specimens taken from the lesion also revealed nonspecific inflammatory findings and vasculitis. As he had a combination of multiple oral aphtha and skin lesions, he was diagnosed with the abortive form of Behcet's disease. After diagnosis, we started administration of PSL (30mg/day). Then, all symptoms and the esophageal lesion improved and PSL were tapered following a combination of azathioprine. However, infliximab was administered due to exacerbation of esophageal ulcer and then he had obtained complete remission. This appears to be an interesting case of Behcet's disease with esophageal lesion.

P2-244

Intestinal Behcet's Disease with Perforation During Anti-TNF-a Antibody Therapy for Sacroiliitis

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Conflict of interest: None

Case report: An 18-year-old woman was admitted to our hospital for oral ulcers, poor appetite and fever. She had been diagnosed as sacroiliitis and administered Infliximab (IFX) four months before the hospitalization. Although IFX improved lower back pain, she presented high fever a few days before admission. She was diagnosed as Behcet's disease (BD) because of the four chief clinical features, oral ulcers, genital ulcers, acneiform eruptions and posterior synechia. The patient suddenly had abdominal pain five days after admission, and abdominal CT revealed intraperitoneal free air. She was diagnosed as gastrointestinal tract perforation and had urgent surgical intervention; ileocecal resection and colostomy with double orifices. The endoscopic and microscopic findings were consistent with intestinal BD. The patient was treated with antibiotics, high dose glucocorticoids and Adalimumab. One month-later colonoscopy revealed that the intestinal mucosa was completely healed and the endoscopic remission was achieved. Discussion: The patient developed intestinal BD although she had been treated with IFX for sacroiliitis. We thought that the dosage of TNFa inhibitor for sacroiliitis was inadequate for intestinal BD.

P2-245

A case of Behçet's disease accompanied by myelodysplastic syndrome with trisomy 8 successfully treated with IFX, MTX and Mesalazine

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Conflict of interest: None

Behçet's disease accompanied by myelodysplastic syndrome (MDS) with trisomy 8 is rare and known as refractory. Bone marrow transplantation may be the best way to treat both MDS and Behçet's disease, however it has a lot of side effects and limitations in age, physical condition and others. We experienced a case of Behçet's disease accompanied by MDS with trisomy 8 successfully treated with IFX, MTX and Mesalazine, so we'll report the case. The case is a 46 years old female patient who has a history of HBV carrier. She was pointed out the pancytopenia several years ago, but no test was examined. She had been had intermittent fever, oral aphta, genital ulcer, erythema nodosum and diarrhea a few years before admission and no complains of abdominal pain and bloody stool. According to those symptoms, the finding of ileocecal ulcer shown by CS and pathological result, we made a diagnosis of Behçet's disease and also of MDS by bone marrow puncture. We started treatment by predonisolone (PSL) and azathioprin at first, however we couldn't reduce PSL less than 15 mg/day because her abdominal symptoms got worse. We added IFX, MTX and Methalazin in order, finally her symptoms disappear and come off PSL. We now maintain the remission of Behçet disease without exacerbation and side effects.

P2-246

Clinical features of Methotrexate associated Lymphoproliferative disorder (MTX-LPD) in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To investigate the clinical features of MTX-LPD in patients

with rheumatoid arthritis (RA). [Methods] We retrospectively identified 16 RA patients who developed MTX-LPD in our hospital from 2006 to 2017. [Results] The median age at onset of MTX-LPD was 76 years. The male-to-female ratio was 6:10. The median duration of RA and MTX administration was 9 years and 4 years, respectively. The median of MTX dosage was 10mg/week. Among 11 patients with extranodal lesion at onset of MTX-LPD, EB virus positive was observed in 4 patients. Pathological diagnosis was DLBCL (Diffuse large B cell lymphoma) in13 patients, PTCL (peripheral T cell lymphoma) in 2 patients and polymorphic LPD in 1 patient. The spontaneous regression after discontinuation of MTX was detected in 4 patients. Of 12 patients who required chemotherapy, 5 patients were dead (non-survival group). Compared to chemotherapy group, the duration of RA and MTX administration tended to be longer in spontaneous regression group (p=0.077, p=0.063, respectively). Male mortality in non-survival group was significantly higher than those in survival group (P=0.017). [Conclusions] This study has suggested that male gender might be associated with prognostic factor of MTX-LPD.

P2-247

Subsequent treatments in rheumatoid arthritis (RA) with lymphoproliferative disorders after discontinuation of methotrexate (MTX)

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Conflict of interest: None

[Object] The subsequent treatment strategy in RA cases with lymphoproliferative disorders (LPD) after discontinuation of MTX has not been determined. [Methods] In our hospital between April 2011 and October 2017, 16 cases of RA with MTX discontinued with the onset of LPD were identified. The records of 11 cases of them who could have been followed for more than 6 months were retrospectively reviewed in terms of treatments for RA after the withdrawal of MTX. [Results] Nine patients were female and two were male. Mean age was 66.1±8.3 year-old when LPD was diagnosed. Nine cases were LPD of B cell type. Four patients did not require additional treatments. Five patients underwent incremental or new introduction of PSL and two cases needed increasing or new introduction of csDMARDs (one case of SASP, one case of SASP + IGT). One case needed change in csDMARDs (AZP → BUC) and bDMARDs (CZP → TCZ), and there was no case newly introduced a bDMARDs. No patients were treated with rituximab or TNF antagonists. [Conclusions] After withdrawal of MTX, patients preferentially received PSL or csDMARDs.

P2-248

Methotrexate-associated lymph proliferative disorders: A report on 5 cases

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Conflict of interest: None

[Object] Methotrexate (MTX) is an anchor drug in the management of rheumatoid arthritis (RA). MTX is commonly used for the elderly; however, elderly patients RA during MTX treatment often develop lymphoproliferative disorders. This disease is called methotrexate-associated lymphoproliferative disorder (MTX-LPD). [Methods] We reported five RA cases with MTX-LPD and their clinicopathological features were discussed. [Results] Mean age of the patients was 69.2 years (4 females, 1 male) and mean disease duration of RA was 10.6 years. They were suspected of having lymphoproliferative disorder in brain, lung, and neck during MTX treatment. Three cases were diagnosed as having diffuse large B-cell lymphoma, one case was diagnosed as having follicular lymphoma, and one case was not well understood. One case was Epstein-Barr (EB) virus encoded small RNAs. Remission was achieved in three cases just by the cessation of MTX. Chemotherapy was needed in two cases, and it is continued presently. [Conclusions] Our cases have long disease duration as reported previously. It is reported that MTX-LPD has relation to EB virus, and it was applied in one case in our series. When MTX-LPD is suspected, cessation of MTX should be considered; however, careful observation is necessary since it might worsen.

P2-249

A case of bone destructive MTX-LPD occurred in the wrist joint

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Conflict of interest: None

[Object] To report bone destructive methotrexate associated lymphoproliferative disorders (MTX-LPD) occurred in the wrist joint. [Case] A 64 years old woman [Medical History] She had rheumatoid arthritis (RA) at 57 years old. MTX was introduced a year later, and the disease activity was controlled well with the dose of 10mg/w. The arthralgia in her right wrist joint occurred at 63 years old, and developed gradually with swelling and redness. The bones in the wrist joint were severely broken in the X-ray analysis. And the right axillary lymph node was swollen in the CT image. The blood test showed CRP 3.39mg/dl and ESR (1h) 85mm/h. A malignant tumor or infection was considered more for the differential diagnosis, that a biopsy was done at first. MTX-LPD was diagnosed pathologically that we stopped MTX immediately. The symptoms in her wrist joint had reduced once, but recurred later, which she is receiving chemotherapy now. [Clinical significance and discussion] The reports concerning to MTX-LPD increased recently, but bone destructive MTX-LPD in the wrist joint was not reported. We should take MTX-LPD into consideration when some joint shows severe swelling and bone destruction under well controlled disease activity during MTX medication.

P2-250

A case of follicular lymphoma with pseudo-high CRP due to nonspecific reaction of IgM type RF during the course of RA

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Conflict of interest: None

[70-year-old female] [Chief complaint] edema and ulcer in the lower leg [Present history] X-6 years ago the patient was diagnosed with RA and treated with MTX. Edema accompanied by skin eruption appeared on the left lower thigh X-1 month before; was consulted to the dermatology in our hospital under suspected cellulitis. Although high values of CRP were observed, the general condition was stable. Even with antibiotics, there was no improvement. MTX - associated lymphoproliferative disorders etc. was suspected. After MTX was discontinued, CRP did not improve though ESR was decreasing. Laboratory tests showed an abnormally high level of beta-2 microglobulin or more as compared with mild increase of soluble IL - 2 receptor. As a result, it was considered that the inspection value was abnormal due to non-specific reaction of IgM type RF. Thereafter it was diagnosed as follicular lymphoma bone marrow infiltration. [Discussion] We experienced a case of follicular lymphoma with pseudo-high CRP which does not meet the condition in patients with RA. RA is a disease that heavily uses CRP for comprehend the disease condition, and it is reported as a suggestive case.

P2-251

Four cases of methotrexate-associated lymphoproliferative disorder at extranodal sites through the clinical course of rheumatoid arthiritis

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Conflict of interest: None

MTX-LPDs not uncommonly occur at extranodal sites. The pathogenesis are poorly understood. We report our 4 cases with literature review. Case 1: A 49 y.o. F. with RA for 14 years has been treated with MTX 4mg and PSL. A liver tumor was pointed out after 12 years' treatment with MTX. The histology of the tumor met for large B-cell lymphoma (DLBCL). After 2 years of MTX cessation, chemotheraphy for DLBCL is currently in discussion because of mildly increasing in size of the tumor. Case 2: A 74 y.o. F. with RA for 30 years has been treated with MTX 8mg. She presented with multiple subcutaneous nodules, after 29 years since MTX initiation. The histology met for DLBCL. After 2 months of MTX cessation, all nodules have disappeared. Case 3: A 72 y.o. F. with RA for 6 years has been treated with MTX 8mg and Infliximab. An ileal perforation had occured, and emergency surgery was performed after 6 years' treatment with MTX. The histology of the resected ileum met for DLBCL. After 6 months of MTX cessation, there has been no changes on her clinical status. Case 4: A 84 y.o. F. with RA for 24 years has been treated with MTX, PSL, BUC and Tac. She was diagnosed with lung cancer after 23 years' treatment with MTX, although the tumor had regressed since MTX cessation for 1 month.

P2-252

Two cases of MTX-LPD with Endobronchial lesions

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Conflict of interest: None

[Case 1] A 69-year old female. He was treated with rheumatoid arthritis (RA) with BUC, MTX, SASP, PSL. Cough and breathing difficulty emerge from November 2016. He was suspected of having an asthma attack and treatment was started with bronchodilator. However, the improvement of symptoms was poor. Tumorous lesions appeared in the bronchus with chest CT. Biopsy was performed after tracheotomy in otolaryngology. In the pathological examination it was MTX-LPD. After discontinuing MTX, the tumor tended to decrease with no treatment, and there was no recurrence. [Case 2] A 72-year-old female. Low disease activity persisted at IFX+MTX against RA. From May 2017, moist cough appears. Tumor shadow appeared on the lower left lobe central side with chest CT, and left lower lobe lung cancer was suspected. TBLB was performed from the same site. Pathological findings showed that CD3 positive cells were diffusely increased, EBER-ISH (in situ hybridization) was positive, and MTX-LPD was considered. After discontinuing MTX, the lesion tends to shrink and has been under treatment. [Clinical Significance] MTX-LPD accompanied by endotracheal lesion is very rare, and cases in the trachea alone have not been reported so far. We report this case because it seemed to be a valuable case.

P2-253

Improvement of joint symptoms after resection of lymphoma in a patient with rheumatoid arthritis

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Conflict of interest: None

A 43 years old female was suffered multiple joint pain in November 2016. In February 2017, her laboratory data revealed positive test for RF, and she was admitted to our hospital in March 2017. Polyarthritis, positive test for RF, and ACPA, abnormal CRP, and symptom duration ≧6 weeks were identified, so she was diagnosed as RA. In addition, positive test for anti-SS-A/Ro antibody and labial salivary gland biopsy, she was diagnosed as SS. Treatment with PSL5mg/day and SASP500mg/day was started. Multifocal cyst was identified in anterior mediastinum in contrast CT, thoracoscopic surgery was done in July. She was diagnosed as MALT lymphoma. After resection of lymphoma, swollen joints were improved and, RF and ACPA titer were decreased. After PSL and SASP were discontinued, RA was not relapsed. RA and SS, and lymphocytic malignancies are related. In addition, patient with blood cancer (ex. lymphocytic malignancies) is frequently complicated by immune disorder, and shows positive test for autoantibodies (ex. ACPA) more frequently than healthy person, so association between autoimmune rheumatic diseases and lymphocytic malignancies is bidirectional. Our data indicated that immune disorder formed by lymphoma complicated by pathology like RA.

P2-254

A case of primary splenic diffuse large cell lymphoma associated with rheumatoid arthritis

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Conflict of interest: None

Case: A 83 years old woman. We started anti TNF-α inhibitor at approximately 13 years ago. We are under the medical treatment in Etanercept (alternation of 25mg/week and 50mg/week) and MTX 4mg/ week. After anti TNF-α inhibitor initiation, CRP passed negative conversion. For one month before hospitalization, the left coxalgia developed, and CRP rose with 7.89 mg/dl. We thought RA aggravated it. We gave ETN 50mg every week and added predonine. However, CRP rose with 22.7 mg/dl one week before hospitalization, and cytopenia was detected. 2% of blast cells appeared. sILL-2R was 13562IU/ml. Marrow hypoplasia was detected in femoral MRI. Spleen showed strong accumulation in PET-CT. Nodal disease was absent by CT. There were atypical lymphocytes in bone marrow biopsy. DLBCL invaded the marrow. Discussion: The splenic primary malignant lymphoma is 0.3-2.0% of all malignant lymphoma. Most have bone marrow infiltration, and nodal disease is rarely detected. We accepted bone marrow infiltration, but clear nodal disease was absent in this case. It was the case that should differentiate blood disorder in a cause of the arthralgia.

P2-255

A case of chronic active Epstein-Barr virus infection in a patient with rheumatoid arthritis

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Conflict of interest: None

A seventy-one male was diagnosed with rheumatoid arthritis on 2007. He was treated with methotrexate (MTX) 8mg/week and prednisolone (PSL) 5mg/day. On April 2016, he was admitted to a local hospital complaining fever and cervical lymphadenopathy. Under the diagnosis of MTX-associated lymphoproliferative disorder (LPD), discontinuation of MTX resolved his symptoms. Since polyarthritis was worsened, PSL was increased to 20mg/day. He was admitted to our hospital on February 2017, complaining a month of fever. Abdominal enhanced CT depicted multiple low density area in the liver. Considering the elevated serum levels of sIL-2R and high viral loads of EBV, we estimated the LPD reactivation. Liver biopsy was performed. Methylprednisolone pulse therapy was initiated for the multiple organ failure thought to be due to cytokine storm and PSL was increased to 75mg/day. Despite the treatment, he died with a rapid clinical course. Subsequently, the liver biopsy revealed infiltration of EBV positive T-cells into the liver tissue. The diagnosis of Chronic active EBV (CAEBV) infection was made. If organ dysfunction appeared with high viral loads of EBV during immunosuppressive thera-

py, we should consider not only the B-cell type of EBV infection, but also T-cell/NK-cell type, such as CAEBV infection.

P2-256

Methotrexate-related lymphoproliferative disorder in a patient with sarcoidosis

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Conflict of interest: None

[introduction] Methotrexate-associated lymphproliferative disorder (MTX-LPD) is a rare but critical complication developing in patients treated with methotrexate. [Case] Patient was 70's y.o Female with Sarcoidosis. She was treated with methotrexate and prednisolone for sarcoid arthropathy for 1 year. She recently presented fatigue, fever, cough, chest discomfort and back pain. Computerized tomography (CT) revealed lymphoadenopathy in her pelvis. CT-guided biopsy was performed, and the histopathological diagnose was peripheral T-cell lymphoma, NOS. So, we discontinued MTX. And then, her symptom and lymphoadenopathy was improved. [Discussion] Many things with MTX-LPD have been unclear such as incidence, demographic characters and risk factors. The frequency of diffuse large B cell lymphoma was significantly high in MTX-LPD, however, the histopathologic finding in this patient presented with peripheral T-cell lymphoma, NOS.

P2-257

Two cases of rheumatoid arthritis and polymyositis associated with (Idiopathic) portal hypertension

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Conflict of interest: None

[Case 1] A 61-year-old man with polymyositis (PM) was maintained with PSL 7mg and Tac 3mg. Then his PM flared with CPK 717U/L and CRP 5.8mg/dl and was improved by PSL 40mg and Tac 4mg. However, hepatic dysfunction prolonged and he suffered from ascites. Liver biopsy showed fibrotic change of portal vein without hepatitis. Direct measurement of portal pressure was elevated at 28mmHg, and therefore he was diagnosed with (idiopathic) portal hypertension ((I) PH). Diuretics and olmesartan in addition to immunosuppressant improved ascites. [Case 2] A 64-year-old woman with rheumatoid arthritis (RA) was treated with MTX. Then MTX was discontinued owing to cytopenia. Exacerbation of arthritis followed by ascites and hepatic dysfunction were revealed. Liver biopsy showed no cirrhosis. The direct measurement of portal pressure was elevated at 31mmHg, and therefore he was diagnosed with PH. Ascites was reduced by tocilizumab (TCZ) and transient use of diuretics, and she has no flare. [Conclusion] (I) PH associated with autoimmune diseases were rarely reported, and therefore, it has been suggested that autoimmunity is possibly related to pathophysiology of (I) PH. We should remind to consider (I) PH as a rare cause of prolonged hepatic dysfunction and ascites associated with PM and RA.

P2-258

Pulmonary arterial hypertension accompanied with autoimmune hepatitis observed in two patients with connective tissue disease

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Conflict of interest: None

Connective tissue disease (CTD) and portal hypertension are well known causes of pulmonary arterial hypertension (PAH), but the precise mechanisms for these associations remains unknown. Recently, some cases of PAH complicated with autoimmune hepatitis (AIH) had been reported, and they could be classified as a new overlap syndrome; AIH/PAH. We herein report two cases of CTD-associated PAH complicated with portal hypertension suggested to be caused by AIH. Case1: 52-year-old woman who had been diagnosed with systemic sclerosis (SSc), PAH, systemic lupus erythematosus (SLE), and rheumatoidarthritis developed esophageal varices with hepatic cirrhosis. Case2: 55-year-old woman who had been diagnosed with SLE, Sjogren's syndrome, and SSc with PAH developed gastric varices with hepatic cirrhosis. In both cases, the diagnosis of hepatic cirrhosis was not done histologically, but the cause was speculated to be AIH by positive antinuclear antibody test. A new disease spectrum of portopulmonary hypertension complicated with AIH and undifferentiated CTD is strongly suggested be these two cases.

P2-259

Two cases of ITP complicated with rheumatic disease, successfully treated with TPO receptor agonist

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Conflict of interest: None

(Case 1) A 67-year-old female developed SLE in1996 and was treated with prednisolone from 2001 in our hospital. In January 2017, platelet count decreased to 1.2×10^9/L and purpura was increased. She was administrated eltrombopag, and then platelet count elevated by 13×10^9/L. (Case 2) A 76-year-old male who developed rheumatoid arthritis (RA) in 2011 and was treated with tacrolimus. Severe thrombocytopenia (0.2×10^9/L) occurred in December 2016, which was refractory to prednisolone. He was treated with romiplostim and platelet increased. In July 2017, articular symptoms worsened and simultaneously platelet count decreased to 1.1×10^9/L. After switching from romiplostim to eltrombopag, platelet count increased to 15×10^9/L. Case 1 was diagnosed with secondary immune thrombocytopenia (ITP) with SLE and case 2 was diagnosed with idiopathic ITP complicated with RA. In both cases, thrombopoietin (TPO) receptor agonists were effective. Recently, thrapeutic options for ITP are increasing, and therefore treatment selection depending on each case should be considered.

P2-260

The autoimmune manifestation associated with myelodysplastic syndrome in Japan

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Conflict of interest: None

Autoimmune manifestation (AIM) occurs in 10-20% of patients with myelodysplastic syndrome (MDS). However, its clinical characteristics in Japan have not yet been examined. In this study, we analyzed 40 patients who were newly diagnosed as MDS at our department between Apr. 2009 and Sep. 2014. 8 of 40 patients (20%) developed autoimmune diseases (PM, SSc and Intestinal Behcet disease) or AIMs (oral aphtha, intestinal ulcer, interstitial pneumonitis, arthralgia, non-infectious fever, etc.). There was no difference regarding age, sex, WHO classification, the absolute number of myeloblasts in bone marrow and IPSS score at the time of MDS diagnosis between patients with and without AIM. The absolute number of neutrophils in the peripheral blood and CRP was higher in MDS patients with AIM. The abnormal karyotype was found in 88% of patients with AIM. The mortality rate was high in patients with AIM (37.5%).

P2-261

A case of poly juvenile idiopathic arthritis with Sjogren's syndrome during treatment of tocilizumab with destructive thyroiditis

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Conflict of interest: None

[Background] Destructive thyroiditis is a condition in which extensive destruction of the thyroid follicle occurs due to rapid exacerbation of inflammation and thyrotoxicosis develops, and it is roughly divided into subacute thyroiditis and analgesic thyroiditis. This is a case of destructive thyroiditis during the treatment of tocilizumab. [Case] 15 year old onset RF positive with juvenile idiopathic arthritis. Autologous antibodies to various thyroid glands were also high, but no goitre was observed, and thyroid hormone always remained normal during the course of treatment. Four months ago, the thyroid suddenly enlarged with no particular trigger, multiple sweat, polydipsia, palpitations, weight loss was observed, and thyroid He was toxic but she did not show fever or sore throat. TSH receptor antibody · thyroid stimulating antibody was normal and in the thyroid scintigraphy, uptake was as the lower limit of normal I diagnosed with destructive thyroiditis. [Discussion] The clinical staure of this case is painless thyroiditis and drug involvement was suspected because it is onset during immunosuppression. However, considering the masking effect of symptoms by TCZ, the pathology of this case seemed to be highly likely to be subacute thyroiditis due to viral infection.

P2-262

Normal weight obesity and sarcopenia in rheumatoid arthritis

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Conflict of interest: None

[Object] Normal weight obesity (NWO) and sarcopenia appears most commonly on rheumatoid arthritis (RA), The purpose of this study was to investigate an association between NWO and sarcopenia in RA patients. [Methods] 93 patients (18 men, 75 women, average age 70.5) received the evaluation of body composition by DXA and physical functions were enrolled in this study. F% men 25%, women 30% or more over and BMI below 25 classified as NWO. SMI below 7.0kg/m^2 in men, 5.4 kg/m^2 in women classified in the muscle mass sarcopenia (MMS), Hand grip strength below 26 kg in men, 18kg in women classified in the muscle power sarcopenia (MPS), and walking speed below 0.8m/sec or TUG over 15 sec in the physical function sarcopenia (PFS). MMS with MPS or PFS was classified as SAR, Prevalence of sarcopenia (MMS, MPS, PFS, SAR) in RA patients with or without NWO were compared. [Results] 45 patients were classified in NMO, The prevalence of MMS: 64.4% in patent with NWO, 41.7% without NWO, MPO: 88.7% with NWO and 72.9% without NWO, PFO: 15.6% with NWO and 25.0% without NWO. SAR: 60% with NWO and 33.3% with out NWO. [Conclusions] In RA patients, prevalence of NWO and sarcopenia was high. Nutrion and physical activity Supports for RA patients should be planned in consideration of NOW, but figure.

P2-263

Efficacy of Neurotropin in acute severe pains related Fibromyalgia

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Conflict of interest: None

Fibromyalgia is a refractory disorder and indicates a chronic widespread pain disorder that has been associated with fatigue, sleep disturbance and other symptoms. Usually the doctors are prescribe several strong medication such as amitriptyline, cyclobenzaprine, SNRI, NSAID, and opioid materials for managing pains of patients. In Japan the solutions and tablet of Neurotropin (NT) including extract from the inflamed skin of rabbits inoculated with vaccinia virus are available. It is a nonprotein substance and commonly prescribed analgesic drug for chronic pain. It consists of multiple components, but what components effective are not clear nor classified. However a deficit of descending pain inhibitory systems has been suggested to contribute to fibromyalgia and several reports has been made. We prescribed NT against patients' pain with fibromyalgia. The effect of oral prescription in 20 cases was limited, and injection of NT was almost no improvement. But intravenous drip infusion of solutions are so effective in 8 severe cases. There was no clinical manifestation of side effect and adverse effects rarely occur even in the massive dose of NT. That means we can safely apply this drugs to manage the pain of patients in any type of fibromyalgia and in log-term treatment.

P2-264

The age-specific prevalence of complications in Rheumatoid Arthritis (RA) - a single center study -

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Conflict of interest: Yes

[Object] Elderly patients with RA have gradually increased year by year. We evaluated the age-specific prevalence of complications in RA. [Methods] This study comprised 1099 patients with RA (female:male, 853:245; age: 64.5±14.2yr). We divided RA patients into 7 groups based on age (20s:-29yr, 30s:30-39yr, 40s:40-49yr, 50s:50-59yr, 60s:60-69yr, 70s:70-79yr, 80s:80yr-), and compared the prevalence of complications among 7 groups. We also evaluated the correlation between age and laboratory findings. [Results] Of 1099 patients, complications was present in 518 (45.5%). The prevalence of complications significantly increased with age (20s:14.8%, 30s:10.0%, 40s:18.8%, 50s:34.0%, 60s:46.6%, 70s:57.6%, 80s:64.0%). The prevalence of hypertension, diabetes mellitus and dyslipidemia increased from 40s, cancers and chronic interstitial lung diseases from 50s, and ischemic heart diseases from 60s. Organizing pneumonia, thyroid diseases, and lymphoproliferative diseases did not increase with age. There was the negative correlation between age and eGFR or albumin level (correlation coefficient: -0.50 and -0.29, respectively). [Conclusions] The results showed that many elderly RA patients had complications and rheumatologists needed to take an attention on both RA and complications.

P2-265

A bullous pemphigoid patient complicated with rheumatoid arthritis and Sjögren's syndrome with various autoantibodies under long-term MTX and anti-TNF-alpha treatment

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Conflict of interest: None

A 65-year-old woman with rheumatoid arthritis (RA) and Sjögren's syndrome (SjS) with various autoantibodies under long-term MTX and anti-TNF-alpha treatment developed bullous disease. Laboratory examination revealed positive anti-nuclear antibody (Homo, Speckle, Centromere, Golgi), anti-ds-DNA antibody, anti-ss-DNA antibody, anti-CCP antibody, RF, anti-SS/A antibody, anti-TPO antibody and PA-IgG. Skin biopsy was performed and pathological examination revealed subepidermal bulla with inflammatory eosinophil-predominant infiltrate, linear deposits of IgG and IgM at the basement membrane zone (BMZ), and IgG- and anti-BMZ antibodies-epidermal pattern, and serum anti-BP 180 antibodies were positive. We diagnosed her with bullous pemphigoid (BP) and eliminated anti-TNF alpha therapy. In parallel, we started topical glucocorticoid and oral doxycycline therapy, then, her symptoms were immediately resolved. BP complicated with RA or SjS are extremely rare with or without anti-TNF-alpha treatment. However, increment of elderly patients or long-term anti-TNF therapy might induce such autoimmune disorders including BP in RA/SjS patient. This case prompted us to speculate the relationship among autoantibodies, biologics, and development of BP.

P2-266

Methotrexate-associated pneumonia (MTX-P), analysis of 7 cases diagnosed at our hospital

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Conflict of interest: None

[Object] MTX plays a central role in the treatment of rheumatoid arthritis. On the other hand, severe adverse event has been concerned. MTX-P has also been noted. We experienced 7cases of MTX-P at our hospital and analyzed the features. [Methods] 7 cases of MTX-P diagnosed and treated at our hospital between 2004 and 2016 are enrolled in this study and retrospectively analyzed. All cases are definite cases with modified criteria of Searlers and McKendry [Results] All patients were female. Average age 73.3 years (68-78), MTX dose 5.6mg (4-8), use period 33.6 months (3-192), all cases except 1were within 24 months and 4 cases were within 6 months. 4 cases were steroids, 1case was tocilizumab being treated. The initial symptoms did not necessarily show cough symptoms. Headaches and malaise were the reasons for visit in 2 cases. In 2 cases, it developed after orthopedic surgery. Diabetes and hypoalbuminemia before onset were not observed. All cases were recovered in treatment including MTX withdrawal and steroid therapy. [Conclusions] MTX-P was considered likely to occur in older patients, within 2 years MTX administration and after surgery. Steroids and biologics will not inhibit the onset. Early detection and discontinuation of MTX are considered important.

P2-267

Low dose Sulfamethoxazole (SMX)/Trimethoprim (TMP) treatment for pneumocystis jirovecii pneumonia (PJP)

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Conflict of interest: None

[Object] PJP is a well-known opportunistic infection and is life threatening in patients using immunosuppressive drugs or biologics for rheumatic diseases. The recommended dosage for PJP is 15-20 mg TMP/kg/day for 2-3 weeks. High dose SMX/TMP for long duration, frequently result in adverse drug reactions such as electrolytic abnormality or renal failure. This study is aimed to evaluate the efficacy of low dose SMX/TMP for PJP patients. [Methods] We retrospectively enrolled patients with PJP diagnosed in our department from 1998 to 2017. [Results] PJP patients were 27 cases (26 RA and 1 dermatomyositis). The average age at the onset of PJP was 77.4 years. All and 19 patients in that had been treated with PSL (mean 7mg/day) and MTX (mean 6mg/week) respectively before the onset of PJP. Biologics were used for 6 patients. 23 cases and 4 cases were treated with SMX/TMP and atovaquone respectively. The average dose of TMP was 4.87mg/kg/day. After the onset of PJP, 23 case were given increased total dose of prednisolone, and 4 case had pulses of mPSL 1g IV. The 28 days survival rate of PJP patients were 100%. No serious adverse events frequently seen in high dose SMX/TMP occurred. [Conclusions] We conclude that low dose SMX/TMP is effective and safe for PJP.

P2-268

Development of Pneumocystis jirovecii pneumonia (PJP) after discontinuation of salazosulfapyridine (SASP) in patients with rheumatoid arthritis (RA)

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Conflict of interest: None

[Object] Recently SASP has been reported to effective for the prevention of PJP (Mizushina K, Mod Rheumatol 2016). We presented the same results in JCR 2017. We here studied on the relationship between the development of PJP and drugs used before PJP. [Methods] Subjects were 22 patients with RA who experienced PJP. The mean age was 72 years (range: 51 - 86). Diagnosis of PJP was done according to the report by Harigai et al (N Engl J Med 2007). Drugs used before the development of PJP were surveyed. [Results] Of 22 PJP patients, 13 had a history of administration of SASP. Two of them were taking SASP at the time of PJP development. The rest of the patients had taken SASP before, but it was discontinued before the development of PJP. The median interval between discontinuation of SASP and PJP development was 7 months (range: 3.2 - 70 months). In patients who had PJP after discontinuation of SASP, PSL (median 8mg) were being taken in every patient, MTX in 10/11 (median 8mg), and bDMARDS in 7/11, which suggest high disease activity. Other risk factors than drugs used were not found. [Conclusions] SASP was again suggested to be effective for the suppression of PJP development.

P2-269

Prognostic factors of Pneumocystis pneumonia in patients with systemic autoimmune diseases

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Conflict of interest: None

[Object] *Pneumocystis* pneumonia (PCP) is one of the representative opportunistic infections. There have been many reports about risk factors for occurrence of PCP in systemic autoimmune disease patients. However, prognostic factors in PCP have not been studied. [Methods] We retrospectively collected patients who developed PCP during immunosuppressive treatments for systemic autoimmune diseases, and assessed baseline characteristics, immunosuppressive treatments prior to the onset of PCP, treatments for PCP and survival. [Results] A total of 95 patients was identified, and 42 deaths (44.2%) were observed. Age at diagnosis of PCP was higher in non-survivors than survivors (74y vs. 64y, $p=0.008$). Non-survivors had more frequent lung involvement than survivors (47.6% vs. 13.2%, $p<0.001$). The majority of the patients (91.5%) received glucocorticoids prior to the onset of PCP, and the median dose of prednisolone at diagnosis of PCP was higher in non-survivors than survivors (20 mg vs. 12.5 mg, $p=0.006$). [Conclusions] Although PCP occurred in patients treated with even no or low-dose glucocorticoids, prognosis of PCP in such patients was generally good. Our results suggest that prophylaxis for PCP is not mandatory for patients treated with no or low-dose glucocorticoids.

P2-270

Pneumocystis Jirovecii Pneumonia complicated with Rheumatoid arthritis from Kansai Consortium for Well-Being of Rheumatic Disease Patients (ANSWER cohort)

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Conflict of interest: None

<Objectives> Pneumocystis jirovecii pneumonia (PJP) is a severe lung infectious disease complicated with RA. Prophylactic antibiotics should be considered for RA patients received immunosuppressive therapy. <Methods> Patients were enrolled from the multicenter observational registry - ANSWR Cohort (Kansai Consortium for Well-Being of Rheumatic Disease Patients) - from August 2008 to October 2017. Patient's characteristics, blood examinations, administrations for RA, DAS, prophylaxis with PjP were analyzed. <Results> A total of 37 patients (10 males,27 females) were included. Mean duration;28.5 months. DAS28-CRP;3.61. The rate of MTX administration;86% (6.75 mg/w), PSL;68% (5.2 mg/d), biologics;37.8%. Two cases were treated with SASP. No patients were administered prophylaxis with ST except for 3 with Atovaquone. Six patients died (16.2%). Prophylaxis rates were over 60% after PjP therapy. Despite the use of MTX and Biologics were decreased, that of PSL and TAC increased. Disease activity of RA remained LDA after PjP in our registry. <Conclusion> This study showed that prophylaxis with trimethoprim-sulfamethoxazole is effective for preventing PjP in RA patients. We should consider optimal use for immunocompromised patients and ones complicated with DM, several lung diseases and prevent future outbreaks.

P2-271

Hypercalcemia with rheumatoid arthritis and pneumocystis pneumonia: a case report

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Conflict of interest: None

An 87-year-old woman was diagnosed with rheumatoid arthritis (RA) 4 years ago, and treated with methotrexate (4mg/week). She presented with of general fatigue and dyspnea that appeared 1 month ago. Her primary doctor diagnosed her anemia by the blood test 3 weeks ago. She was emergently hospitalized because of fever. Blood examination revealed pancytopenia, high inflammatory reaction, kidney dysfunction, and hypercalcemia. She was diagnosed with pneumocystis pneumonia (PCP) based on high β-D-glucan levels and diffuse ground-grass opacity of bilateral lungs in chest computed tomography scans. She was administered sulfamethoxazole-trimethoprim, and her condition improved. Despite no medication history of Ca or vitamin D supplements, serum 1, 25-dihydroxyvitamin D level was elevated and i-PTH level was suppressed. There was no evidence of acid-fast bacteria, lymphoproliferative disease, or granulomatous disease. Hypercalcemia was considered the cause of PCP. As pneumonia resolved, serum 1,25-dihydroxyvitamin D level normalized along with hypercalcemia resolution. I report a rare case of a patient with RA who developed PCP who developed hypercalcemia. In immunocompromised patients, pulmonary infection accompanied by hypercalcemia should raise the suspicion of PCP.

P2-272

Pneumocystis jirovecii pneumonia prophylaxis for rheumatoid arthiritis -Data from Kansai Consortium for Well-Being of Rheumatic Disease Patients (ANSWER) cohort-

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Conflict of interest: None

[Background] Pneumocystis pneumonia (PCP) is an important complication in treatment for rheumatoid arthritis (RA). Prophylaxis with trimethoprim-sulfamethoxazole (SMX-TMP) is well-established. [Methods] We evaluated the usage of PCP prophylactic agents (PCP-PAs) on the first visit day in 2016 among the RA patients registered in the ANSWER Cohort. [Results] The number of patients was 1538 (336 males and 1202 females, age: 64.5±21.8 years old, DAS28-CRP: 2.30±1.01). Methotorexate (MTX), salazosulfapyridine (SASP), predonisolon (PSL) and bDMARDs/JAK inhibitor (JAKi) were used for 898 (58.4%), 304 (19.8%), 418 (27.2%) and 558 cases (36.3%). PCP-PAs were administered for 155 cases (10.1%; SMX-TMP for 147 and atovaquone for 8). The PCP-PAs were used for 18.5% of bDMARDs/JAKi users, 5.8% of bDMARDs/JAKi non-users. According to dose of PSL and MTX, PCP-PAs were administered as below; PSL0mg: 5.2%, PSL0mg< ≦5mg: 18.3%, PSL5mg< ≦10mg: 35.4%, PSL10mg<: 64.3%, MTX0mg: 13.1%, MTX0mg< <6mg: 10.7%, MTX6mg≦ <12mg: 6.5%, MTX-12mg≦: 10.4%. PCP-PAs were used for 7.9% of under 65 years old, and 12.0% of 65 years old or older. Among all patients, PCP developed in 3 cases without SMX-TMP and SASP. [Conclusion] PCP-PAs were tended to be administered for bDMARDs/JAKi users, PSL users and elderly patients.

P2-273

Assessment of the cases performed hyposensitization of the sulfamethoxazole-trimethoprim (TMP/SMX) and the relationship of a pharmacist

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Conflict of interest: None

Object For an allergy by the TMP/SMX (T/S) for the PCP prevention during immunosuppression treatment, there are many reports of the usefulness of the hyposensitization. In our Rheumatic division, we also try to do the hyposensitization and readministration. We here report the cases of the hyposensitization therapy and review. **Method** We intended for 8 cases that performed hyposensitization of the T/S from July 2016 to 2017, investigated retrospectively the status of allergy such as duration of illness, T/S starting dose, history of allergy, time of allergy appearance.I, as a pharmacist, explained the necessity of the therapy to the patients. **Result** 6 patients were within 2 months of disease duration. The starting amount was varied in each patient.6 patients had past history of allergic to medicine. Appearance time of allergy was an average of 13 days. We could readministrate in 6 of 8 patients who underwent hyposensitization therapy. **Conclusion** In our study, hyposensitization therapy enabled the readministration of T/S in many cases.I'd like to continue consideration and utilize for the explanation when administrate the drug. In addition, not only the doctor, the pharmacist have to explanation before the hyposensitization, to reduce the anxiety of the patient and understand the necessity of taking T/S.

P2-274

Nontuberculous mycobacterium infections in patients with rheumatoid arthritis: a single-center experience in Japan

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Conflict of interest: None

[Object] To identify the clinical characteristics of NTM infections in patients with rheumatoid arthritis (RA). [Methods] We assessed 11 RA patients complicated with NTM (mean age, 66.6 years) at our institute. [Results] Average values obtained with SD were as follows: age (years), 66.6 ± 8.0; Steinbrocker stage I, 1; II, 0; III, 1; and IV, 9; Class 1, 2; 2, 5; 3, 4; and 4, 0; disease duration (months), 274.9 ± 126.9; positivity of anti-CCP antibody, 80.0%; positivity of rheumatoid factor, 100%; HAQ-DI,

1.35 ± 0.72; DAS28-ESR, 3.61 ± 0.90; detection by sputum culture, 81.8%; NTM species, *M. avium*, 8 cases and *M. intracellulare*, 3 cases; bronchiectasis, 90.9%; interstitial pneumonia, 0%; methotrexate use and dosage (mg/week); 63.6% and 7.4 ± 3.4; prednisolone use and dosage (mg/day); 81.8% and 4.3 ± 2.0; biological agent use, 45.5%; and anti-NTM therapy, 36.4%. [Conclusions] RA patients complicated with NTM were long-standing, had high disease activities and worse HAQ-DI. In all five patients (45%) who were treated with biologics, 3 who had preceding episodes of NTM infection were treated with anti-NTM therapy before treatment with biologics, and the other 2 who had asymptomatic NTM infection after treatment with biologics were not treated with anti-NTM therapy thereafter.

P2-275

Prognostic factors of non-tuberculous mycobacterial (NTM) infections in patients with rheumatoid arthritis

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Conflict of interest: None

[Introduction] Recently, the numbers of patients with pulmonary mycobacterium avium complex diseases have been increased in Japan, especially in patients with rheumatoid arthritis (RA) under immunosuppressive therapy. We examined factors influencing the prognosis of pulmonary NTM diseases complicated with RA patients. [Methods] We retrospectively reviewed 36 RA patients who were diagnosed or suspected with NTM infections at Tokai University Hospital between 2006 and 2016. We analyzed age, biochemical markers, RA disease activity, drug therapy for RA, antimicrobial agents and radiographic findings as prognostic factors. [Results] All patients were female and the mean age was 65.9 years. Isolated species of NTM was as follows; M. avium 73%, M. intracellulare 18%, and M abscessus 9%. The course of CT findings were classified into 3 groups; progression (6 cases), unchange (19 cases), and improvement (11 cases) by the CT findings. Immunosuppressive therapy was reduced in 34 patients. Advanced age, poor control of RA activity, extensive lesions with cavity formation and hypoalbuminemia were poor prognostic factors. [Conclusion] In pulmonary NTM diseases complicated with RA patients, reduction of the immunosuppressive therapy is important with the control of RA disease activity.

P2-276

Clinical course of RA patients suspected of nontuberculous mycobacterium (NTM)

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Conflict of interest: None

[Object] To investigate clinical course of RA patients with confirmed/suspected NTM infection. [Methods] We extracted NTM culture positive RA patients in ANSWER cohort, and surveyed patients profile and clinical course (RA disease activities, RA and NTM treatments). [Results] 64 RA paitents (mean age 67; disease duration 103 months) were extracted. 46 cases (MAC 40, Abscessus 3, Kansasii 1, unknown 2) fulfilled NTM bacteriological criteria. 33 patients were treated with MTX, 27 patients with GCs, 18 patients with biologics and 4 patients were no medication. After one year, 16 cases were added other DMARDs or increased dosage, and 12 cases were reduced or discontinued DMARDs. 27 patients were received NTM treatments and only 2 cases showed exacerbation of NTM infection. Further in evaluable 28 cases, we examined RA disease activity at baseline and one year later. In these cases, Mean CDAI decreased from 8.08±6.82 to 7.05±6.06 but not significantly, and 5 cases changed LDA to MDA. [Conclusions] In this study, RA disease activity of almost patients were controlled and few patients were NTM exacerbation, But NTM infection is slowly progressive disease, and we should confirm our results by long term follow up.

P2-277

A surgical case of spondylodiscitis due to Mycobacterium abscessus in a patient with rheumatoid arthritis treated with biologic agent

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Conflict of interest: None

[Case] 58 year-old female with the history of RA (11 years) introduced our hosptal becouse of sever back pain and gait disturbance. Administration of ETN to the patient contnued for 3 years combined with MTX and PSL at the previous hospital. Under the diagnosis of lumbar disc herniation block injection was performed couple of days before administration. Bilateral lower leg paresthesia and muscle weakness was observed and bladder/rectal disturbance were examined from the patient. From the MRI L4/5 dicitis and extra dular abscess and iliopsoas abscess were revieled. Emergent irrigation of the abscess and posterior lumbar cannal decompression were performed on the day. Subsequentry posterior paravertebral and sacroilliac fusion was performed 19 days after emergency operation. While acid-fast bacterium was observed in abscess, antiTB treatment was started without delay. Based on the result of TB/MAC PCR negative and culture plus CAM+AMK+IMP/CS treatment were performed assuming M. Abscesssus as a causative agent. After administration of 122 days patient dicharged without back pain and neurological symptoms. Anti-bacterial treatments were performde for 2 years.

P2-278

A case of systemic lupus erythematosus complicated by tuberculous fasciitis

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Conflict of interest: Yes

A 42-year-old Chinese woman in whom systemic lupus erythematosus (SLE) had been diagnosed 7 month previously, was referred to our clinic with fever and painful swelling of right forearm. She had received 30 mg/day prednisolone and azathioprine for the treatment of mesenteric panniculitis. Physical examination was unremarkable except for swelling and tenderness of right forearm, and chest x-ray was normal. She was initially treated with intravenous antibiotics, but this treatment did not improve her symptoms. A few days later, she developed newly painful swelling in her buttock and both femoral regions. MRI findings of right forearm and both femurs indicated increased T2 signal intensity within fascial layers. Muscle biopsy from the left vastus lateralis was performed, and this tissue specimen revealed a *Mycobacterium tuberculosis* infection. She was diagnosed with tuberculous fasciitis. Clinical significance: Tuberculous fasciitis, a type of mycobacterial soft tissue infection, is uncommon disorder and it encountered in immunocompromised patients. It may mimic lupus panniculitis clinically, and delayed diagnosis can lead to serious results. Rheumatologists should be aware of tuberculosis fasciitis for the differential diagnosis of soft tissue inflammation.

P2-279

Examination of the tuberculosis screening results in the patients of rheumatoid arthritis in our hospital

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Conflict of interest: None

[Object] In immunosuppressive therapy (IST) for the articular rheumatism (RA), the onset of tuberculosis becomes the remedial problem. We report the actual situation of the examination of tuberculosis in the RA patients in this hospital. [Methods] We examined tuberculosis RA patients 319 whom we screened backward for from August, 2007 to July, 2016. [Results] Men 49, women 270 cases, the age were 61.6±13.8 years old. The patients with IST were 262 patients. IGRA was carried out in all cases. 14 patients were positive, and 201 patients were with negative results of IGRA. The patients who had a diagnosis of a latent tuberculosis infection (LTBI) were 86 patients. As for the sensitivity of IGRA, 9.3%, the specificity were 86.6%. ACPA was measured in 295 cases. The patients with positive both ACPA and IGRA were 12 patients. Of these, LTBI and the patients who had a diagnosis were eight patients, and the sensitivity was 66.7%. The patients with negative both ACPA and IGRA were 39 patients. Of these, the patients that LTBI was denied were 36 patients and were 92.3% of specificity. [Conclusions] It was confirmed that the patients in IST had decreased sensitivity of IGRA. The possibility that sensitivity and the specificity improved both was suggested by measuring both IGRA and ACPA.

P2-280

A case of developing active pulmonary tuberculosis during remission induction therapy of lupus nephritis

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Conflict of interest: None

Case: 32 year old Filipino woman. She was diagnosed with systemic lupus erythematosus with type IV lupus nephritis (IV LN) 7 years before admission. Remission was induced with high-dose steroid and cyclophosphamide and maintained with prednisolone (PSL) 15 mg + cyclosporine 100 mg. She was admitted for relapsing IV LN. T-SPOT on admission was negative. IV LN relapse or migration to type V was suspected; treatment started with PSL 30 mg, mycophenolate mofetil (MMF) 2000 mg, and tacrolimus 2 mg. Due to treatment resistance, treatment was changed to PSL 60 mg + MMF 2000 mg on IV + V type on the 35 day. CT on the 71 day found that a nodule in S1, which was 5 mm on admission, grew to 15 mm, and the nodule grew to 25mm. Though acid-fast bacterial tests were negative, acid-fast bacilli were cultured from bronchoalveolar lavage, 3 weeks after bronchoscopy, and identified as *M. tuberculosis (TB)*. Sputum on the 120 day showed Gaffky No. 9 and she was diagnosed of active pulmonary TB. LN was still active; she was transferred to a specialized hospital on the 127 day. Active pulmonary TB occurred during induction therapy. T-SPOT has a window period and induction therapy increased the false negative rate; patients from high-burden countries need to be monitored by different modalities.

P2-281

A case of SLE complicated by disseminated nocardiosis which was difficult to diagnose and treat

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Conflict of interest: None

A 72-year-old woman visited our hospital with a low grade fever of refractory to antibiotics in 2011. After detailed examination, she was diagnosed as having SLE. As there was no remarkable organ lesions, she was treated with prednisolone 5mg/day. In August 2015, she was hospitalized due to lung abscess and treated successfully. After she was discharged, she got a fever again, and diagnosed as having subcutaneous abscess in the back. Stab culture of the right lower back revealed a gram positive rod. Since Nocardia infection was suspected from the history of lung abscess and elevation of serum β-D glucan level, we administered with trimethoprim-sulfamethoxazole and minocycline. Later the pathogen was reported to be N.farsinica. However, 2 weeks later, abcess of the same site relapsed. According to susceptibility, we initially administrated with imipenem/cilastatin and amikacin for 9 weeks, switched to oral administration of amoxicillin/clavulanate and sitafloxacin, and the symptoms stabilized. It was suggested that Nocardia infection should be considered in the immunocompromised hosts like this case.

P2-282

Plumonary cryptococcosis in a patient receiving abatacept for rheumatoid arthritis: a case report

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Conflict of interest: None

[Object] Special attention should be given to opportunistic infections in RA patients (Pts) treated with biologics (BIO). We report a case of pulmonary cryptococcosis (PC) in a Pt receiving ABT. [Case report] A 79-year-old female Pt, who had developed RA in1991, was in low disease activity with MTX 10mg/week, BUC 200mg/day and TAC 2mg/day. In September 2016, a therapy with ABT SC was started due to flare up of arthritis, and improved it. After 6 months, she had intermittent low fever. She was consulted to respiratory medicine due to abnormal shadow in chest CT. A course of antibiotics with discontinue of ABT could not improve the pneumonia. The Cryptococcus neoformans antigen was detected from her serum and bronchial lavage fluids, indicating a diagnosis of PC. Antifungal treatment with fluconazole was started and effective. [Clinical importance] For the safe use of BIO, the JCR has developed guidelines. Pts should have comprehensive TB screening and prophylactic treatment, and a peripheral leukocyte and lymphocyte count test, and a negative test for (1-3)-β-d-glucan (BG). The value of BG level usually does not change in spite of fungal infection in PC. Therefore, Pts should regularly have chest imaging including CT test as well as blood test to monitor PC.

P2-283

Pulmonary nocardiosis caused by *Nocardia concava* in patient with systemic lupus erythematosus associated with mantle cell lymphoma

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Conflict of interest: None

A 76-year-old Japanese male with 18 year history of mantle cell lymphoma was admitted to our hospital because of fever and cough. One year before, systemic lupus erythematosus developed and he received oral PSL. Laboratory examination showed as follows; CRP 19.3mg/L, WBC 19400/μL (NETU 95%), β-D-glucan <6.0pg/mL. Computed tomography revealed multifocal consolidation with nodular infiltration in the bilateral lung lobe. Cultures from the sputum showed *Nocardia concave* and we confirmed the identification result using a sequence analysis of the 16S rRNA gene. MINO was administrated and subsequently his symptoms improved without relapse. Pulmonary nocardiosis is a common disease in immunocompromised hosts. Furthermore, the reduction of infection prevention ability in pulmonary local area is considered to be one of important risk factors for pulmonary nocardiosis. *Nocardia concava* is a new Nocardia species identified in 2005. To date, there have been few reported cases in the English literature. Here, we report a rare case of *Nocardia concave* infection in systemic lupus erythematosus associated with mantle cell lymphoma.

P2-284

A case of the Legionella pneumonia which it was difficult to distinguish from polymyositis because she suffered rhabdomyolysis

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Conflict of interest: None

[Case] The patient was 66-year-old woman. She was prescribed fever, cough, muscle pain, muscle weakness, and joint pain. WBC level was 13030/μl. CRP level was 31.76 mg/dl. CK level was 14008 U/l. Aldolase level was 31.1 U/l. Chest X ray showed reticular shadow in the lower left lungs. We met diagnostic criteria five items of the polymyositis. So we considered polymyositis and interstitial pneumonia and she admitted to our hospital. We started to give ceftriaxone, because myositis by infection and rhabdomyolysis were undeniable. The autoantibody was negative. Urinary Legionella pneumonia antigen positive became clear. By history taking, we knew that she stayed at the hot-spring hotel in kyoutango before 8 to 9 days. So we diagnosed Legionella pneumonia. Pneumonia was cured, her muscle symptom was improved and CK level was normalized by levofloxacin, and she left our hospital. [Clinical significance] Legionella pneumophilia is the most in a cause microbe of community-acquired pneumonia to be complicated with rhabdomyolysis. It was reported that the death rate is high when accompanied by rhabdomyolysis for Legionella pneumonia. When community-acquired pneumonia to be complicated with rhabdomyolysis present, we should perform an examination for urinary Legionella antigen.

P2-285

Clinical characteristics of urinary tract infection in patients with rheumatic disease

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Conflict of interest: None

[Object] To investigate the clinical features and the prognostic factors of urinary tract infection (UTI) in patients with rheumatic disease (RD). **[Methods]** We retrospectively identified UTI patients with RD (n=41, RD/UTI group) and without RD (n=407, non-RD/UTI group) who were admitted to our hospital from April 2008 to December 2016. Clinical features were compared between the two groups, and prognostic factors of UTI patients with RD were investigated. **[Results]** RD/UTI group had a significantly younger age at onset of UTI (72.1±9.9 vs 78.2±12.5, p=0.014) and a higher rate of complicating urolithiasis (10.4% vs 3.2%, p=0.032) compared with non-RD/UTI group. After adjusting for age and gender, RD/UTI group had a higher incidence of septic shock (12.5% vs 4.7%; OR, 3.87; p=0.019). Although no risk factor of septic shock was identified by univariate analysis, use of prednisolone (≧5mg/day) and non-use of methotrexate could be associated with the risk of septic shock. In-hospital mortality was similar in both groups (4.2% vs 5.2%; OR, 1.39; p=0.69). **[Conclusions]** It should be noted that patients with RD had a higher risk of septic shock caused by UTI. The management of septic shock and urolithiasis is required in treatment of UTI with RD.

P2-286

Gait disturbance caused by multiple gouty tophi: a case report

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Conflict of interest: None

[Case Presentation] A 29-year-old man with an 8-year history of gout was referred to our hospital for surgical removal of gouty tophi. He complained of multiple joint pain and gait disturbance for several months. Physical examination revealed that there were multiple large tophi over bilateral elbows, wrists, and ankles. Range of motion was limited in bilateral knees and ankles. MRI showed soft tissue swelling with multiple tophi deposition inside and around the bilateral knees and ankles. Laboratory tests revealed the following values: sUA 6.9mg/dl, sCr 1.14mg/dl, eGFR 64 ml/min/1.73m^2, sCRP 2.7mg/dl, ESR 44mm/h. He continued medication therapy with potassium citrate, sodium citrate, and febuxostat. Arthroscopically assisted surgical management was performed with resection of tophi in bilateral knees and ankles. After several-month physiotherapy courses, these joints functions were significantly improved. He returned to work as a cram school teacher at 4 months postoperatively. [Clinical Value] Surgical treatment should be considered when tophi causes decreasing activity of daily living. The potential advantages of the arthroscopically assisted surgery include minimal tissue damage, less wound complications and earlier joint mobilization.

P2-287

Case report: Orthopeadic infections complicated with autoimmune disease

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Conflict of interest: Yes

[Object] We reported on orthopeadic infections complicated with autoimmune disease. [Methods] There are 4 cases, all cases were females, the mean age at onset was 63.8 years (62 - 66 years). The original diseases were rheumatoid arthritis, optic neuromyelitis, polymyositis, dermatomyositis, respectively, one was treated with methotrexate (MTX), two were treated with prednisolone (PLS) and tacrolimus (FK 506), and three cases had diabetic complications. [Results] Infected areas were a hip joint after THA, two knee joints, and a gluteus medius including the hip joint. In 2 cases, inflammation had spread to the bone marrow. The causative organisms were methicillin - sensitive S. aureus and extended spectrum β-Lactamase producing E. coli. In all cases, surgical treatments were performed and Hicmann catheters were placed. After surgery, daily washing and high concentration local injection of amidoglycoside antibiotic agent were performed. Two patients had merger of pneumonia, but all cases were resolved infections. [Conclusions] Although they were infectious diseases associated with autoimmune disease, surgical procedures succeeded in resolving the infections relatively early.

P2-288

Two patients with rapidly progressed streptococcosis

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Conflict of interest: None

Case 1. 78-year old man was admitted to Dept. of Orthopedics in our hospital with lower back pain and polyarthralgia and transferred to our division due to persistent fever and erythema on extremities. Labo; WBC 22260 CRP 24 mg/dl ESR 101mm/h ACPA (-) ASO 388 IU/ml ASKx20480. Streptococcus dys. Cquisimilis was detected by blood culture. P-R prolongation on ECG was investgating. We diagnosed him as rheumatic fever. Penicillin G/clindamycin and celecoxib were continued. Symptoms were improved. Case 2. 58-year old woman was admitted by polyarthralgia with high fever and right sore eye. She was seen by a general practitioner who prescribed an antipyretic. Physical examination revealed conjunctivitis and corneal erosion of right eye and erythema on extremities. Labo; WBC 10580 CRP 16 mg/dl RF (-) ASO 72 IU/ml ASKx320 blood culture; streptococcus pyogenes. Sulvasilin was started but she transferred to University Hospital because of ophtalmectomy. Streptococcosis including rheumatic fever is important, even in adult patients as a differential diagnosis of acute onset polyarthritis. As our patients did not have typical tonsillitis, the final diagnosis was done by our division. Since streptococcosis can rapidly fall into critical condition, quick diagnosis and treatment are necessary.

P2-289

A case of PR3-ANCA positive infectious endocarditis that could be distinguished from granulomatosis with polyangiitis because ofby appropriate infection screening

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Conflict of interest: None

[Case] 67 years old, male [Onset and coarse] He had a history of gingival abscess in February 201X. He admitted because of 4-month history of fever. He had visited clinics and treated by anti-tuberculotic drugs and low dose of oral prednisolone (5 mg/day) for pulmonary cavitary and multiple nodular lesion detected by chest CT scan. Even though those treatment have been administered, his fever have not been resolved. On September 201X, he showed acute renal dysfunction with glomerular hematuria and positive of various auto-antibodies including PR3-ANCA. He satisfied the ACR classification criteria for granulomatosis with polyangiitis (GPA). We performed some examination to rule out infectious disease before the beginning of immunosuppressive therapy and found a vegetation on tricuspid valves by echocardiogram and Enterococcus faecalis was detected from all three sets of blood culture. He satisfied Modified Duke's criteria for infectious endocarditis (IE) and combination of antibiotics were administered. The titer of PR3-ANCA were soon decreased. He gradually recovered and discharged from hospital on 60th day. [Conclusion] PR3-ANCA is a specific marker for GPA, however some IE patients showed positive of PR3-ANCA. Thus, we have to rule out infectious diseases in such patients.

P2-290

A case of abscess formation around pubic joint by P. aeruginosa during secukinumab therapy

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Conflict of interest: None

[Background] Secukinumab is now available for psoriatic arthritis (PsA) in addition to psoriasis vulgaris. It is reported that severe bacterial infection occurred only in 1% of cases 52 weeks after initiation of secukinumab, and pelvic abscess has never been documented. We report a case of abscess formation around pubic joint by *P. aeruginosa* during secukinumab therapy. [Case] A 72-year-old woman with PsA was attending to our clinic, who was treated with MTX and PSL. She had a history of cervical cancer, for which she received radiation therapy and developed vesicovaginal fistula as a complication. On June 201X, secukinumab was started due to worsening psoriasis. Two months later, she complained severe pain around the pubis, which was accompanied by inflammatory response of unknown origin. Pelvic CT showed space occupying lesion around pubic joint. *P. aeruginosa* was identified from culture specimen obtained by CT-guided biopsy of the lesion. [Discussions] Because IL-17 activates neutrophils, IL-17 inhibitor might have served as an integral part in development of abscess in this case, due to lack of neutrophil activity. [Conclusions] When we see patients on IL-17 inhibitor with inflammatory response without obvious etiology, infection including abscess formation must be ruled out.

P2-291

A case of progressive multifocal leukoencephalopathy in patient with systemic lupus erythematosus treated with mycophenolate mofetil

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Conflict of interest: None

[Case] A 55-year old female was diagnosed with systemic lupus erythematosus (SLE) by arthritis, renal dysfunction, positive of anti-nuclear antibody and anti-dsDNA antibody, and hypocomplementemia. She has been administered with prednisolone (PSL). From one year ago, 1 g mycophenolate mofetil (MMF) was added to 8 mg PSL. She falled down several times, and brain MRI showed high intensity area in cortex white matter in the right frontal lobe. Although antiplatelet therapy was started, headache, left hemiplegia, and articulation disorder were appeared, and the high intensity area by brain MRI was extended. IL-6 level and immunoglobulin G index in the cerebrospinal fluid were normal, but 16,400 copies/mL of JC virus was detected by PCR. Brain biopsy revealed oligodendrocyte with enlarged nucleus and star cells with heteromorphism, and JC virus antigen was observed by immunohistochemistry. She was diagnosed with progressive multifocal leukoencephalopathy (PML). Mefloquine was administered to the patient. [Clinical Significance] PML is a subacute central nervous system infection caused by JC virus. It is known to develop during immunosuppressant treatment for autoimmune diseases. However, there are only a few reports that MMF was considered as the causative agent.

P2-292

Pancytopenia and cytomegalovirus infection during treatment with leflunomide and methotrexate for rheumatoid arthritis

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Conflict of interest: None

A 55-year-old woman who had been diagnosed with rheumatoid arthritis seven years previously was admitted to our hospital because of fever. She had been under treatment with leflunomide and methotrexate. At the time of admission, blood tests revealed WBC 900/μL, neutrophil 600/μL, Hb 7.4 g/dL, and platelets 1.6 × 104/μL. Cytomegalovirus (CMV) antigenemia assays were positive and she had signs of CMV retinitis. She was diagnosed with febrile neutropenia, drug-induced pancytopenia, and CMV infection. We stopped the treatment with leflunomide and methotrexate and administered antibiotics, G-CSF, calcium folinate, cholestyramine, and ganciclovir, which gradually improved her status. Both leflunomide and methotrexate can cause pancytopenia. Little is known in Japan about the risks of methotrexate combined with leflunomide for adverse events. This case report described pancytopenia and cytomegalovirus infection in a patient with rheumatoid arthritis under treatment with leflunomide and methotrexate.

P2-293

A Case of Parvovirus B19 Infection Concurrent with Pulmonary MAC Infection that Showed Typical Features of SLE and Multiple Lung Nodules

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Conflict of interest: None

[Introduction] Patients with parvovirus B19 infection can present typical symptoms of SLE such as cytopenia, hypocomplementemia, skin rash and arthritis. Although both images and culture results are needed for diagnosis of pulmonary MAC infection, the utility of MAC antibody had been recognized. We are reporting a case of parvovirus B19 infection concurrent with pulmonary MAC infection that showed SLE features and multiple lung nodules. [Case] A 43-year-old woman presented with chronic cough and malaise followed by myalgia, arthralgia and erythema. Laboratory tests revealed leukopenia, lymphopenia, hypocomplementemia and ANA positivity. SLE was suspected initially, but the result of parvovirus B19 antibody IgM was positive. Chest CT showed multiple nodules. Although both sputum mycobacterium cultures and TSPOT were negative, a diagnosis of pulmonary MAC infection was made based on MAC antibody positivity and imaging findings. Myalgia, arthralgia and skin rash improved spontaneously. Treatment for MAC infection was started by pulmonologist. [Conclusion] It is important to rule out parvo-

virus B19 infection when we consider the possibility of SLE. The MAC antibody is useful when diagnosing pulmonary MAC infection in cases where we can't get appropriate specimens.

P2-294

Intracranial viral infection in early period of treatment NPSLE

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Conflict of interest: None

A 55-years-old woman presenting numbness of both lower limbs, granular casts in urine, lymphocytopenia, positive of anti-nuclear antibody, and anti-DNA antibody titer over 300IU/ml on October 2016. She fulfilled criterion in SLE. Anti-PCNA antibody and anti-ribosomal-P antibody were detected, and left tibial and sural nerves showed multiple mononeuritis. She admitted to the examination and treatment for NPSLE. She developed cognitive disorder, and her IL-6 in CSF increased to 8.8pg/ml. Her brain MRI showed multifocal leukoaraiosis. We started high-dose methylprednisolone at 1000 mg/day for 3 days, followed by 45 mg of PSL. Her cognitive disorder was improved, we added the IVCY. However, following HSV-DNA assay in CSF on the 22nd hospital day increased from under detectivity to 2.3×10*2copies/ml, and we started acyclovir therapy. On the 29nd hospital day, HSV-DNA assay decreased to under detectivity. We withdrew from IVCY because of active infection, and we added HCQ from the 47th hospital day. NPSLE has poor specific findings in CSF or imaging, and it requires differential diagnosis of infectious diseases and neurological diseases. We report that we treated the case with NPSLE suffered from intracranial infection of HSV in treatment on 22nd hospital day.

P2-295

One case of - Reactive arthritis by HB Virus, that arthritis showed something like RA

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Conflict of interest: None

Patient: 57years old, clerk Present illness: RF positive was since 10years ago. But since two months ago, light swelling and pain in the large joints and small joints were noticed out. She was HBV carrier, she was consulted at this clinic on July 30, 2016. Blood exa. (at. First visiting): General biochemical exa, peripheral blood count, blood picture are normal. Anti-ccp antibody (-), CRP0.33, RF32, erythrocyte sedimentation rate 17mm/h, ANA normal. HBV-real time 5.2Log-C (+), HBe antigen (-), HBe anti body 99.7/CLLA (+), HBs antigen Iu/ml:2048 (+++), HBs anti body (-), HBV geno type: B.Course; Treatment of Tenozet300mg was started on August2016. At the fourth month after starting, on December 2016; Wrists joints, right hand PIPs and right knee joints pain were diminished out bud swelling in the left knee joint was remained. Left knee joint fluid finding on January 2017: CH50 10.0↓, RF (+), HBs antigen 50Iu/ml (normal 0.05↓), Blood exa. on May, 2017: HBs antigen174Iu/ml (+), HBe antigen (-), HBe anti body 99/CLIA. Left knee joint fluid on May 2017: HBs antigen 21.6Iu/ml (+), CH50 10↓, HBV real time:not detected. Left knee joint fluid on July 2017: HB antigen 148Iu/ml, HBV real time (-). This case can be considesed reactive arthritis by HBV Virus and so this case will be treated by only Tenozet the more.

P2-296

A case of ANCA-associated hypertrophic pachymeningitis with bilateral pleural effusion and Sjögren syndrome

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Conflict of interest: None

A 48-year-old-woman was admitted to our hospital because of cough, chest pain, and bilateral pleural effusion. Causative agents or malignant cells were not detected in pleural effusion. Antibiotic therapy was not effective for pleural effusion and then swelling of bilateral knee joints appeared. After admission she complained of a headache and PR3-ANCA was 7.5 U/ml. Brain MR imaging showed hypertrophy and contrast enhancement of occipital lobe meninges, indicating ANCA-associated hypertrophic pachymeningitis. She complained mouth dryness, and the volume of salivary secretion by gum test was 7 ml per 10 minutes. Hypofunction was also revealed in salivary gland scintigraphy and the grading of labial salivary gland histopathology was 4. She satisfied the revised Japanese diagnostic criteria for Sjögren syndrome. With the administration of 55mg of prednisolone daily, headache got better, pleural effusion decreased, and swelling of bilateral knee joints went down. Finally her symptoms disappeared and C-reactive protein decreased to normal level. After combination with prednisolone and tacrolimus, she was discharged from the hospital. We report the case here because it was very difficult to diagnose her illness, and ANCA-associated vasculitis with pleuritis is very rare.

P2-297

Mycophenolate mofetil was successful histopathologically for Lupus nephritis Class V: a case report

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Conflict of interest: None

[Clinical Case] 30-year-old man. In 2003, he was diagnosed as systemic lupus erythematosus (SLE) from findings of butterfly erythema, hair loss, antinuclear antibody positive, anti ds-DNA antibody positive, anti-Sm antibody positive, low complementation, cytopenia, proteinuria and started prednisolone (PSL) 60 mg. This renal pathology was Lupus nephritis (LN) ISN/RPS classification ClassIIa. After that, relapse and remission were repeated. Renal biopsy was performed because SLE flared in 2006. The renal pathology at this time was LN ISN/RPS classification Clas V. Mizoribine and tacrolimus were added, but urinary protein 1-2 g/g·Cr was sustained. Therefore, when mycophenolate mofetil (MMF) was introduced in 2015, complete remission was obtained. In 2016, renal biopsy was performed for the purpose of disease condition evaluation. It was LN ISN/RPS classification class V, but the disappearance of deposits was confirmed by electron microscopy. There has not been a recurrence after that. [Conclusion] It is known that MMF is effective against SLE·LN, but histopathological changes before and after treatment have not been reported rarely. This case is a valuable case suggesting histopathological course of treatment and report it.

P2-298

A case of dialysis-related amyloidosis diagnosed with fever of unknown origin (FUO)

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Conflict of interest: None

A 67 years old woman on long term hemodialysis therapy had developed unstable angina during hemodialysis and admitted to the department of cardiology. Approximately 8 years before this admission, she had been introduced to orthopedics for the treatment of polyarthralgia, fever and iliopsoas abscesses. Emperic antibiotic therapy and focal curettage failed to improve her symptoms, however, she was successfully treated with prednisolone (PSL). 7 years before, she underwent operation on a left

femoral neck fracture. On admission, she had presented fever and polyarthralgia. Gallium scintigraphy demonstrated abnormal uptake in multiple joints, and she was referred to our department. Infection, connective tissue diseases, malignancy were ruled out by close inspection. Re-staining of the specimen from the past orthopedic surgeries, demonstrated the deposition of the Aβ2M amyloid. We diagnosed her with dialysis related amyloidosis (DRA) and her symptoms were resolved by PSL. Generally, in the setting of FUO, it is necessary to exclude the infection in immunocompromised patients undergoing hemodialysis. However, in some patients, systemic inflammation and synovitis are caused by cytokine production from the activated macrophage at the site of Aβ2M amyloid deposition.

P2-299

Cytomegalovirus retinochoroiditis diagnosed by taking aqueous humor in rheumatoid arthritis patiant treated with methotrexate and tofacitinib

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Conflict of interest: None

[Clinical Case] A 71-year-old woman. In 1995, she was diagnosed with multiple mononeuropathy associated with Sjogren's syndrome and treated with prednisolone (PSL). In 2008, she was diagnosed with rheumatoid arthritis. Her RA was did not improve with various biologicals, and in February 2017 finally it was treated with tofacitinib (TOF) 10 mg, methotrexate 8 mg / w, PSL 5 mg. In July 2017 visual acuity decline appeared. Retinochoroiditis was observed, and she was admitted. The CMV antigen was 52/5000 cells, therefore ganciclovir was started. However, βD glucan in blood became positive, and exacerbation of left vitreous opacity was observed, so fungal retinochoroiditis could not be ruled out. Aqueous humor was collected to determine the cause, followed by viral coverage PCR. Only CMV-PCR test is positive, diagnosed with CMV retinochoroiditis. [Conclusions] Although the risk of shingles is reported in TOF, there are few reports of CMV infection and CMV retinochoroiditis is less frequent. Diagnosis of CMV retinochoroiditis is often difficult, but there is also a risk of blindness, so prompt response is required. In this report, we report an example in which diagnosis of CMV retinochoroiditis was obtained by aqueous humor PCR, and lightness of visual acuity was obtained.

P2-300

A case of protopulmonary hypertension due to primary biliary cirrhosis complicated with systemic lupus erythematosus

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Conflict of interest: None

The present study reported a case of portopulmonary hypertension (POPH) due to primary biliary cirrhosis (PBC) complicated by pulmonary arterial hypertension (PAH) due to systemic lupus erythematosus (SLE). We would like to highlight the risks and benefits of continuous epoprostenol infusion therapy (INEPO) and intravenous cyclophosphamide (IVCY). The patient was diagnosed with Sjogren's syndrome at the age of 31 years. At the age of 34, his condition was rapidly deteriorating, and he was diagnosed with PAH. Because of the disease severity (mean pulmonary arterial pressure: 49 mmHg), he was initiated with IVEPO immediately. Five days later, He was diagnosed with SLE. He was managed with 1 mg/kg/day prednisolone therapy. 3 months later, he was newly diagnosed with PBC, and we confirmed portal hypertension. Through these treatments, he got total recovery from PAH. As reported, IVCY is highly effective in the patients with PAH due to SLE. However, pathophysiology of PAH is often complicated, especially in connective tissue disease. In this case, the reasons of PAH are not only SLE activity but also underlying portal hypertension. We would like to emphasize we should not hesitate the induction of IVEPO.

P2-301

A case of bucillamine nephropathy developed after long term use of bucillamine

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Conflict of interest: None

<Introduction> Bucillamine (BUC) was developed in Japan in 1987 and is one of DMARDs. Proteinuria is the famous side effect, it often occurs within 6 months after use, sometimes exhibiting nephrotic syndrome.<Case> A 82-year-old woman developed RA in March 2015. She had history of HBV infection. BUC (200mg/day) was started in May 2015. Because that the effect of BUC was poor and moderate disease activity continued, tacrolimus (TAC) was added on BUC in October 2015. However, in June 2016, hand tremor as a side effect of TAC was recognized and TAC was withdrawn. Since then BUC monotherapy was continued. In August 2017, she showed bilateral severe lower extremity edema and her blood exam and urinalysis presented serum albumin was 1.5 g/dl urine protein was 9.38 g/g·cr. She was diagnosed as nephrotic syndrome. Renal biopsy was performed because urine protein did not decrease despite 1 month of BUC withdrawal. An image of typical membranous nephropathy was obtained by electron microscopy, and a fine granular deposit often found in bucillamine nephropathy (BN) was observed. <Discussion> As the use of BUC decreases, the recognition of it's side effects is diminished. There are few reports that proteinuria developed after long-term use. We consider BN with literature reviews.

P2-302

Successful use of golimumab in a patient with anti-CCP antibody positive chronic monoarthritis of the knee: A case report

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Conflict of interest: None

[Case] A 65-year-old woman has had 4months history of right knee joint pain and swelling. She had no other joint symptoms. A laboratory evaluation revealed elevated inflammatory markers (CRP 10.4 mg/dL, MMP-3 579 ng/mL). Anti-CCP antibody (ACPA) was 28.4 U/mL and rheumatoid factor (RF) was positive. Antinuclear antibodies were negative and UA was 5.5 mg/dL. Calcium pyrophosphate crystals were not found in synovial fluid. Gram-staining, bacterial culture, acid-fast bacilli culture and PCR of synovial fluid were all negative. Despite of intraarticular steroid injection, it lacked efficacy. Treatment with 6 mg of weekly MTX relieved her right knee joint pain and CRP decreased to 4.0 mg/dL. However after increase of MTX doses to 8 mg/week, hepatic injury appeared (AST 94 U/L, ALT 232 U/L) and MTX was discontinued. Thereafter right knee arthritis got worse and CRP increased to 13.7 mg/dL. After the administration of subcutaneous golimumab at a monthly dose of 100 mg, arthritis of the knee joint improved and CRP decreased to 0.29 mg/dL. Therapy was well tolerated. [Summary] The use of golimumab may be an alternative treatment strategy for some patients with anti-CCP antibody positive chronic monoarthritis.

P2-303

Diagnostic and therapeutic utility of tetracycline to the fever of unknown origin (FUO) cases

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tal

Conflict of interest: None

[Object] To investigate the efficacy of tetracycline administration to FUO cases. [Methods] 200mg per day of minocycline were administrated to 9 patients (male 4, female 5) of FUO who visited our hospital. [Result] 7 of 9 cases improved completely after 7-30 days of minocycline administration, and no relapse was observed after the treatment. 2 nonresponse cases were diagnosed with adult onset Still's disease (AOSD) and familial Mediterranean fever, respectively. 2 of 7 responded cases were diagnosed with Japanese spotted fever and tsutsugamushi disease, respectively using PCR test. Final diagnosis of 5 responded cases were unknown, and clinical characteristics were poor except for headache were observed in 4 of 5 cases. 4 of 5 responded cases showed no response to at least one of cephem, macrolide, and quinolone antibiotics before minocycline therapy. In the case of 60 years old female, autoantibodies, bacterial cultures, imaging examinations including enhanced CT, bone marrow and cerebral fluid examinations, and biopsies of skin and liver were all negative, therefore steroid therapy was considered. However, her symptoms improved quickly after minocycline administration. [Conclusion] Tetracycline is useful for differentiation and treatment in FUO cases.

P2-304

A case of rheumatoid arthritis with a high level of KL-6 associated with pancreatic cancer

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Conflict of interest: None

A 82-year-old woman diagnosed with rheumatoid arthritis (RA) in 1992 and treated with methotrexate and prednisolone. The subjective symptoms of pneumonitis were poor. However, the KL-6 values were elevated to 13809U/ml in April 2017. Abdominal computer tomography findings revealed a pancreatic-head tumor and multiple liver nodules, diagnosed as a primary pancreatic adenocarcinoma with multiple liver metastasis. The stage of pancreatic cancer was stage 4, and curative surgery of the tumor was not indicated. The patient died in July 2017. If a high level of KL-6 is found without the increasing activity of lung disease containing interstitial pneumonia in RA patients, examination for the internal malignancies including pancreatic cancer should be performed.

P2-305

A case of bone sarcoidosis of the right shoulder with significant hyper IgG

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Conflict of interest: None

[Case] A 35-year-old woman complained of the right shoulder pain persisted for 3 months. Both the pain and the limitation in range of motion of the right shoulder became exacerbated gradually. Although there were no inflammatory physical findings in the right shoulder joint, she could bend and abduct her right shoulder joint only up to 90-degree. Both ACE and lysozyme were normal. IgG was over 5000mg/dL. Although magnetic resonance imaging of the right shoulder showed no specific findings, computed tomography of the lung revealed diffuse small nodular shadow. [Clinical course] Bronchoscopy showed "network formation" of the trachea and main bronchi, and transbronchial lung biopsy revealed non-caseating granuloma. Based on the above results, the patient was diagnosed with sarcoidosis. The limitation in range of motion of the right shoulder was improved completely nine weeks after receiving systemic glucocorticoid therapy (initial dose of prednisolone 0.6mg/kg/day). IgG was kept high even after achieving remission. [Discussion] The frequency of bone sarcoidosis is low. Although the predilection site is phalanx, both axial and appendicular skeleton are involved infrequently. In part of sarcoidosis, serum IgG may correlate with the state of the disease.

P2-307

The review of 10 cases of the adult human parvoviral B19 infectious diseases

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Conflict of interest: None

[Object] The adult human parvoviral B19 infectious disease often presents similar clinical manifestations and laboratory findings of systemic lupus erythematosus (SLE). I verified this through own cases this time. [Methods] I examined clinical manifestations and laboratory findings of 10 cases of the adult human parvoviral B19 infectious diseases that I experienced in two years recently. [Results] All ten cases were female; the mean age was 38.2 (the range: 16-59) years old. As for the onset time, there were the most from June to August with five cases, and four cases from March to May, December was one case. Five cases presented fever. Eight cases presented arthralgia. Seven cases presented erythema. The mean of WBC was 4263/μl, Hb11.7g/dl, Plt19.7×10^4/μl. Three cases presented WBC<4000/μl and Plt<15.0×10^4/μl The mean of CRP was 0.29 mg/dl. Of all cases CRP level was within normal limit. Complement was measured in seven of ten cases; the mean of C3 was 69.9 mg/dl, C4 13.2 mg/dl. Six cases presented hypocomplementemia. [Conclusions] The adult human parvoviral B19 infectious diseases often occur young female and present symptoms and findings similar to SLE, fever, arthralgia, erythema, leukopenia, thrombocytopenia, normal CRP level, hypocomplementemia, and so on.

P2-308

A case of Tubulointerstitial Nephritis and Uveitis (TINU) Syndrome with unknown fever

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Conflict of interest: None

[Case] A 51-year-old man with complaints of Fever, chills. Even though antibiotics were administered, it didn't improve. After hospitalization, ophthalmologic examination revealed non-granulomatous uveitis. Blood tests revealed high leukocytosis and inflammatory response, urinary tests revealed urinary protein and high urinary beta 2 microglobulin. There was no findings include pneumonia in the image findings. Based on the above findings, tubulointerstitial nephritis / uveitis syndrome (TINU syndrome) was suspected and a renal biopsy was performed, which was a diagnosis of interstitial nephritis. Thus we diagnosed TINU syndrome after distinguishing infection by antibiotic administration. After PSL 60 mg (1 mg / kg / day) were administered, symptoms improved promptly. The reminiscences were not recognized after steroid was gradually tapered and finished. In addition, various autoantibodies, HLA, sarcoidosis etc. were also examined, but neither of them got a significant finding, which was due to idiopathy. [Clinical Significance] I experienced an example of diagnosis of TINU syndrome with chief complaint of unknown fever of antibiotic refractory. Thus we reports with literature consideration.

P2-309

Two cases of intravascular lymphoma patients showed ground glass opacities in bilateral lung fields during treatment for rheumatic diseases

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Conflict of interest: None

[Introduction]: We report two cases of intravascular lymphoma (IVL) patients showed ground glass opacities (GGO) during treatment for rheumatic diseases. [Case 1]: A 73-year-old woman diagnosed as granulomatosis with polyangiitis 3 years ago presented fever under treatment with azathioprine and prednisolone. Because her symptoms were not improved by antibiotic therapy, she got an CT of her lungs. Chest CT showed GGO. We suspected interstitial pneumonia, so steroid therapy was started. But she had persistent fever. We suspected malignant lymphoma, because she showed low platelet count and high level of atypical lymphocytes. Bone marrow aspiration and random skin biopsy revealed IVL. [Case 2]: A 84-year-old woman presented with right shoulder pain and fever. She presented symmetry multiple arthritis after one month, so we suspected elderly onset RA and started salazosulfapyridine and prednisolone. After that, dry cough were emerged and persisted. So she got an CT of her lungs. Chest CT showed GGO. We suspected malignant lymphoma, because she showed persistent fever and monocytosis. Random skin biopsy revealed IVL. [Clinical importance]: In the practice of rheumatic diseases, we should take into consideration that there is a possibility that malignant lymphoma if Chest CT shows GGO.

P2-310

Clinical characteristics of tophaceous gout

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Conflict of interest: None

Objective: To investigate the clinical manifestation of gout patients with tophus. Methods: 983 patients (men/women: 970/13) with gout were included in the study. The clinical manifestations at the first visit of our outpatient clinic were analyzed retrospectively. Results: The mean age of gout onset was 44 years. The mean duration of gout at the first visit was 6.0 years. 71 patients (7%) had tophus at the first visit. The frequency of tophus increased with longer disease duration and the frequency of tophaceous gout was 30% in patients with disease duration ≧ 21 years. In tophaceous gout patients, the proportion of women was higher, the age at gout onset was younger and the disease duration was longer than those in non-tophaceous gout patients ($p=0.011$, $p=0.009$, $p<0.0001$). The frequency of hypertension was significantly higher in tophaceous group, however, the renal function was not significantly different between tophaceous and non-tophaceous patients. Discussion: This study shows that tophaceous gout was found 7% of patients with gout. The frequency increased with disease duration. It is recommended to keep in mind the development of cardiovascular disease because of increased frequency of hypertension in patients with tophaceous gout.

P2-311

Analysis of binding of Nivolumab in lung cancer patients

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Conflict of interest: None

[Object] Biological durability of the PD-1 blocking antibody, Nivolumab, in patient blood, was reported to continue beyond 12 weeks after last infusion. However, maximum duration of its efficacy remains unclear. [Methods] To evaluate the efficacy of the treatment, we developed an efficient technique to identify Nivolumab binding status: complete binding, partial binding and no binding in the T cells from patient samples using flowcytometry. [Results] While the decrease in frequency of Nivolumab binding after discontinuation was observed in all cases where long term monitoring was possible, Nivolumab binding in T cells from peripheral blood was detected beyond 20 weeks of the last infusion. Though effective binding could have ceased before that time point. [Conclusions] It is possible that monitoring of Nivolumab binding to T cells is valuable.

P3-001

Importance of TNFa on CTLA4-Ig induced inhibition of human osteoclastogenesis

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Conflict of interest: Yes

[Object] Abatacept (CTLA4-Ig) binds to CD80 and CD86 on antigen presenting cell and suppresses T cell functions. The authors have reported the inhibitory effect of CTLA4-Ig on RANKL-induced osteoclast differentiation. Here we report on the effect of TNFa on this inhibitory action. [Method] Monocytes were isolated from peripheral blood of healthy volunteers and cultured in the presence of RANKL and M-CSF. In addition, CTLA4-Ig and/or TNFa were added, and osteoclasts were identified by TRAP staining and bone resorption activity using osteoplates. Expressions of CD80 and CD86 was assessed by real-time PCR and flow cytometric analysis. [Results] CTLA4-Ig inhibited RANKL-induced osteoclast generation in a dose-dependent manner. Next, Peripheral monocytes with TNFa for 24 hours induced expression of CD80 at the level of mRNA. In addition, the inhibitory effect on the osteoclastogenes is by CTLA4-Ig was enhanced. [Conclusions] TNFa acts on peripheral blood monocytes to induce the expression of CD80 molecule and enhance inhibition of osteoclast differentiation by CTLA4-Ig. Since TNFa is strongly expressed in RA synovium and osteoclast precursor cells of the joint locus, CTLA4-Ig may strongly exert its inhibitory effect on osteoclast differentiation at the inflamed joint in RA.

P3-002

Inhibitory effect of a statin on arthritis and its mechanism

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Conflict of interest: None

[Object] Some cohort studies demonstrated that statins inhibited arthritis, however, the mechanism remains unknown. The aim of this study is to clarify the mechanism. [Methods] The env-pX rats, which develop spontaneous arthritis, were used. (Exp.1) Eleven male rats (7-10-week-old) were divided into fluvastatin group (500 μg/kg/day p.o, n=6) and placebo group (n=5). At day 0, 10, 20 and 30, visual assessment of joint swelling and blood sampling were carried out. At day 30, the ankle joints were subjected for histological analyses after sacrifice. (Exp.2) At day 0, 10, 20 and 30, ultrasonography of ankle joints was conducted on the fluvastatin group (n=4) and placebo group (n=2). (Exp.3) Serum microRNAs (at day 0 and 30) were comprehensively analyzed between the fluvastatin group and placebo group. [Results] Joint swelling and histological scores in the fluvastatin group were smaller than in the placebo group. Additionally, ultrasonography revealed chronological inhibitory effect of fluvastatin on arthritis. We noted that 3 microRNAs, which target a common gene, demonstrated similar behavior. [Conclusions] Inhibitory effect of fluvastatin on arthritis was confirmed.

P3-003

Clock gene Bmal1 regulates the proliferation of RA fibroblast-like synovial cells via the cycle regulator

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Conflict of interest: None

[Object] The cross-talk of clock genes and cell-cycle regulators was recently reported. In this study, we examined the regulation between the clock gene and cell cycle or cell proliferation in primary cultured rheumatoid fibroblast-like synovial cells (RA-FLSs). [Methods] RA-FLS was stimulated by *Bmal1* siRNA and cultured with 50% horse serum/DMEM to synchronize the oscillation of the clock gene. RA-FLS was further cultured with serum-free DMEM until 32hr, and total RNA was extracted periodically to measure expressions of *CyclinE1* by qPCR. After synchronized the oscillation of clock genes, RA-FLS was also cultured with 10 %FCS/ DMEM, and cell viability was measured by WST-8 assay. [Results] Under the condition of interfering *Bmal1,* expressions of *CyclinE1* was significantly decreased after 8hr and cell viability was also decreased after 24hr. [Conclusions] Bmal1 regulates clock genes by binding E-box, placed in their transcriptional regions. Similarly, analogue sequences of E-box are present in the transcriptional region of *CyclinE1*. Results suggested the regulation of Bmal1 is a possible therapeutic strategy for controlling the proliferation of RA-FLS.

P3-004

Involvement of mucosal-associated invariant T (MAIT) cells in lupus pathogenesis

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Conflict of interest: None

[Object] Mucosal-associated invariant T (MAIT) cells are innate T cells that are restricted by MHC-related molecule-1 (MR1). We have reported that the activation state of MAIT cells correlated with SLE disease activity index (SLEDAI) score, suggesting their association with lupus pathology. [Methods] FcγRIIB$^{-/-}$*Yaa* mice were crossed to MR1 deficient mice lacking MAIT cells, and disease progression was compared between MR1$^{-/-}$ and MR1$^{+/+}$FcγRIIB$^{-/-}$*Yaa* mice. The frequency, activated status, and cytokine producing capacity of immune cells were analyzed by using flow cytometery. [Result] The lack of MR1 improved survival rate and reduced serum levels of anti-dsDNA antibody and glomerular IgG and C3 deposits. There was a trend of reduced glomerulonephritis in MR1$^{-/-}$FcγRIIb$^{-/-}$*Yaa* mice. MR1 deficiency reduced cytokine producing capacity of T cells and innate-T cells. Germinal center B cells, plasma cells and T follicular helper cells were markedly reduced, and regulatory T cells were increased in MR1$^{-/-}$FcγRIIb$^{-/-}$*Yaa* mice. Activated MAIT cells are accumulated in the kidney. [Conclusion] These data suggest that MAIT cells exacerbated pathological process of lupus. Further studies are undergoing to understand the mechanisms by which MAIT cells are involved in pathogenesis of lupus.

P3-005

Role of chemokine-producing T-bet+ effector B cells in rheumatoid arthritis

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Conflict of interest: None

[Object] Efficacy of B-cell depletion therapy underscores novel Ab-independent effector functions of B cells in rheumatoid arthritis (RA). This function requires collaboration between CD4+ T cells and B cells. Given the abundant existence of Th1 cells in synovial fluid of RA, here we have focused on B cell effector functions, in particular chemokine production, in the Th1 milieu. [Methods] B cell subsets from peripheral blood and synovial fluid in healthy controls as well as patients with RA were subject to the following analyses. Upon Th1 stimulation we evaluated mRNA and protein expression of B cells using microarray, quantitative PCR, and flow cytometric analysis. [Results] Microarray analysis showed pronounced CXCL9 and CXCL10 mRNA expression in memory B cells upon BCR/CD40/IFNg stimulation. By coculture with Th1 cells, B cells produced CXCL9/10 proteins. Intriguingly, these chemokine-producing B cells were characterized by expression of T-bet. Expression of CXCL9/10 was noted in the CXCR3+ B cells. Synovial fluid in RA consisted of an abundant number of activated Th1 and T-bet+ B cells. [Conclusions] These findings suggest that Th1 environment generates CXCR9/10-producing T-bet+ effector B cells that in turn facilitate the recruitment of CXCR3+ T/B cells into inflammatory sites.

P3-006

Role of IL-21-producing CD8+ T cells in rheumatoid arthritis

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Conflict of interest: None

[Object] CD8+ T cells have recently gained attention as an IL-21-producing cell population. In mice a novel subset of CD8+ T cells, like Tfh cells, is capable of producing IL-21 that supports B cell differentiation into Ab-producing cells. However, little is known about human IL-21-producing CD8+ T cells, in particular in autoimmune diseases. Here, we have investigated a role of IL-21-producing CD8+ T cells in HC and patients with RA. [Methods] CD8+ T cells in peripheral blood (PB) from HC and patients with RA in the absence or presence of CD3/28 stimulation were subject to the analysis of IL-21 expression at both mRNA and protein levels. [Results] CD3/28 stimulation promoted IL-21 production in CD8+ T cells from HC and memory (CD45RA-) CD8+ T cells were a main producer of IL-21. Notably, central memory (CD45RA-CCR7+) CD8+ T cell subsets were remarkably enriched in PB from patients with RA compared with HC. The surface phenotype of IL-21-producing CD8+ T cells was CD28+CD69+CD95+, and these cells also have potential to produce IFNγ, but not IL-17. [Conclusions] These findings suggest that a novel subset of human IL-21-producing CD8+ T cells, similar to Tfh cells, plays a pivotal role in B cell differentiation into Ab-producing cells in the pathogenesis of RA.

P3-007

Autoantibody-inducing CD4 T cell (*ai* CD4 T cell) that induces SLE includes not only follicular helper T cell but also IL-21-producing CXCR5^{-}ICOS^{hi}PD-1^{hi} cell

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Conflict of interest: None

[Object] Autoantibody-inducing CD4 T (*ai*CD4 T) cell is indispensable for our 'self-organized criticality theory' that induces SLE. We previously showed that the *ai*CD4 T cell belongs to CD45RB^{lo}122^{lo} CD4 T cell subpopulation. Here we further dissected the phenotype of *ai*CD4 T cell. [Methods] BALB/c mice were repeatedly immunized with OVA and SLE was induced. Cell surface marker of CD45RB^{lo} CD4 T cell was detected using flow cytomery. These CD4 T cells were stimulated with anti-CD3 and CD28 antibodies *in vitro*, and cytokine in culture supernatant was detected using ELISA. [Results] After repeated immunization with OVA, CD4^{+}CXCR5^{+}ICOS^{hi}PD-1^{hi} follicular helper T (Tfh) cell was increased, and these Tfh cells were CD45RB^{lo}. Further, CXCR5^{-}ICOS^{hi}PD-

1^{hi} cell was also increased in CD45RB^{lo} CD4 T cell of OVA-immunized mice. We found that CXCR5^{-}ICOS^{hi}PD-1^{hi} CD4 T cell highly produced IL-21 rather than Tfh cell after repeated immunization with OVA. [Conclusions] In addition to Tfh, the CXCR5^{-}ICOS^{hi}PD-1^{hi} CD4 T cell that produces IL-21 was increased in line with induction of SLE. This novel CXCR5^{-}ICOS^{hi}PD-1^{hi} CD4 T cell population appears to be responsible for helping B cell to induce varieties of autoantibodies and driving CD8 T cell to cause lupus tissue injury.

P3-008

Pathogenic role of fractalkine in interstitial pneumonia

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Conflict of interest: None

[Objective] Treatment strategy for interstitial pneumonia (IP) associated with collagen diseases has not been established yet. It is expected to elucidate the pathogenesis of IP and development of novel therapy. In this study, we aimed to clarify the role of fractalkine (FKN) in IP. [Methods] *In vitro*, expression of FKN and its receptor CX3CR1 in human lung fibroblasts was analyzed by RT-PCR. Bleomycin was intratracheally administered to C57BL/6 mice to develop IP. The mice were treated with administration of anti-FKN mAb or control Ab intraperitoneally for 2 weeks. The lung was stained with hematoxylin-eosin. Collagen eluted from the lung with dilute acid and pepsin was quantified by ELISA. [Results] Human lung fibroblasts expressed FKN and CX3CR1. FKN expression was increased by stimulation with TNF-α and IFN-γ, and markedly increased by stimulation with TNF-α + IFN-γ. Treatment with anti-FKN mAb did not significantly alter inflammatory cell infiltration of bleomycin-induced IP. However, collagen in the lung was decreased by the treatment with anti-FKN mAb. [Conclusion] Interaction of FKN-CX3CR1 may contribute the fibrosis of IP.

P3-009

Effects of iguratimod on protein profiles of chondrocytes

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Conflict of interest: None

[Object] To analyze precise mechanisms for the effect of iguratimod (IGU), we analyzed protein profiles of chondrocytes. [Methods] OUMS-27 was cultured in the presence or absence of 100μM IGU. Extracted proteins were separated by 2 dimensional-differential gel electrophoresis (2D-DIGE). Proteins of interest were identified by mass spectrometry. [Results] 776 and 803 protein spots were detected in the 2D-DIGE results of 24 hour- and 6 day-stimulation with IGU, respectively. In the 6 day-stimulation, 22 spots showed 1.3-fold or higher intensity in the presence of IGU compared to the absence, whereas 15 spots showed -1.3-fold (1/1.3) or lower intensity ($p<0.05$). We identified 15 out of the 37 spots, which included proteins involved in packaging and splicing pre-mRNA, regulating signaling pathway and protein folding, innate immunity and inflammation, transcription, ATP synthesis, cytoprotection, and cytoskeleton. Interestingly, intensity of multiple spots ofhnRNPA2/B1 and A1 was decreased by IGU, which are autoantigens and proinflammatory regulators in RA andpossibly locate at the upstream of NF-kB, the known target of IGU. [Conclusions] IGU affected protein profiles of chondrocytes. The reduction of hnRNPs may indicate novel and precise mechanisms for anti-rheumatic effects of IGU.

P3-010

The induction of eGFP in the central nervous system in the knee arthritis model in the c-fos-eGFP transgenic rats

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Conflict of interest: None

[Object] We evaluated whether a c-*fos*-enhanced green fluorescent protein (eGFP) transgenic rat line, which expresses the c-*fos* and eGFP fusion gene, can be useful for the study of nociceptive pathways and processing in the knee arthritis model. [Methods] We used adult male c-*fos*-eGFP transgenic rats. The knee arthritis was induced in both tibiofemoral joint by intra-articular injection of 100 μL of 3 % carrageenan. Control rats were injected with 100 μL of physiological saline. Carrageenan-treated rats were perfused at 3, 6, 12 and 24 hours post injection. [Results] The number of the eGFP positive cells in lamina I-II of the dorsal spinal cord, paraventricular nucleus (PVN) and supraoptic nucleus (SON) was counted. The number of them in all regions were significantly increased after nociceptive stimuli. Following Carrageenan treatment, eGFP was maximally expressed at 12 hours post injection in the all regions. [Conclusions] These results suggested that *c-fos*-eGFP rat line can be useful for the study of nociceptive pathways and processing in the knee arthritis model.

P3-011

The fate of synovial fibroblasts in chronic joint inflammation of a rheumatoid arthritis model, D1BC mouse

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Conflict of interest: None

[Object] Rheumatoid arthritis (RA) is a type of chronic inflammation, characterized by the onset of synovitis and progressive bone destruction in joints. Fibroblast differentiates into chondrocyte. To create the B7.1 transgenic mouse (D1BC for DBA/1J, B7.1 gene; transcribed from the rat CII, rCII promoter and enhancer), we analyzed the fate of synovial fibroblasts (SFs) in model animal. [Methods] D1BC mice were treated with a low-dose of bovine CII for induction of chronic articular inflammation. Joint damage was analyzed by *in situ* hybridization and histopathological examination using *B7.1* transgene as a lineage tracing marker. [Results] D1BC mice shared common features of RA such as chronic inflammation and ankylosis. FSP1 and vimentin together with *B7.1* were expressed in SFs and articular chondrocytes. SFs in the pannus also expressed *col2a1* and *col10a1*, but not ColX, thus they were classified as chondrocyte and pre-hypertrophic chondrocyte (HC). These SFs underwent differentiation into osteoblastic cells via HC at the end of the chronic phase to involve in the progression of ankylosis. [Conclusions] The ectopic expression of *B7.1* in chondrocytes and SFs leads to an increased susceptibility to chronic inflammatory arthritis and subsequent new bone formation, reminiscent of ankylosis.

P3-012

Role of allograft inflammatory factor-1 in bleomycin-induced lung fibrosis

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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 asso-

ciated with the pathogenesis of rheumatoid arthritis and skin fibrosis in sclerodermatous graft-versus-host disease mice. Here, we used an animal 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. AIF-1 was also expressed in lung fibroblasts. Recombinant AIF-1 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.

P3-013

Blocking of CD11b-positive cell activation prevents spontaneously occurring arthritis in a novel arthritis-prone mouse model

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Conflict of interest: None

[Object] Osteoclasts are derived from osteoclast precursors involved in peripheral $CD11b^+$ monocytes and play an important role for bone destruction in rheumatoid arthritis. Here, we examined whether antagonistic anti-CD11b mAb (5C6) can prevent the disease in the novel arthritis-prone mouse model. [Methods] Arthritis-prone FcγRIIB deficient B6 mice (designated KO1) were treated with 5C6 mAb, and examined the effect on the disease severity. [Results] Arthritis was significantly prevented in 5C6-treated group compared with control antibody-treated and non-treated KO1 mice groups. 5C6-treated group also showed lower mRNA expression levels of B cell activation cytokines in spleen, the decreased frequencies of activated B cells and plasma cells, and the lower serum levels of autoantibodies. [Conclusions] Blocking of $CD11b^+$ cell activation is a possible new therapeutic strategy for rheumatoid arthritis.

P3-014

Critical epitope of anti-rabbit podoplanin monoclonal antibody PMab-32 for immunohistochemical analysis in rabbit arthritis model

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Conflict of interest: None

[Object] Podoplanin (PDPN) is a type I transmembrane O-glycoprotein, which is used as a specific lymphatic marker. Expression of PDPN has been reported in various inflammatory lesions and neoplastic lesions. PDPN is drawing attention as a biomarker and a molecular target. We revealed expression of PDPN in knee synovitis of lipopolysaccharide-induced rabbit arthritis model, using newly established anti-rabbit PDPN monoclonal antibody, PMab-32. In this study, we identified the epitope of PMab-32. [Methods] Substitutions of amino acids to alanine in rabbit PDPN were performed. Chinese hamster ovary-K1 cells were transfected with the mutated plasmids using an electroporation system. We performed epitope mapping using western blot analysis and flow cytometric analysis. [Results] Western blot analysis showed that several point mutants, such as S61A, G65A, T67A, and A68G, completely lost the reaction by PMab-32. Flow cytometric analysis revealed that PMab-32 did not react with G65A. Taken together, the epitope of PMab-32 is Ser61-Ala68, and Gly65 is the most important amino acid. [Conclusions] The critical epitope of PMab-32 is Ser61-Ala68, and Gly65 is the most important amino acid. Elucidation of epitopes is considered to be very important in preparing antibody drugs targeting podoplanin.

P3-015

Immunohistochemical analysis of inflammatory rheumatoid synovial tissues using anti-human monoclonal podoplanin antibody panel

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Conflict of interest: None

[Object] Podoplanin (PDPN) is a transmembrane sialoglycoprotein, which is expressed in several normal tissues and malignant tumors. In this study, we examined PDPN expression in inflammatory synovial tissues using anti-human PDPN mAb panel to assess which mAb was the most useful for evaluating of synovitis. [Methods] Synovial tissue samples were obtained from eleven RA patients undergoing upper and lower limb joint surgery. The degree of synovitis was evaluated using Krenn histopathological grading system (KS). PDPN positive cells were immunostained by panel of PDPN mAbs (NZ-1, LpMab-3, LpMab-10, LpMab-12, LpMab-13, and LpMab-17). The area of immuno-positive cells per reference area was calculated digitally using BZ H3C Hybrid Cell Count Software (KEYENCE). [Results] KS was 7.4±1.0. In quantitative analyses, LpMab12 attained the highest score, and was significantly higher than that of NZ-1, LpMab-3, and LpMab-17 in RA (NZ-1; 28.8±5.6%, LpMab-3; 29.5±7.6%, LpMab-10; 30.1±9.9%, LpMab-12; 41.3±6.6%, LpMab-13; 37.5±7.9%, LpMab-17; 30.4±7.4%) ($p < 0.05$) [Conclusions] In various anti-human PDPN mAbs, we demonstrated that LpMab-12 was the most stainable anti-human PDPN mAb for inflamed synovial lining layer of RA patients in immunohistochemistry.

P3-016

IL-6 induces the resistance for apoptosis via circadian clock genes in synovial cells

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Conflict of interest: None

[Object] IL-6 is involved in the pathogenesis of rheumatoid arthritis (RA), while the interaction between clock gene and IL-6 has not been elucidated. In this study, the effect of IL-6 on the expression of clock gene Per2 and pro-apoptotic factor Bik, and also the clock gene transcription factor PAR bZIP (Dbp, Tef, Hlf) was examined [Methods] Synovial cells were treated with/without IL-6 (100μg/ml) and real time PCR was performed to examine expressions of *Per2, Bik, Dbp, Hlf*, and *Tef*. Luciferase plasmid constructs with/without D-box sequence on Per2/Bik promoter were transfected to cells, then promoter activities were measured after IL-6 stimulation. Cells were pre-treated with IL-6, and dexamethasone (DEX, 10μM) was added to measure cellular viabilities. [Results] IL-6 decreased the expression of *Tef*, *Dbp, Hlf, Per2* and *Bik*. Promoter activities of Per2/Bik containing D-box sequence were decreased by IL-6 stimulation. DEX decreased cellular viabilities, while it was suppressed by IL-6 pre-treatment. [Conclusions] PAR bZIP regulates gene expressions of Per2/Bik through the D-box sequence present in their promoter region. Inhibited expressions of PAR bZIP by IL-6 could lead to suppress Per 2/Bik expression via D-box to contribute to acquisition of resistance for apoptosis.

P3-017

Adenosine inhibits the TNFa-induced MMP-3 production on RA synoviocyte cell line MH7A via A2A adenosine receptor signaling

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Conflict of interest: None

[Object] Adenosine (Ado) is the effector molecule of anti-rheumatic effects of methotrexate (MTX). The function of Ado receptors on synoviocytes, however, is yet to be clarified. In this study, MH7A, a cell line of human rheumatoid synovial cells, was used to investigate the role of A_{2A} AdoR on TNFα-induced production of MMP-3. [Methods] MH7A was cultured for 24 hours in the presence or absence of TNFα (25 pg/ml) with or without the selective A_{2A} AdoR agonist HE-NECA (10, 50, 100, or 1000 nM). MMP-3 concentration of the culture supernatants was then measured using "Panacurea MMP-3 (Sekisui Medical Co. Ltd.)." [Results] TNFα stimulation induced the MMP-3 production on MH7A, which was inhibited by HE-NECA in the concentration-dependent manner. In addition, pretreatment of MH7A with the selective A_{2A} AdoR antagonist to block the signaling via A_{2A} AdoR resulted in the cancelation of the observed inhibitory effects of HE-NECA. [Conclusions] MMP-3 is considered important for the joint destruction on RA because of the highest concentration among MMPs inside the joints and of the lowest substrate specificity. Our results indicate that Ado via A_{2A} AdoR is capable of reducing the MMP-3 production induced by TNFα, which may contribute to the anti-rheumatic mechanisms of MTX.

P3-018

The influence of glucocorticoid on the validity of estimated glomerular filtration rate calculated by serum cystatine C in patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] It has been known that serum cystatin C (cysC) is not influenced by muscle mass in the body, but is by glucocorticoids. Thus, we evaluated the influence of glucocorticoid dosage to the validity of estimated glomerular filtration rate (eGFR) calculated by cystatin C (cysC) in patients with rheumatoid arthritis (RA). [Methods] Fifty patients with RA who had been admitted to Niigata University Hospital were included in this study [12 males and 38 females, the mean dosage of daily prednisolone (PSL) was 9.6 mg]. Renal inulin clearance (Cin) was measured and compared to eGFR using serum creatinine (Cr) (eGFRcreat) or cysC (eGFRcysC). [Results] The mean eGFRcreat (78.9±28.9 ml/min/1.73m^2) was significantly higher ($p<0.001$), and the mean eGFRcysC (57.7±25.0ml/min/1.73m^2) lower ($p<0.001$) than the mean Cin (65.2±26.9ml/min/1.73m^2). As the PSL dosage was higher, eGFRcysC was significantly less estimated ($r=0.371$, $p=0.008$). However, in 30 patients taking PSL less than 10mg/day, the mean eGFRcysC (63.0±25.1 ml/min/1.73m^2) was not different from that of Cin (65.4±24.8 ml/min/1.73m^2) ($p=0.400$). [Conclusions] Whereas higher PSL dosage may lead underestimation of eGFRcysC, it was accurate when PSL was less than 10mg/day in patients with RA.

P3-019

The titers of anti-CCP antibody (ACPA) and RF are significantly higher in patients with rheumatoid arthritis (RA) associated with bronchial asthma (BA)

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Conflict of interest: None

[Object] ACPA and RF turn positive before the onset of RA, which suggests close relation between them in terms of pathogenesis. BA is characterized by chronic eosinophilic inflammation. We studied whether eosinophilic inflammation contributes to pathogenesis of RA particularly to elevation of ACPA and RF. [Methods] Subjects were 17 patients with RA associated with BA. Control subjects were 229 RA patients with RA without pulmonary disorders evaluated by chest CT scan. [Results] The mean age of BA development was 32.2 (10.4 - 59.9), and that of RA was 54.7 (40.4 - 82.5). The development of RA was almost the same time in 2, but in the rest of the patients, BA came earlier than RA. Even in the 2 patients, they had symptoms compatible with cough variant asthma before. The median value of anti-CCP Ab in BA/RA and RA patients were 88.4U/ml (1 - 703) and 25U/ml (0.4 - 2958), respectively, and the difference was statistically different. The median values of RF of each groups were 64U/ml (12 - 517), and 37U/ml (15 - 1698), respectively, and difference wan also significant. [Conclusions] It was suggested that in patients with RA associated with BA, pre-existing eosinophilic airway inflammation contributes to citrullination of peptides and ACPA formation.

P3-020

The study of 4 kinds of serum fatty acid level and EPA/AA ratio in patients with rheumatoid arthritis

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Conflict of interest: None

Objective: We evaluated the role of 4 kinds of fatty acid, such as eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), arachidonic acid (AA) and dihomo-gamma-linolenic acid (DHLA), in rheumatoid arthritis (RA) patients. Within these fatty acids, especially EPA/AA ratio is a good marker for susceptibility of ischemic heart disease and a factor affecting to activity in other immunological diseases such as RA. Method: We examined the 4 fatty acids in 145 patients with RA who visit to our private clinic regularly. The relationship with EPA/AA ratio and other clinical features were evaluated. Results: In 145 RA patients, there were no significant correlation with EPA/AA ratio and stage, class, age, sex, disease duration, serum CRP level and DAS28CRP. An original index of joint destruction (the ratio of stage/disease duration) was positively correlated with EPA/AA ratio. The comparison of a group with ≧0.2 of EPA/AA ratio (92 cases) and a group with <0.2 (53 cases) indicated that the tender joint count tends to be more than the swollen joint count in low (<0.2) EPA/AA ratio group (not significant). Conclusion: EPA/AA ratio could be an indicator of RA progression although further studies with a large number of patients are required in the future.

P3-021

Relationship between anti-cyclic citrullinated antibodies and disease activity, medication for RA patients

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Conflict of interest: None

Objective: To investigate relationship between Anti-CCP antibodies and disease activity, medication for RA patients. We examined anti-CCP antibodies of 323 RA patients who admitted our clinic. We identified 84 patients of anti-CCP antibodies negative (less than 0.45U/ml), 20 patients of anti-CCP antibodies low value (less than 13.5U/ml), and 219 patients of anti-CCP antibodies high value (more than 13.5U/ml). Results: Mean CRP value is 0.26mg/dl in negative group, 0.32mg/dl in low value group, and 0.55mg/dl in high value group. There is marginally significant that CRP value of negative group is lower than that of high value group. In order of negative group, low value group, high value group, remission of DAS-CRP is 73%, 65%, 72%, low disease activity is 16%, 5%, 11%, moderate disease activity is 12%, 25%, 14%, high disease activity is 0%, 5%, 3%. The use rate of SASP is 42% in negative group, 10% in low value group and 16% in high value group. The use rate of MTX is 37% in negative group, 41% in low value group and 49% in high value group. The use rate of Biologics is 14% in negative group, 40% in low value group, 20% in high value group. The use rate of SASP in negative group

is more significantly than that of low value group and high value group.

P3-022

Liver function of patients with rheumatoid arthritis

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Conflict of interest: None

[Object] Recently, patients of rheumatoid arthritis (RA) are aggressively treated by methotrexate (MTX) and biological drugs. However, HBV reactivation is most critical problem, and also, cases suspected of drug-induced liver damage are not uncommon in RA patients. So, we investigated liver function of RA patients in our department. [Methods] We investigated liver functions, virus markers for 240 patients with RA continuously hospitalized in our department at the time of October 31, 2017. In addition, we examined RA treatment contents and disease activity. [Results] Only about 3% of the cases were positive of HBs antigen, but about 20% were positive of HBs antibody or HBc antibody. About 25% of the total cases were positive for some HBV markers. Furthermore, HBV-DNA was detected in about 10% of them. Then, of these, 40% were HBs antigen negative cases. Especially in 40% of elderly people, HBV marker was positive. AST and ALT exceeded normal values in about 10% of the cases, but no significant correlation was found between the use of therapeutic drugs and folic acid use. [Conclusions] There are many HBV marker positive cases, especially in elderly people, so it is necessary to pay attention to reactivation by surely screening.

P3-023

Tocilizumab increased the numbers of peripheral eosinophil ?

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Conflict of interest: None

Objective] In clinical situations, we experienced several patients who increased eosinophil number after starting tocilizumab (TCZ). The purpose of this study is to determine whether TCZ increases eosinophil numbers through analysis of clinical records of RA patients who receive TCZ. [Methods] Consecutive 95 RA patients who received TCZ were enrolled. Medical records, including eosinophil % and WBC were reviewed. [Results] Subjects were 26 male and 69 female, 23 bio-naïve and 72 bi0-switch cases whose prior bio were TNF Ab in37, ETN in 23 and ABT in 7). Percentage and number of eosinophil before TCZ were 2.1±1.8% and 154±129/mm3, respectively. In 3month starting TCZ, 86% and 77% of the patients showed increases in the percentage (3.95±4.8%) and numbers (264±396/mm3) of eosinophil, respectively, which were statistically significant. There were no relation between the eosinophil change and bio-naïve/ switch, prior bio-agents, or RA responsiveness to TCZ. Glucocorticoid dose was negatively correlated with eosinophil number before therapy, but not with eosinophil change. [Conclusion] IL-6 blockade by TCZ might increase the numbers of peripheral eosinophil.

P3-024

The association between cytoplasmic staining pattern and anti-ARS syndrome

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Conflict of interest: None

[Object] To evaluate the association of cytoplasmic staining pattern and anti-ARS syndrome. [Methods] This study comprised 75 cases that were positive for cytoplasmic among 1416 patients who measured antinuclear antibodies from October 2014 to October 2017 in the Department of Rheumatology and the Department of Respiratory Medicine in our hospital. [Results] The mean age was 62.0±13.9 years old. 21 males and 54 females. There were 25 ILD, 21 Sjogren's syndrome, 19 RA, 6 systemic scleroderma, 6 dermatomyositis, 4 polymyositis, and 5 systemic lupus erythematosus patients. Anti-SS-A antibody was detected in 24 (35%) out of 68 cases in total and 6 (25%) out of 24 cases of ILD, whereas, anti-ARS antibody was detected in 8 (50%) out of 16 cases in total and 8 (73%) out of 11 cases of ILD patients. ILD complication was observed in 9 out of 19 RA patients with cytoplasmic, among which all 4 patients who measured anti-ARS antibody were positive. [Conclusions] Cytoplasmic is associated with anti-SS-A antibody and anti-ARS antibody, and detection rate of anti-ARS antibody is particularly high in ILD patients. In RA patients and ILD patients who are positive for cytoplasmic, it is necessary to consider the possibility of anti-ARS syndrome.

P3-025

The clinical utility of the serum interleukin-18 measurement in the rheumatic disease

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Conflict of interest: None

[Object] Interleukin (IL)-18 is a one of the key cytokine in adult onset Still's disease (AOSD). We considered the serum levels of IL-18 elevation in the rheumatic disease (RD). [Methods] We measured the serum levels of IL-18 (normal range<128 pg/ml) by enzyme-linked immunosorbent assay kit in the thirty untreated RD patients. The number of RA patient was 12, AOSD 3, SLE 2, polymyositis (PM) 2, dermatomyositis (DM) 2, MCTD 2, ANCA related vasculitis 2, systemic sclerosis 1, Bechet disease 1, periarteritis nodosa 1, PMR 1 and spondylarthritis 1. [Results] The serum levels of IL-18 in AOSD patient were 60267 pg/ml, but in the RD without AOSD were 410 pg/ml on average. Additionally in the RA patient the serum levels of IL-18 were 293 pg/ml on average, which elevated in the one of both DM (2490 pg/ml) and PM (917 pg/ml) patient. [Discussion] It was recently reported that the serum levels of IL-18 is an efficient marker during the active phase of AOSD, but also might be a useful predictor of remission. Furthermore, both IL-18 and interferon-γ are effective markers during active disease in muscle inflammation such as PM. [Conclusions] We suggested that the serum levels of IL-18 may be a valuable surrogate marker to predict the disease activity in the inflammatory myositis.

P3-026

Detection of Anti Stress Granule Antibody in Arthritis Patients

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Conflict of interest: None

[Object] An autoantibody against RPL23A, a cytoplasmic antigen, was reported in RA. We focused on stress granule (SG), which is a complex of RNA and proteins in cytoplasm that appears in response to various stresses. We attempted to detect anti-SG Ab in patients with arthritis and to determine the clinical characteristics of anti-SG Ab positive patient. [Methods] 89 patients with arthralgia who visited Hiroshima University Hospital were examined. SG was induced in U2OS cells by sodium arsenite (0.5mM) treatment for 60 minutes. The SG-induced cells were incubated with anti eIF3η (a SG marker) antibody and patients' sera (40-fold dilution). Sera that recognized eIF3η-positive SG was considered as positive for anti-SG Ab. The subcellular localization of RPL23A was examined. [Results] 17 cases (19%) were positive for anti-SG Ab. Undifferentiated arthritis was the most frequent in the anti-SG Ab positive cases, and titers of RF and anti-CCP Ab tended to be low in anti-SG Ab positive cases, however there was no statistically significance. Since RPL23A is not localized in SG, anti-SG Ab is a novel autoantibody different from anti-RPL23A Ab. [Conclusions] Anti-SG Ab was found in arthritis cases. It is necessary to conduct more clinical analyzes and to identify antigens for anti-SG Ab.

P3-027

5 patients with dual Myeloperoxidase (MPO) and proteinase3 (PR3) anti-neutrophil cytoplasmic antibodies (ANCAs) positivity: A case series

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Conflict of interest: None

[Object] ANCAs are specific antibodies and regarded as a biomarker for AAV. They are also seen in other rheumatic disease and inflammatory bowel disease. However, clinical features of dual ANCAs positivity are little known. This study report and evaluate the cases with dual ANCAs positivity. [Methods] 5 patients with dual ANCAs positivity had medical examination at our unit between AUG 2010 and SEP 2017. We evaluate their primary disease, affected organs, and the activity. [Results] Our study included 2 cases of AAV (one was MPA, the other one was GPA), 2 cases of Ulcerative colitis, and a case of drug-induced ANCAs positivity. Dual ANCAs positivity, IP and microscopic hematuria (MPA) or hearing impairments (GPA) were detected when AAVs were diagnosed. The ANCA titers were decreased with remission. UC patients were revealed dual ANCAs positivity with colitis worsened, however, the titers were not decreased after remission. A case of drug-induced ANCAs positivity was concluded by that the ANCA titers were decreased after Minomycin withdrawal, which was prescribed for chronic osteomyelitis. [Conclusions] Any consistent tendency of dual ANCAs positivity was not shown through the 5 cases. Further cases and studies are needed for revealing clinical features of dual ANCAs positivity.

P3-028

Supplemental treatment of rheumatoid arthritis with a whey protein preparation containing natural milk antibodies against enteric pathogenic bacteria and their toxins: Effects of milk antibodies against intestinal microflora composition and the disease activity

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Conflict of interest: None

[Objective] To investigate the effects of natural milk antibody (Ab) on intestinal bacteria composition, and consequent therapeutic effect on disease activity in RA. (Double blind multi-center study) **[Methods]** Eighty-seven patients with RA with DAS28-ESR (DAS) above 3.2 were divided into 3 groups (29 patients each) and treated with 600mg, 300 mg of Ab plus 10 g of skim milk, and 20 g of skim milk, respectively, for 12 weeks. Fecal bacterial composition analysis by PCR were performed before and after 12 weeks of treatment. **[Results]** A significant reduction in DAS was observed in Ab 300mg group after 4 weeks, and lasted through the 12th week. DAS returned to original levels after discontinuation of the treatment. Characteristic effects of milk antibody treatment were observed in the improvement of SJC, TJC, and pain VAS. Microflora analysis indicated dysbiosis in RA, which is characterized by low Bacteroides fragilis (less than 1/100 compared to healthy adults) and high S. aureus (1000x higher). The improvement of DAS, pain VAS in the Ab treated-group were associated with an increase in the Lactobacillus, B.fragilis population, respectively. **[Conclusion]** Natural milk antibodies modulate the intestinal bacterial composition, and may contribute to improving disease activity in RA.

P3-029

The efficacy of joint injection with hyaluronic acid under the ultrasound guide

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Conflict of interest: None

(Objective) It was selected to only wrist arthritis with ten rheumatoid arthritis patients, they are not more medication during this study. (Method) Sodium purified hyaluronic acid under ultrasonic guide is administered intra-particularly. The continued to evaluate of weekly dose 5 times, after the 5 weeks, no efficacy patient were continued this injection per 2 weeks. (Result) Immediately after hyaluronic acid injection is all cases PDUS signal is lost. In five weeks 2 patients decrease, but 8 patients remained. In a half year, 6 patient were achieved the G1 signal level, but 2patient were remaind. (Conclusion) Results of hyaluronic acid was injected directly into the synovia to dorsal wrist under ultrasound guidance, after the injection immediately PDUS signal was lost. This we suspect that the pressure of the joint cavity has happened disruption elevated fine blood flow by precise intra-articular injection. In a half year, 6 patient were achieved the G1 signal level. It seemed the alternative pathway of the hyaluronic acid effected the joint inflammation.

P3-030

A case report: Tocilizumab was effective for repairing of large bone defect in patient of rheumatoid arthritis

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Conflict of interest: None

[Background] There are few reports on the effect of bDMARDs including TCZ for large bone defect lesions. Here we present the case that the large bone defect lesion of the elbow joint was greatly improved with TCZ in rheumatoid arthritis (RA) patient. [Case] A 66-year-old man. From 2013 bilateral elbow pain appeared and gradually worsened. In September 2015 he was introduced to our hospital because of his remarkable joint deformation. We diagnosed as RA because joint swelling, tenderness and severe bone destruction were seen in his elbow and wrist, and the result of blood test was as follows, CRP 2.4, anti-CCP antibody 156. A large bone defect image of 29.7 mm × 21.0 mm was found in the distal region of the left upper arm. MR image showed the legion to be synovial cyst inside bone. Since we diagnosed as RA with high disease activity (DAS28-ESR 5.18), we started the treatment with MTX and gradually increased the dose to 12 mg/week. However disease activity was not controlled, TCZ subcutaneous injection was applied. The disease activity became to remission (DAS28-ESR 1.73) at 24 weeks after introduction and humeral bone absorption lesion was remarkably reduced to 10.4 mm×8.6 mm with 36 weeks treatment of TCZ. [Conclusions] TCZ might contribute for the treatment of large bone defect lesions.

P3-031

Case report of elbow joint infection in rheumatoid arthritis patients treated with tocilizumab

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Conflict of interest: None

[Object] The purpose of this study was to report the case report of elbow joint infection in rheumatoid arthritis patients treated with tocilizumab. [Results] Case 1 was a 63-year-old woman who used TCZ and diagnosed with elbow pyogenic arthritis postoperative TEA. Listeria monocytogenes detected from discharge. We conducted debridement and replacement of the hinge part and administered Ampicillin (AMPC) intravenously. During this course CRP remained almost negative. It was possible to preserve the artificial elbow joint with good progress without replacement. [Conclusions] I experienced a case in which inflammation occurred around the artificial joint during use of the biological preparation and it was difficult to diagnose. The artificial joint was preserved and the infection could be calmed down.

P3-032

Successful treatment of rheumatoid arthritis (RA) using Certolizumab Pegol (CZP) after exacerbation by granulocyte-colony stimulating factor (G-CSF): a case report

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Conflict of interest: None

G-CSF is widely used for treating neutropenia. We herein report a case of RA successfully treated by CZP after exacerbation by G-CSF. A 70-year-old woman, who had been diagnosed as having RA at the age of 52 and treated with PSL (2mg), MTX (4mg), developed RA-associated interstitial lung disease. After withdrawal of MTX, she was treated with oral high-dose PSL and intravenous cyclophosphamide. However, she was admitted to the hospital due to drug- or infection-induced neutropenia. She was administered filgrastim and her ANC increased from 345 to 10295 cells/μl on day six. On day seven, severe arthritis of both wrists appeared, and serum CRP levels elevated as high as 13 mg/dl with a high numerical rating scale score. On day ten, she was treated with CZP, and the arthritis and elevated CRP restored after the commencement of the treatment. Granulocyte-macrophage colony stimulating factor (GM-CSF) plays an important role in the pathogenesis of RA. There are some reports of RA exacerbation by G-CSF or GM-CSF administration, and a similar case may happen in different clinical states including RA patients treated with anticancer drugs. Our case provides evidence that biologics are effective for the treatment of G-CSF-induced arthritis in patients with RA.

P3-033

Pulmonary cryptococcosis occurring shortly after starting certolizumab pegol for rheumatoid arthritis

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Conflict of interest: None

[Case] A 70-year-old female had a diagnosis of rheumatoid arthritis (RA) 4 months before. She started to take predonisolone and methotrexate. Two months after starting the initial medication, she got a start to treat with certolizumab pegol. Two months from starting biologics, routine chest CT scan was performed. The patient had no chest symptoms, but CT scan showed multiple pulmonary nodules. Because serum cryptococcal antigen test was positive, we made a diagnosis the lung nodules as cryptococcoma. [Conclusion] The patient developed pulmonary cryptococcosis only two months after stating certolizumab pegol. Cryptococcosis is a rare disease, In one study, only 0.22% patients with RA had cryptococcosis. The same study shows time to crypotococosis diagnosis among RA patient receiving anti-TNF biological was shorter than in patients not receiving anti-TNF biologicals. Cryptococosis can be critical, so we think of crypococcal infection in patients with RA, especially receiving anti-TNF agents.

P3-034

A case report: D-penicillamine-induced myasthenia gravis in patient with rheumatoid arthritis and scleroderma

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Conflict of interest: None

It is well known that rheumatoid arthritis often complicated myasthenia gravis. A seventy-two year old woman with rheumatoid arthritis and scleroderma developed right ptosis after taking D-penicillamine for sixteen years. Investigation including ice pack test, EMG and anti-acetylcholine receptor anti body assay are shown the diagnosis of myasthenia graves. The myasthenic symptoms gradually subsided after the treatment discontinued D-penicillamine and added ambenonium and prednisolone. The incidence of side effects of myasthenia gravis with D-penicillamine is reported to be about 0.5%. We report a case of long-term administration of D-penicillamine induced myasthenia gravis.

P3-035

Tocilizumab was effective for rapidly distructive coxoarthrosis: a case report

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Conflict of interest: None

[Objective] Rapidly destructive coxoarthrosis (RDC) is a refractory disease and the cause is unknown. Ti is also so rapidly progressive disease tha only arthroplasty can relief pain and recover the ADL. In this case, tocilizumab (TCZ) was effective for RDC. [Case] 47 year old female [Chief complain] right hip pain [History of present illness] 9 month before she came to our hospital, she had right hip pain without any trauma history, and it had got worse gradually. Her previous dotor suspected RA, and introduced to us. X-ray indicated sightly joint space narrowing and MRI showed remarkable joint fluid but no evidence of necrosis, bone bursa and erosion. She complained joint pain in her bilateral knees and hand. Labo data showed RF 25.4IU/ml, ACPA 144U/ml, MMP-3 136ng/l, but CRP was low level. We confirmed diagnosis of RA and prescribed 10mg PSL and 8mg MTX. 3months later TAC was added to them. 6 months later X-ray showed progressed joint space narrowing, and we started TCZ prescription. [Results] After 3 months, hip pain was dissapeared, and labo data was improved. [Conclusions] We reported a case of prolonged prognosis of RDC by TCZ. TCZ may be a new treatment option as long as it is prescribed at an early stage of arthrisis.

P3-036

Effectiveness of subcutaneous tocilizumab therapy every week in two patients with active rheumatoid arthritis with inadequate response to subcutaneous tocilizumab every other week

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Conflict of interest: None

[Case1] A 69-year-old man with a history of RA at the age of 68 was seen to our hospital because of persistent high disease activity. He was prescribed PSL at the dose of 15mg, but high disease activity had persisted. He was administered abatacept and golimumab, but they were ineffective. Eight months before, he received IFX, and the dose of IFX was increased to 500mg (8mg/kg). But he experienced infusion reaction, IFX was stopped and he received subcutaneous tocilizumab (TCZ-SC) every other week (q2w). However, he responded to TCZ-SC q2w inadequately, and so we shortened the interval of TCZ-SC to every week (qw). Following two months, DAS28-ESR decreased 7.9 to 4.67. [Case2] A 54-year-old woman with a history of RA at the age of 48 was referred to our hospital because of high disease activity. Five years before our evaluation, ETN was administered and her symptoms improved. But 14 months before, PSL was initiated at the dose of 15mg with increased disease activity of RA. We initiated TCZ-SC q2w. However, she responded to TCZ-SC q2w inadequately, and so we shortened the interval of TCZ-SC to qw. Following three months, DAS28-ESR decreased 6.49 to 2.79. [Conclusion] In patients with high disease activity and inadequate response to TCZ-SC q2w, TCZ-SC qw is an effective treatment option.

P3-037

Efficacy of TNF inhibitor switch against discontinuation of other TNF inhibitor by adverse drug reaction

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Conflict of interest: None

[Object] Biological agents sometimes have to be discontinued due to adverse events. In particular, in the case of adverse drug reaction (ADR) such as an allergic reaction, re-administration of the same drug is often difficult, and how to switch to other drugs is an important issue. In this study, we investigated whether cases that were terminated by ADR other than infectious diseases could switch between TNF inhibitors. [Methods] Among 90 patients with bio naive who had newly introduced TNF inhibitor in our department after March 2013, we extract the case that 1st bio was discontinued due to non-infectious ADR, and 2nd bio was switched to other TNF inhibitor. Then, three cases were extracted. We investigated retrospectively about patient background, drugs used, and disease activity in each case. [Results] The discontinued biologics in the subject cases were IFX 1 case, ETN 1 case, and CZP 1 case. The ADRs that caused drug withdrawal were anaphylactic shock, fever, and generalized pruritus sensation, respectively. After drug withdrawal, all TNF inhibitors changed were golimumab, no new adverse events were observed, and treatment was continued. [Conclusions] It was suggested that golimumab can be used effectively and relatively safely even in RA cases with an ADR to TNF inhibitor.

P3-038

Achieving biologic-free remission after Etanercept use: a case report

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Conflict of interest: None

Object: The need for biological drug increases as treatment of the rheumatoid arthritis. However, the next goal is to aim for biologic-free from the burden of expensive medical expenses and the mental burden of treatment continuation. We reported in our hospital that patients with Etanercept (ETN) have experienced a case of achieving biologic-free remission. Patient: 69years, Male, SATGE1, CLASS1, smokerOnset, in winter 2011, MHAQ0 DAS28-CRP:3.03, CDAI:10, SDAI:10.86 Treatment: MTX started from 6mg/W and was increased to 10mg in 2 months, but since improvement is good, ETN 50 mg/W was added additionally. After 4 months RA improved disease activity (DAS28-CRP:1.19, CDAI:2, SDAI:2.03). It gradually tapering and became biologic-free remission four years and six months after the start of treatment. It has not exacerbation after one year. Disscusion: As for the PRESERVE examination, ETN reports that the patient who continued use than the patient whom I stopped can hold down disease activity to predominance. However, the ENCOURAGE Study showed that if remission was achieved both at 6 months and 1 year after administration, half could keep remission for 1year even after discontinuation of ETN administration thereafter. Conclusion: I reported a patient who achieved biologic-free remission using ETN.

P3-039

A case in which fingolimod was effective for rheumatoid arthritis control in multiple sclerosis complicated with rheumatoid arthritis

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Conflict of interest: Yes

[Case] A 55-year-old female diagnosed with multiple sclerosis 8 years ago. Although it had prevented reoccurrence by steroid or self-injection of interferon β1a against multiple sclerosis, recurrence continued, and about a year and a half ago, it was changed to medicine treatment of fingholmod. Finger joint pain was seen from 5 months ago and it was introduced to Rheumatology Department. Rheumatoid arthritis was diagnosed based on findings of polyarthritis pain and anti-CCP antibody strongly positive and erosion with X-ray. It was predicted that the activity was high and the progress of joint destruction was early, but after the addition of only salazosulfapyridine, there was no pain thereafter and the control of rheumatoid arthritis was good. [Discussion] Fingolimod suppresses the process of T cells leaving the lymph node via sphingosine 1-phosphate receptor type 1 (S1 P1 receptors), and regulation of the circulation of T cells allows immune regulation to exert its effect. Efficacy to rheumatoid arthritis has also been suggested, but there are few reports on clinical practice. We report that fingolimod is useful for the control of rheumatoid arthritis in patients with multiple sclerosis with rheumatoid arthritis combined.

P3-040

A case of RA patient who had been complicated with cryptic organizing pneumonia under the treatment with golimumab, followed by anti-IL-6 receptor antibody, tocilizumab, showed minimal response to arthritis. But when he again received anti-TNF therapy, certolizumab-pegol, she dramatically improved clinical symptoms

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Conflict of interest: None

77 years-old RA patient, who had been treated with golimumab, developed cough and fever with the high-inflammatory reaction (high CRP and WBC elevation) by blood examination. Computer-tomography scanning of her chest revealed the existence of ground-glass occupancy in both lungs. By CT-guided biopsy, she was diagnosed as cryptic organizing pneumonia (COP). Corticosteroid therapy improved all of her clinical symptoms immediately. However, when her dosage of steroid reduced to 12.5mg, arthralgia relapsed. Considering the cause of COP, she received the treatment with anti-IL-6 receptor antibody, tocilizumab (TCZ). But TCZ therapy showed minimal efficacy. Then, she was administrated another TNF inhibitor, certolizumab-pegol (CZP), and CZP showed dramatically improvement of her arthralgia. COP has not been occurred again until now.

P3-041

A case with rheumatoid arthritis (RA) who developed methotrexate (MTX)-related lymphoproliferative disorder (LPD) leading to prominent necrosis of lymph nodes

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Conflict of interest: None

A 65-year-old man with a 10-year history of seropositive RA presented with gradual enlargement of right cervical lymph nodes (LN) followed by persistent fever (>38 C) 2 months later, when he had achieved sustained remission by MTX 6mg/w therapy. The size of tender supraclavicular LN was 7 cm in diameter. The LN in the left neck and groin areas were also palpable (2 cm). CRP was elevated (15 mg/dl). Ga scintigraphy showed intense accumulation in superficial and mediastinal LN. The cessation of MTX led to amelioration of fever and elevated CRP 14 days later, which was compatible with MTX-related LPD. Notably, the right supraclavicular LN became elastic soft, and CT scan revealed LN necrosis. EB VCA-IgG was positive (320x) without EBNA, and EBV DNA was detected (1000 copies/million), suggesting EBV activation. Although LPD did not recur after 1-year cessation of MTX, EBV activation still persisted with positive EA DR-IgG (40x), EBNA (10x) and EBV DNA (580 copies). Here we have described a case of MTX-LPD leading to prominent LN necrosis. It is reported that LN necrosis is rare in MTX-LPD, while it was relatively common in EBV-induced LPD. We therefore suggest that EBV could be involved in the swelling as well as necrosis of LNs in our case.

P3-042

2 cases of rheumatoid arthritis patients who developed systemic lupus erythematosus following anti- TNF-antibody agents

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Conflict of interest: None

[Object] To investigate on the frequencies and characteristics of SLE eruption due to anti-TNF-α agents. [Methods] We present two such cases and investigate on them. [Results] We experienced two cases of RA patients who developed SLE following the use of anti-TNF-α. The first case, a 57-year-old male patient, stage II, class 1, who was on infliximab, erupted SLE with a rash on his forehead, fever and pleuritis at 21 months. The second case, a 56-year-old female, stage III, class 1 was on adalimumab for 4 months when SLE erupted with execerbation of arthritis, followed by fever, venous thrombosis and rash on the lower limb. Anti-TNF-agents were withdrawn from both patients. The first patient with pleuritis improved with steroid, but later experienced RA execerbation and was on MTX again. The second case required the use of HCQ and MMF in addition to steroid. We often experiece a rise in anti DNA antibody due to anti-TNF-α, but eruption of SLE itself is less common. [Conclusions] In our study, we found fever, rash, arthritis to be common features, and serum tests like ANA positivity, rise in anti-DNA-antibody titers should lead to suspicion of anti-TNF-α induced SLE and mere cessation of anti-TNF-α agents will often not ameliorate its course, steroid is required for treatment.

P3-043

Protective Effects of Denosumab on Carpal Bone Erosion in Early RA: A Case Report

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Conflict of interest: None

<Case> 68y Female <Chief Complaints> Bilateral wrist pain and swelling <Clinical Course> October 2016, morning stiffness and bilateral wrist pain occured. In December, she visited our hospital. At first visit, hematology revealed inflammation. In MRI findings, carpal bone erosion appeared, so diagnosed early RA. Although prescribed MTX, VAS was not recovered. So ABT injection therapy started. CRP decreased, but wrist pain still continues. In DEXA study, Bone Mineral Density was marked decreased. Denosumab therapy began. Gradually wrist pain decreased, and VAS increased. In MRI, Bone erosion diminished. <Conclusion> In early RA, Denosumab had protective effects on carpal bone erosion.

P3-044

Preexisting interstitial pneumonia deteriorated only during a limited period of the use of specific disease modifying anti-rheumatic drugs: report of two cases

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Conflict of interest: None

<Cases> Case 1: A 72 year-old man with stable interstitial lung disease (ILD) was diagnosed with rheumatoid arthritis (RA). Ground glass opacity (GGO) and reticulation deteriorated during the use of tacrolimus (TAC), while it had efficacy for RA. After TAC had been discontinued, active lesions diminished with remaining fibrosis and no ILD progression occurred. Case 2: A 48 year-old woman with RA accompanied by fibrotic NSIP discontinued MTX due to infection. Subsequent use of bucillamine (BUC) showed efficacy but after 6 months she had cough and dyspnea, regarding which CT showed worsening of ILD. Upon the cessation of Buc her symptoms improved, active lesions diminished, and no ILD progression occurred. <Discussion> To date the most typical drug-induced ILD (DILD) associated with disease modifying anti-rheumatic drugs (DMARDs) is considered to be bilateral shadows located in the non-peripheral middle/upper lung fields, presumably reflecting circulatory distribution; in contrast, our cases showed a different pattern, the exacerbation of preexisting ILD. The fact that the ILD activity was observed during a limited period between the start and cessation of the suspected medicines suggested the probable involvement of specific DMARDs in evoking exacerbation of preexisting RA-ILD.

P3-045

Differences of clinical performance between 50mg and 100mg of golimumab in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] This study evaluated the differences of clinical performance between 50mg and 100mg of golimumab in patients with rheumatoid arthritis. [Methods] The clinical background and the changes of disease activity score (DAS28-ESR) were analyzed for fifty-nine patients (50mg group; 35 cases, 100mg group; 24 cases) who were treated with golimumab at least three months. [Results] The rates of concomitant use of methotrexate (MTX) were 94.3% in 50mg group and 50.0% in 100mg group. The mean doses of MTX were 8.2 and 6.7 mg/week respectively. Also, the rates of concomitant use of prednisolone (PSL) were 60.0% in 50mg group and 41.7% in 1000mg group. The mean doses of PSL were 4.5 and 7.1 mg/week respectively. The DAS28-ESR at baseline were 3.86 in 50mg group and 3.95 in 100mg group (n.s.). The rates of remission at 12 and 24 weeks were 25.9%, 28.6% in 50mg group and 44.4%, 46.7% in 100mg group. The averaged differences of DAS28-ESR from baseline at 12 and 24 weeks were -0.91, -0.97 in 50mg group and -1.36, -1.35 in 100mg group (n.s.). [Conclusions] Although there were no statistically significant results from our data, the administration 100mg of GLM tended to show better clinical efficacy in early period of treatment.

P3-046

Clinical Usefulness of Adalimumab in elderly RA Patients

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Conflict of interest: None

[Object] RA patients are also aging. For elderly patients restrict biological products from the viewpoint of concomitant drug restriction and organ reserve. In order to aim for a high therapeutic goal, it is considered that TNF antibody preparation is excellent, so we examined the effectiveness and safety of adalimumab with elderly RA patients. [Methods] Subjects were 234 analyzable RA patients that were introduced to ADA treatment at this institution from May 2009 to May 2014. Mean age was 54.2 years, mean duration of illness 76 months, rate of concomitant MTX use 97% (mean dose of 11.5 mg/week), and mean DAS28CRP (DAS) 3.9. Efficacy of ADA treatment after 152 weeks was comparatively investigated in each group, namely, the elderly patients (E group) and non-elderly patients (Y group), Efficacy was evaluated by DAS change, remission rate, EULAR response, HAQ score change amount. [Results] DAS score change (average: E group -2.1, Y group -2.1), remission rate (E group 83%, Y group 72%), EULAR good response (E group 72%, Y group 60%), HAQ score change (average: E group - 0.406, Y group - 0.404) did not differ in either group. [Conclusions] It was suggested that ADA is a useful treatment option even in the elderly.

P3-047

Comparison of the retention rate of biological DMARDs ~ the data from patients with RA who were followed up for over 10 years

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Conflict of interest: None

[Object] In Japan, infliximab (INF) was applied in 2003 for RA treatment, and etanercept (ETN) in 2005, adalimumab (ADA) and tocilizumab (TCZ) in 2008. Since 2003, RA treatment by ADA and TCZ had been conducted by clinical trials. In this study, we evaluated the retention rate of these bDMARDs for over 10 years. [Methods] RA patients who started the treatment with INF, ETN, ADA, or TCZ before 2007 and were observed for over 10 years were included in this study. INF group included 95 out of 111 cases, ETN group included 95 out of 119 cases, ADA group included 24 out of 27 cases, and TCZ group included 21 out of 25 cases. The retention rate of the bDMARDs was calculated using Kaplan-Meier survival analysis. [Results] There was no statistically significant difference in the retention rate of these bDMARDs. The retention rate of INF and TCZ decreased with time and was 10.5% and 33.3% at the final survey in November 2017, respectively. That of ETN and ADA plateaued at 9 years after the start of treatment and was 22.1% and 8.33% at the final survey, respectively. [Conclusions] The retention rate of over 10 years was the highest in TCZ and the lowest in ADA. The rate of INF and TCZ continued to decrease, and that of ETN and ADA was almost constant after 9 years from the start of treatment.

P3-048

Clinical Usefulness of Adalimumab in High Disease Activity RA Patients ~Remission Induction Rate at 152 weeks in 71 Patients~

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Conflict of interest: None

Objective Clinical usefulness of 152-week adalimumab (ADA) treatment in high disease activity (HDA) RA patients (DAS28ESR>5.1) was investigated over time. **Methods** Subjects were 71 analyzable HAD RA patients that were introduced to ADA treatment at this institution from May 2009 to May 2014. Mean age was 58.9 years, mean duration of illness 7.2 years, rate of concominant MTX use 93% (mean dose of 11.2mg/week). and mean DAS28ESR (DAS) 6.2. Efficacy of ADA treatment after 152 weeks was comparatively investigated in each group, namelr, the Bio Naïve (N group) and Switch (S group), duration of illness below 2 years (<2 group) and over 2 years (≧2 group), MTX ≧12mg/week (≧12 group) and <12mg/week (<12 group). **Results** At 152 weeks, DAS remission rate in the overall patients was 52% with significantly high efficacy for the N and <2 groups, and a high tendency for the ≧12 group. At 152 weeks, HAQ remission rate for the overall patients was 66%, which was good. **Conclusions** Good responsivity was achieved with ADA even in HDARA patients. In particular, it was demonstrated that the potential of ADA can be exploited maximally producing better treatment efficacy when it is given concomitantly with an adequate dose of MTX to early onset and Bio Naïve patients.

P3-049

Evaluation of adalimumab continuation rate from the point of view of combined dose of methotrexate

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Conflict of interest: Yes

[Objectives] We investigated the combination dose of MTX and the effectiveness of ADA from the continuation rate. [Methods] RA cases in which ADA was introduced were examined. MTX combination dose (6 mg / week or less, 8 mg / week or more, and not used in combination) was classified into 3 groups. The number of continuous cases (%) was analyzed in each group at the first year, the second year, the third year, and the fifth year from the introduction of ADA. [Results] There were 88 RA cases, 20 males and 68 females. The average age was 56.7 years. The continuation example (%) of the whole (88 cases) was 1 year: 79.5, 2 years: 64.7, 3 years: 47.0, 5 years: 20.5. Adverse events, dropout examples due to weakness of effect were 14 cases, 6 cases, 1 case, 5 cases respectively, and 4 cases, 7 cases, 15 cases and 18 cases were discontinued cases due to transfers and withdrawal of remission. Continuation rate (%) of each group was 86.3, 72.7, 49.1, 31.8, in MTX 6 mg / week or less group (22 cases), 83.3, 66.7, 44.4, 27.8, in MTX 8 mg / week or more group (18 cases), and 75.0, 60.4, 41.7, and 12.5 in without MTX group (48 cases), respectively. [Conclusions] The continuation rate of ADA tended to be higher in the MTX combined group. MTX combination dose did not affect the continuation rate.

P3-050

Onset age of rheumatoid arthritis on the effectiveness of biologics

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Conflict of interest: Yes

[Objective] Patients with rheumatoid arthritis (RA) also have advanced aging, with half of cases of those aged 65 years or over being momentum. Elderly onset RA (EORA) is often inflammatory as compared with young onset RA (YORA) and is often refractory to treatment. We examined whether there is a difference in the effectiveness of biologics (BIO) from onset age. [Methods] We targeted 95 RAs who were 65 years of age or older and treated by BIO. Patients' background before treatment, change amount of DAS28 ESR at 52 weeks, remission rate, etc. were analyzed retrospectively. We defined YORA group as under-65 years of age and EORA group as onset over 65 years. [Results] On the patient background, there were more women and younger patients, and MTX combined rate and BIO naïve were rate higher in the IFX group. The amount of DAS28 ESR change tended to be large in the YORA group in IFX and ABT. The remission rate tended to be higher in the EORA group in IFX and in the YORA group in ABT. On the other hand, in TCZ both groups had the same trend. [Conclusions] As a result of examining the effectiveness of BIO as seen from the onset age of RA, the tendency varied depending on the type of BIO.

P3-051

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: Results from long-term period of the SHINOBI study

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Conflict of interest: Yes

Objective: To investigate the long-term 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 the 12 week double-blind (DB) period, followed by an open-label period where all pts received TCZ-SC QW up to Week 52. **Result:** Of the 21pts in each group (total 42) in DB period, 19 pts in TCZ-SC QW and 17 pts in TCZ-SC Q2W entered the open-label period. 14 pts in each group completed the 52 weeks. In the open-label period, improvement in ΔDAS28-ESR [12 weeks -> 52 weeks] was continued in TCZ-SC QW group [-2.31 -> -3.19] and observed in TCZ-SC Q2W group [-1.13 -> -2.93]. Most common adverse events were infections and the trend of events observed over the long-term period was similar to previous Japanese clinical trials of TCZ-SC Q2W. There were no clinically problematic changes in the laboratory data. **Conclusion:** The efficacy was sustained in long-term administration of TCZ-SC QW in RA patients with IR to TCZ-SC Q2W, and safety profile of QW were similar to previous clinical trials of TCZ. Shortening TCZ-SC dosing in-

terval up to QW might be a considerable treatment option for RA.

P3-052

Clinical characteristics and management in elderly rheumatoid arthritis

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Conflict of interest: None

[Object] Although the number of patients with elderly rheumatoid arthritis (RA) is increasing, there is no clear guideline for elderly RA. Objective of this study was to clarify clinical characteristics and treatment strategy of elderly RA. [Methods] In this study, elderly RA was dedined more than 65 years old. This retrospective study comprised consecutive 476 with elderly RA and 314 with non-elderly RA in Obihiro Kosei Hospital. Clinical characteristics, treatments and disease activity were analyzed. [Results] The rates of past history of HBV, positive T-spot, less than 10 mg/dl of Hb and less than 60 ml/min of eGFR were significantly higher in elderly RA compared with non-elderly RA (39.3% vs 17.2%, 5.7% vs 2.0%, 8.7% vs 2.9%, 48.6% vs 16.0%, respectively). The rate of MTX use was significantly lower in elderly RA (61.3% vs 83.8%). The rate of biologics use was not different (30.3% vs 29.9 %). The rates of DMARDs except MTX and PSL use was significantly higher in elderly RA (44.7% vs 33.1%, 45% vs 24.5%, respectively) and 57.1 % of elderly RA with TAC was not treated with MTX. The disease activity was not different (DAS28/CRP remission rate, 66.1% vs 69.6%). [Conclusions] Complications, organ dysfunctions and drugs should be considered in elderly RA patients.

P3-054

Evaluation using joint echo to the foot lesions of rheumatoid arthritis (ankle mtp arthritis tendon synovitis) in our clinic and clinical investigation on efficacy and safety of local injection of triamcinolone under echo guidance

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Conflict of interest: None

[Object] Evaluation of foot lesions using joint US and intra-articular injection of triamcinolone will be examined to evaluate its treatment. [Methods] Ankle and MTP joint US was performed on 186 patients diagnosed as RA. GS 2 or more PD 2 or more 35 joints 60 joints were recognized, local injection under US was performed on them, and the evaluation at 2 to 24w was performed by US. [Results] Asymptomatic group was observed in 8 cases 12 joints, PD disappearance in 24w was 31 cases 55 joints, recurrence ineffective group (#2) were 4 cases 5 joints. When comparing the remission group (#1) and #2 Age duration period MTX Bio use rate Although there was no significant difference in DAS before administration, the PSL usage rate in the #2, the prevalence of GS 3 and bone erosion before administration was significantly In the #1, PD was disappeared within 2w in all cases, and VAS was also significantly improved. There was no significant difference when grouping with symptomatic and asymptomatic group. [Conclusions] In the #1, structural remission was obtained at a high rate (91%). Asymptomatic cases requiring therapeutic intervention accounted for 20% of the total and periodic evaluation was considered necessary. Effectiveness of combined use of DMARDs and joint injection has been reported.

P3-055

Ultrasonography images of early response to certolizumab PEGol in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To evaluate the early responsiveness of ultrasonography (US) for assessing synovitis in biologic-naïve patients with rheumatoid arthritis (RA) starting certolizumab PEGol (CZP). [Methods] Articular synovitis was assessed by US in 4 RA patients starting CZP at baseline, and weeks 2, 6 (or 8). Tested joints, with swelling or arthralgia, were different among patients. [Results] 4 RA patients (3 women and 1 man) were included. At the first visit, mean disease duration was 6.0 months, and aged 39-76 years. They were treated with methotrexate (mean 9.5mg weekly), prednisolone (mean 5.1mg daily), and mean DAS28-CRP was 3.88 at the start of CZP. In all patients, the degree of synovial inflammataion of multiple joints decreased at 2 weeks and 6 (or 8) weeks. The levels of improvement were affected by both the sites and individuals. In spite of the patient education, patients tended to be active. The findings of US were were worsened in some joints. After 5 or 10 months, US findings of two patients improved, another swithed to golimumab because of secondary failure. [Conclusions] CZP with loading dose improves clinical response. It is said that RA disease activity at 8~12 weeks is predictors of CZP 12 months response. Ultrasonography image is useful to evaluate early response to CZP.

P3-056

Patients with rheumatoid arthritis whose age at onset were over 70 years

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Conflict of interest: None

[Objectives] We evaluate the patients with rheumatoid arthritis (RA) whose age at onset were over 70 years old. [Methods] Thirteen RA patients (female 9, male 4) whose onset of RA were between April, 2010 and June, 2013 were registered. Their age was 76.5±5.0 (mean±SD) and disease duration was 7.1±7.1 months. At October 2017, these patients were examined. Disease activity with DAS28ESR (4), and treatment progress were studied. [Results] At the first visit, mean DAS28 was 5.9±1.4, the number of high disease activity was 10, six patients had arthritis in large joint, five patients were seronegative and 4 of them were high disease activity. Treatment with MTX were started in 11 patients, and each of 2 patients treated without MTX had lung cancer and bronchiectasis. bDMARDs were used in 2 patients, one was treated with Etanercept, and one was treated with Tocilizumab after the insufficiency treatment with Golimumab. Total hip arthroplasty was made in one patient who were treated with Tocilizumab. Synovectomy of wrist joint was made in 1 case. At October 2017, 9 cases were in DAS remission, and one of them was drug free remission. [Conclusion] Seventy months follow up of 13 RA patients whose age at onset were over 70 years old was performed, nine cases were in DAS remission.

P3-057

Study of elderly patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To clarify the treatment situation of Japanese elderly patients with rheumatoid arthritis (RA). [Methods] 51 RA patients older than 65 years were subjected for the study. The mean age was 73±5.7

year-old (range 65~84), male:female=16:35, mean disease duration was 18±12 years (1~50y). Stage1/2/3/4: 11 (22%)/9 (17.5%)/9 (17.5%)/22 (43%), class 1/2/3/4: 5 (10%)/41 (80%)/5 (10%)/0 (0%). [Results] Mean DAS28-CRP was 2.43±1.02, and high disease activity was 2 (4%), moderate 15 (29%), low 8 (16%), and remission 16 (33%). The most common comorbidities were lung problems (57%), followed by cardiovascular (25%), diabetes (24%), and chronic kidney disease (22%) etc. Methotrexate (MTX) was used in 25 cases (49%), and mean MTX dosage was 6.8±2.9 mg/week. bDMARDs were used in 22 cases (43%), and csDMARDs other than MTX were used in 31 cases (61%). Glucocorticoids were used in 17 cases (33%), and mean prednisolone dosage was 4.4±2.0 mg/day. [Conclusions] MTX cannot be used satisfactorily in many elderly RA patients due to comorbidities in several important organs. It is necessary that these patients are treated properly with bDMARDs and csDMARDs other than MTX.

P3-058

Examination of disease activity course of RA patients switching from the original IFX to IFX biosimilar

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Conflict of interest: None

[Object] Since 2016, in the treatment of patients with rheumatoid arthritis (RA), we have changed from the original IFX to IFX biosimilar (IFXBS) after obtaining consent from patients. We examined the middle-term clinical results containing the disease activity after the change. [Methods] We examined 44 RA patients. They were treated with original IFX at the time of August 2016 and then switched to IFXBS. Disease activity worsening was defined that DAS28CRP got worse more than one stage, or that IFXBS was required to increase by arthritis symptoms worsening. [Results] There were 6 patients who showed disease activity worsening after changing to IFXBS. In these patients, increasing dose (average dose 5.7mg/kg→8.8mg/kg) was necessary, but all patients showed disease activity improvement after increasing dose. In addition, these groups showed a higher tendency for DAS 28CRP before IFXBS change ($p=0.041$), as compared with the group in which disease activity was maintained even after change to IFXBS. [Conclusions] Almost good disease activity could be maintained with IFX to IFXBS change, but in some cases increasing dose was required. However, even if these cases continued the original IFX, it seems that there is a possibility that it may be a case group which had weakened effectiveness.

P3-059

The 36 months efficacy and safety of certolizumab pegol in Elderly patients with Rheumatoid arthritis

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Conflict of interest: None

Object] Elderly patient with Rheumatoid arthritis (ERA) has several comorbidities, especially renal failure and chronic lung disease. In many cases Methotrexate (MTX) was not used. Efficacy of Biologic DMARDs in ERA was seemed to decrease without MTX. ERA patients that were treated by CZP over 36-month were analyzed efficacy and safety Method] 36 Elderly RA patients (11mens and 25women) over 36-month were analyzed. Mean age was 78.4years old (65-91). Mean of disease duration is 6.6years. 20cases are bio-naive.16cases were administrated MTX (22%). The number of CKD classification were G1 (2cases)/G2 (17cases)/G3 (13cases)/G4 (1case)/G5 (1case). We investigated SDAI, DAS 28-ESR, eGFR, participation rate and safety. Result The mean of participation rate was 55.6% over 36month with CZP therapy (75%withMTX,50%without MTX, naive case 70% switch cases 43.8%).9cases were altered another biological DMARDs because efficacy of CZP therapy were not sufficient. 6cases were discontinued for adverse event. The level of eGFR was stationary within an observation period of 36months. Conclusion] MTX tends to be not used in ERA compared with Young onset RA because of comorbidities. CZP treatment for ERA without MTX excellent efficacy and participation rate.

P3-060

Experience of using Golimumab for RA patients in orthopedic clinic

Toshiharu Okuda
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Conflict of interest: None

[Object] We report on the continuation situation, treatment effect, etc. of rheumatoid arthritis (RA) patients who used Golimumab in our orthopedic clinic. [Methods] Beginning use of Golimumab at our clinic since July 2012, 14 cases (2 men and 12 females) who passed 52 weeks or more were targeted. The mean age was 67.1 years, mean RA disease duration was 23.6 years, there were no bio naïve cases, all cases were examples from other TNF inhibitors (Etanercept 10, Adalimumab 4). For these cases, we investigated and evaluated continuation rate, transition of inflammatory marker / disease activity, etc. [Results] Twelve patients (continuation rate: 85.7%) continued at 52 weeks of age, and two cases which seemed to be ineffective were changed to other biological products at the request of patients. Changes in the average value of DAS 28-CRP in the case of continuation improved to 2.17 at 4.31 before administration and 52 weeks after administration. There was no appeal of pain at the time of injection as compared with other drugs, and the number of injections decreased, and patient satisfaction was high in the case of symptom improvement. [Discussions] Golimumab seems to be useful as one of the options for biological products after using other TNF inhibitors.

P3-061

Altered expression of multiple miRNAs including miR-223, miR-451a, miR-150-5p by Leukocytapheresis for rheumatoid arthritis patient

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Conflict of interest: None

[Object] Leukocytapheresis (LCAP) is a safe, unique therapy pertaining to intractable rheumatoid arthritis (RA) even in cases of drug allergy or infectious states. LCAP is also known to improve inflammatory bowel disease, pyoderma gangrenosum, chronic demyelinating neuropathy and skin ulcers caused by rheumatoid vasculitis. However, details of the LCAP efficacy mechanisms are still unknown. Aimed to elucidate that, we have investigated the alteration of microRNA (miRNA) expression in the LCAP procedure for RA patient. [Methods] Blood samples were collected from a RA patient who underwent the LCAP therapy at our hospital, just before and after the procedure and at the time of 750ml blood treatment. Total RNA was extracted using miRCURY™ RNA Isolation Kits (Exiqon) according to the manufacturer's instructions. miRNA expression was comprehensively analyzed using a 3D-gene™ miRNA Oligo chip (Toray). [Results] After LCAP procedure, enhanced expression of hsa-miR-19b-3p, reduced expression of hsa-miR-223-3p, miR-451a, miR-150-5p, miR- 26a-5p, miR-363-3p were observed. [Conclusions] Alteration of multiple miRNAs expression which were reported to be associated with the pathology or prediction of therapeutic effect of RA previously, were also observed. It may be related to the therapeutic effect.

P3-062

Disease activity in rheumatoid arthritis during pregnancy

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Conflict of interest: None

(Objectives) In previous studies, disease activity of rheumatoid ar-

thritis (RA) can ameliorate spontaneously during pregnancy and flare postpartum. However, recent reports suggested that the patients with RA often flared during pregnancy. Herein, we investigated retrospectively disease activity of RA during pregnancy. (Methods) From June 2012 to April 2017 in total 28 pregnant RA patients were enrolled in this study. Disease activity were assessed before conception, each trimester during pregnancy and postpartum. Disease activity was measured with the DAS28-CRP. (Results) Age at conception is 33.0±4.1 years. Twenty-five patients (89%) were RF and ACPA positive. Seven patients were anti-SSA antibody positive. The patients were treated with prednisone (n=6), sulfasalazine (n=5), tacrolimus (n=9), and biological (b) DMARDs (n=13) within 4 months before conception. Mean DAS28-CRP significantly elevated from 1.76±0.47 in before conception to 2.28±0.51 in second trimester (p=0.046). In second trimester, the patients who treated with bDMARDs tend to have low disease activity compared to not treated with bDMARDs (DAS28-CRP 1.51±0.50 vs 2.71±0.58 p=0.057). (Conclusions) In this study, RA disease activity may flare during pregnancy, particularly, in the patients without bDMARDs treatment.

P3-063

Three-dimensional printing for preoperative planning of revision total hip arthroplasty

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Department of Bone and Joint Surgery, Ehime University School of Medicine

Conflict of interest: None

[Object] There are decreasing tendencies of total hip arthroplasties (THA) to RA patients due to MTX and biological products. However, loosening of THA prior to introduction and giant bone defects have been found, and its reconstruction is technically difficult. In recent years, 3D printers can create 3 - dimensional full - size solid bone models that accurately reproduce deformed bones from CT images, and it is possible to compensate for difficult parts that are difficult to evaluate with images. This time, preoperative planning and simulation of revision THA of RA patient with giant bone defect are reported using gypsum scale full bone model (Biotec Bones). [Methods] Three cases subject. All patients were RA and having large bone defect after THA. [Conclusions] The 3D model allowed for trialing of the acetabular component to determine cup size and position. Furthermore, With 3D printing technology, complex pelvic deformities were better evaluated and treated with improved precision. Life-size models allowed accurate surgical simulation, thus improving anatomical appreciation and preoperative planning.

P3-064

Outcomes of cementless total hip arthroplasty in rheumatoid arthritis

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Conflict of interest: None

(Object) We investigated the outcomes of cementless total hip arthroplasty (THA) for RA patients, whose bone quality is considered to be comparatively poor. (Methods) The study subjects were 40 hips of 38 patients with RA who had undergone cementless THA. Their mean age was 62.4 years, and mean follow-up was 7.3 years. The parameters investigated were preoperative and postoperative modified Harris Hip Score (mHHS), aseptic loosening on X-ray, the implant replacement rate, and complications. (Results) Mean preoperative mHHS improved significantly from 35.2 points preoperatively to 76.9 points postoperatively. Aseptic loosening occurred on the cup side and the femoral side in 1 hip each. Revision surgery was performed in 2 hips because of septic and aseptic loosening. Complications comprised implant infection in 2 hips, and periprosthetic fracture in 2 hips. (Conclusions) In our evaluation of patients who all underwent cementless THA, postoperative mHHS score improved significantly. The presence of infection and periprosthetic fracture in 2 hips each, however, indicates that full consideration should be given to RA-specific immunodeficiency and poor bone quality when determining surgical indications.

P3-065

Treatment of periprosthetic femoral fracture in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] We invested 6 cases of [Object] We investigated 6 cases of periprosthetic femoral fracture after bipolar hemiarthroplasty and total knee arthroplasty in patients with rheumatoid arthritis. [Methods] All 6 cases were female and the mean age of these patients was 74.8 years and the duration of illness was 26 years at operation. The surgeries included bipolar hemiarthroplasty (n=2) and total knee arthroplasty (TKA) (n=4). [Results] According to Vancouver classification, one case was type B1 and the other was type B2 in periprosthetic femoral fracture after bipolar hemiarthroplasty. We fixed using long stem with CCG band in type B2 and NCB periprosthetic femur plate (Zimmer) in type B1. In periprosthetic femoral fracture after TKA, we fixed using Supracondylar intramedullary nail in 3cases and Periarticular distalfemoral plate in one case. After operation, X-ray revealed that all cases resulted in union. [Conclusions] Treatment of periprosthetic fractures was a good result in these cases. Also important osteoporosis treatment along with the need to tight control in the treatment of RA.

P3-066

The predictive factors of the radiolucency around the highly porous cup in cementless Total Hip Arthroplasty

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Conflict of interest: None

[Object] The coefficient of friction of the acetabular cup of a cementless total hip arthroplasty (THA) reported as an important factor affecting initial stability. Increasing the coefficient of friction could potentially eliminate micro-motion at the interface. As a result, highly porous metal acetabular cups have been introduced the reports over the past decade that these were established the osseointegration in primary and revision hip arthroplasty. [Methods] We performed both clinical and radiographic evaluation of 100 patients (108 hips) who had undergone cementless THAs using the highly porous cups (SQRUM TT socket; KYOCERA Medical) after an average 1.5-year follow-up period. [Results] The JOA hip scores improved from 52.8±1.2 points preoperatively to 88.5±1.0 points postoperatively. 93 hips were obtained primary stability and secondary osteointegration, remaining 15 hips had radiolucent line accompanied with sclerotic line on the circumferential of the highly porous cups. [Conclusions] The highly porous cups obtained immediate and long-term implant stability in the cases with the good bone conditions. On the other hand, there is a possibility that poor bone quality induced radiographic evidence of poor osseointegration.

P3-067

The clinical evaluation of acetabular cup with 3D porous structure for RA patients

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Conflict of interest: None

[Introduction] We used acetabular cup having a 3D porous structure for seven RA patients (eight joints), so we report on their usefulness. [Method] The evaluation items were 1) implant placement angle (inclination angle / anteversion angle), 2) presence / absence of screw fixation, 3) presence or absence of complications, 4) JOA score before and after operation, 5) JHEQ. [Results] Average inclination angle was 43.6 ° and anteversion angle was 11.9 °. 7 cups were inplanted in the safe zone. In five joints screw fixing was unnecessary. There were no intraoperative and

postoperative complications, JOA score improved from 54.4 points to 85.6 points, JHEQ 28.5 points improved to 64.1 points. [Conclusion] There are cases in which osteoporosis is complicated in RA, and 3D-cup is thought to be more useful in RA.

P3-068

Short term result of silver oxide-containing hydroxyapatite coating total hip arthroplasty in patients with rheumatoid arthritis

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Conflict of interest: None

[Objectives] Prosthetic joint infection is a serious complication of implant therapy. To prevent prosthetic joint infection, we developed the features of silver oxide-containing hydroxyapatite (Ag-HA). We have performed cementless THA using an Ag-HA-coated implant in patients with RA. The purpose of this study was to investigate the short-term clinical results of this procedure. **[Methods]** Seven hip joints in 7 RA patients, all 12 females, with a follow-up of at least 1 years after surgery were retrospectively enrolled. The average age at surgery was 68.0 years old, and the mean follow-up period was 1.1 years. We evaluated the clinical results (in terms of JOA score) and radiographic findings. **[Results]** The mean JOA score before surgery was 37.9 points, improving to 81.3 points at the time of follow-up. No adverse reaction to silver was noted, and argyria was not observed in any case. No patients have developed infection after surgery. In radiographs, the stability of cup were bone in growth in all hip joints. As for the stability of the stem, bone ingrown fixation was obtained in all hip joints. **[Conclusion]** In spite of the short follow-up period, the clinical results of the cementless THA using the Ag-HA-coated implant in patients with RA were good.

P3-069

Early aseptic loosening after revision THA with Trabecular Metal Acetabular Revision System in RA patient

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Conflict of interest: None

[Introduction] Trabecular Metal Acetabular Revision System (TMARS) have been used in Japan since 2014. In other countries, there are already many reports showing good results and a few failure cases. We experienced a case of early aseptic loosening after revision THA with TMARS, which has never been reported in Japan. [Case report] A 72y.o. female with Rheumatoid Arthritis had undergone THA before. Revision THA using trabecular metal (TM) augment and TM shell was performed for aseptic loosening and severe acetabular defect. The patient started partial weight bearing (PWB) from post-operative day (POD) 2 and was discharged on POD23. 3 months after the operation, she felt thigh pain. 5 months after, re-revision THA using bulk bone allograft and TM shell was performed for aseptic loosening. The patient started PWB from POD4 and was discharged on POD30. 1 year has passed, bone allograft is stable. [Discussion] There has been several surgical methods to reconstruct acetabular bone defect, but the best method remains unclear. Many authors have reported on stability and good results of reconstructing with TMARS. The cause of aseptic loosening in this case would be the fragility of the bone, the lack of proper fit between bone and TMARS and the limitation of fixed screws.

P3-070

Comparison between total knee arthroplasty with and without patellar resurfacing in patients with rheumatoid arthritis

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Conflict of interest: None

Routine patella resurfacing in total knee arthroplasty (TKA) remains controversial. This study compared the clinical and radiological outcomes of TKA performed with and without the patella resurfaced in patients with rheumatoid arthritis (RA). A total of 27 patients (36 knees) treated with TKA between October 2010 and July 2014 were retrospectively studied. These patients were divided into 2 groups, 1 of which received primary patella resurfacing (21 knees) and 1 of which did not (15 knees), with an average follow-up of 52.8 months. Range of motion (ROM), JOA score, J-KOOS, incidence of postoperative anterior knee pain, and radiographic findings were compared between the groups. No significant differences were identified between the two groups in terms of the ROM, JOA score, J-KOOS, or anterior knee pain. The thickness of the patella in the patellar retention group significantly decreased with time. Although no significant differences were identified between the two groups clinically, the thickness of the patella decreased with time in the patellar retention group, so the indication for patella retention should be decided seriously.

P3-071

A case report of TKA for a RA patient with the ankylosing flexion knee

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Conflict of interest: None

[Aim] To report a TKA which was performed for a RA patient whose knee joint had ankylosis in slight flexion angle. [Patient] Fifty-three-y-o female [Clinical history] The patient had been suffered from RA (class 3 and stage 4) since 2008. Her right knee pain had been getting worse since 2009, and ROM was severely restricted. She received orthopedics department for main complaint by ADL restrictions in June,2017. [Physical examinations] She was walking with T-cane. She had limping and some difficulty in walking. In spite of the ankylosing FT joint, the patellar mobility and robust quadriceps muscle contraction were observed. [Findings from image] CT image showed bony ankylosis in the FT joint but not in the PF joint. [Operation] In August,2017, TKA was performed. Bony ankylosis was cut using a curved chisel and FT joint was manipulated. After that, ordinary MIS-TKA was performed. She left the hospital by T-cane walk after 16 days after TKA. At 3 month after TKA, ROM of the knee was from -10 to 60 degrees. JOA score was improved from 25 points preoperatively to 65 points postoperatively. [Discussion] Preoperative quadriceps muscular strength and PF joint mobility probably be regarded as a key of good outcome after TKA for an ankylosing knee.

P3-072

Total knee arthroplasty with lateral approach for severe valgus deformity of rheumatoid patients

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Conflict of interest: None

[Object] With the rheumatoid knee, high grade valgus deformity often seen, and there is a problem of patellar subluxation and medial instability on the occasion of the total knee arthroplasty (TKA). [Cases] Six TKAs with lateral approach for valgus-knee were performed for two men and four women. Mean age of the patients at operation was 62 years old. Five Nexgen and one Persona of Zimmer company were used and CCK surface three cases, PS surface for three cases. Mean knee function score was improved from 29 points to 60 points and range of motion increased from an average of 30-98 degrees to an average of 9-113 degrees after operation for an average of 48 months. The femorotibial angle became 172 degrees from an average of 154 degrees. Skin necrosis two cases, peroneal nerve paralysis occurred in one case as complications. [Conclusions] Lateral approach in TKA is the method that can be chosen among heteromorphic correction and an aspect of the joint stability as needed.

P3-073

A case of rheumatoid arthritis with patella fracture and patella tendon rupture in bilateral total knee arthroplasty

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Conflict of interest: None

[Case] A case was 69-year-old woman with a 33-year history of rheumatoid arthritis (RA). We performed total knee arthroplasty (TKA) in right knee RA. Her pre-operative right knee range of motion (ROM) was 20°-105°, Knee score (KS) was 21 and Function score (FS) was 45. She began exercise range training and gait training from 1 day after surgery. She had patella fracture in X-ray on Keating classification type 2A after 2 weeks surgery. After 2 months surgery, bone union in conservative treatment was tended to be accepted. After 1 year surgery, bone union was accepted. We performed TKA in left knee RA after 17 months surgery. Her pre-operative left knee ROM was 20°-95°, KS was 31 and FS was 45. And total hip bone mineral density was 72% by young adult mean. In surgery, partial rupture of patella tendon at tibial insertion of patella tendon was occurred, and the patella tendon was sutured by anchor. She had pain of knee after 2 weeks surgery, avulsion fracture of tibial insertion of patella tendon in X-ray. We cured by conservative treatment because patella wasn't displaced. Her post-operative 3 years right knee/19 months left knee ROM was 0°-95°/10°-110°, KS was 74/72 and FS was 55/55. [Conclusions] We need attention to TKA complications associated with patella in long history of RA.

P3-074

Investigation of periprosthetic fractures in total knee arthroplasty for rheumatoid arthritis

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Conflict of interest: None

[Object] We examined the features and the problems of periprosthetic fracture of TKA for RA. [Patients and Method] 8 cases undergoing treatment for periprosthetic fracture of TKA for RA, all females. The mean age was 74.0, follow-up period was 2Y 5M. The analysis was the cause of the bone fracture, catching period of RA, THA passed years, fracture type, operation methods, RA and osteoporosis drugs, complications. [Results] The cause of the bone fractures were 7 falls and one fall down. Catching average period of RA was 19Y 8M. TKA passed years, average of 9Y 4M. Bone fracture type, as for patellar fracture 2, Lewis-Rorabeck type 1-one, 2-5, the operation methods, as for 6 osteosynthesis. Other joint replacement, THA 4, the other side TKA 7, TEA 1. Drug of RA were Bio. drug one, MTX 6, steroid 6. Bisphosphonete drugs used 2. The implants of osteosynthesis were LCP plate 4, NCB plate 2, all cases bone union[Comclusions] The infection and the bone union imperfection were not seen in this examination. There are many osteoporosis cases 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 osteoporosis with the medication were thought to be important.

P3-075

A case report of the revision total knee arthroplasty using patient matched instrument

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Conflict of interest: None

[Object] We reported a revision total knee arthroplasty (TKA) because of the femoral and tibial shaft deformities after fracture using a patient matched instrument (PMI). [Patient] A 72-years old rheumatoid arthritis patient after TKA with the femoral and tibial shaft deformities was operated because she was injured in frequently falls. We revised a TKA using a PMI because we could not use existing devices due to a shaft deformity. [Results] We could place a femoral component in a five degree varus and a tibial component in a three degree varus using PMI. [Conclusions] PMI was useful to revise a TKA with the femoral and tibial shaft deformities.

P3-076

A case of third revision total knee arthroplasty

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Conflict of interest: None

Rare case of a 3rd revision TKA of female patient. On 17/09/1993, 55 ys female patient was performed primary TKA (Y/S4 model). Because of HDP wear out, revision TKA (Stryker: Osteonics7000 modular knee) was performed. Caused by late infection, On 20/11/2006 Implants were removed and antibiotics included cement module was implanted. On 26/01/2007 Hinged type Knee components (Stryker: HMRS rotating hinged knee) were implanted. On 01/03/2016 the patient complained that she was easy to fall down. By X-ray patella dislocation was detected. On 29/06/2016 (patient was 78 ys) lateral release of patella and medial derangement such as a low invasive operation were done. After 3week-cast-fixation patient started to walk. But 8weeks later Knee pain and weakness of left knee extension mechanism were recurrent. Breakage of femoral component stem was detected by X-ray. Retrospectively stem breakage was found in former X-ray examination. On 2016/09/16 third revision TKA was performed. New femoral component (HMRS rotating hinged knee) was implanted. [Result] Patient was good for gait and had no knee pain and knee weakness. She was advised to use double canes. [Result] If a patellar dislocation was occurred in a stable TKA, change of rotation alignment should be considered.

P3-077

Clinical results of total knee arthroplasty in rheumatoid arthritis patients with severe valgus deformity and femorotibial angle below 160 degrees

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Conflict of interest: None

[Objective] To investigate the clinical results of total knee arthroplasty (TKA) in patients with rheumatoid arthritis (RA) and severe valgus deformity. [Subjects and Methods] The subjects were 20 patients who could be followed up among 30 RA patients with a femorotibial angle (FTA) of≦160º undergoing TKA. Their mean age at surgery was 58.4 years. A cruciate sacrificing posterior-stabilized prosthesis was employed for 11 joints with removal of the posterior cruciate ligament (PCL), while a cruciate retaining prosthesis was used for 9 joints and the PCL remained intact. The items investigated were clinical parameters, plain radiographic findings, and complications. [Results] The extension angle, flexion angle, JOA score, and FTA before/after surgery were -18/-0.5º, 108.4/115.3º, 44.2/89.8 points, and 156.0/175.4º, respectively. Regarding complications, edema, insert displacement, and infection occurred in 1 joint each, but there was no loosening or ligament instability. **[**Discussion**]** Regarding selection of the prosthesis, we consider that favorable postoperative results can be obtained even when using a CR model if PCL function is maintained and intraoperative trial insertion does not reveal marked varus-valgus instability.

P3-078

Clinical Results of Simultaneous Bilateral Total Knee Arthroplasty in Patients with Rheumatoid Arthritis

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Conflict of interest: None

[Object] In cases with severe deformity and flexion contracture, simultaneous bilateral TKA postoperative rehabilitation progresses smoothly, and hospitalization and anesthesia are required only once, so it is assumed that the burden on patients will be reduced medical, economic, physical and mental. On the other hand, it is pointed out that surgical invasion is large compared with unilateral TKA and there are many complications, and sufficient care is required for perioperative management. We investigated the clinical results of bilateral TKA in patients with RA. [Methods] It was investigated 29 cases 58 knee were performed on bilateral TKA in patients with RA. Average age at operation was 67.9 years, mean disease duration was 12.4 years. [Results] Mean operation time was 120.3 minutes, mean total bleeding volume was 692.9 ml, and 9 patients were transfused allogeneic blood transfusion. Range of motion of the knee joint and JOA score were significantly improved. Postoperative complications were 2 hemorrhagic gastric ulcers and 3 knee deep infections. [Conclusions] Clinical results of bilateral TKA in RA Patients was good, but the allogeneic transfusion rate was high. If measures are taken against infection and bleeding, it is considered that bilateral TKA is a useful method.

P3-079

High Tibial Osteotmy for RA patient

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Conflict of interest: None

[Object] High tibial osteotomy (HTO) is a very useful joint preservation method for medial osteoarthritis patient. RA patients is not indicated for HTO till now, but we report 3 acses of RA patites treated with HTO. [Methods] Higi tibial osetetomy was perforemed for 3 RA pattients. All patients were female with a mean age of 68.3 years, and a mean follow up of 9.7 months. RA medication, operetion method, The clinical score (Japanese Orthopaedic Association-JOA score), XP analysis and ROM of the knee were evaluated. [Results] Mead dose of MTX is 6.0mg/weak, PSL 2.5mg/day before operation, golimmub and abatacept was used for one patient. The clinical score (Japanese Orthopaedic Association-JOA-score improved from 60.0 points to 75.0 potins. The leg alignment (Mechanical axis) improved from 24.0% to 57.6% range of motion of the knee changed from -10^115 degree to -1.7~118.3 degree at the final follow up. [Conclusions] HTO as a joint preservation operetion can be one of method for RA knee accoding to tight control.

P3-080

Influence of preoperative analgesics on postoperative physical function and disease activity after total knee arthroplasty in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] The aim of this study is to clarify the influence of preoperative analgesics, especially opioids, on changes in physical function and disease activity after TKA in patients with RA. [Methods] We conducted a retrospective study using multivariate analysis to identify factors that affect postoperative physical function and disease activity. From 2013 to 2016, a total of 52 knees of 41 patients were enrolled in this study. We investigated patients' medication and evaluated CRP and other biomarkers, Larsen grade, SDAI and mHAQ before and 1 year after TKA. [Results] Analgesics were administered regularly as below before surgery: 27 knees NSAID alone, 5 knees combined with NSAID and opioid, 2 knees opioid alone, 2 knees acetaminophen alone. No analgesics were used in 16 knees of 13 patients. Comparing before and after 1 year TKA, SDAI improved -4.70 ($p < 0.01$), and the number of patients in SDAI remission increased from 1 preoperatively to 8 postoperatively. There was no significant difference in the improvement of SDAI and mHAQ with or without opioid use. After TKA in RA patients, mHAQ was more improved in the group without preoperative NSAIDs ($p = 0.03$). [Conclusion] Clinicians should consider limiting pre-TKA analgesic prescriptions to optimize the benefits of TKA in RA patients.

P3-081

Simple calculation method of finger function for rheumatoid hands

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Conflict of interest: None

[Object] Disabilities in rheumatoid hand are assessed by various kinds of evaluation, which evaluate hand function in total, but the impact of each finger deformity is unclear. In contrast, the Nalebuff classification evaluates each finger deformity separately. We considered that this deformity score can be used for a whole hand assessment. Then, we conducted a cross-sectional and longitudinal analysis comparing the sum score and hand function. [Methods] We registered 153 patients 297 hand for cross-sectional study, and 37 patients 63 hands for longitudinal analysis from our rheumatoid hand cohort. Each finger deformities were evaluated by the Nalebuff classification. We summed the deformity scores of each finger from index to little for 'sum score'. For the evaluation of disability, we used a part of Kapandji Index. [Results] In the cross-sectional analysis, there were significant correlations between sum score and FF+FE; SD: $r=-0.335$ ($p<0.05$); BD: $r=-0.427$ ($p<0.001$); combined deformity: $r=-0.423$ ($p<0.01$). In the longitudinal analysis, there was a slight correlation between the changes in sum score and the changes in Kapandji Index; $r=-0.203$ ($p<0.05$). [Conclusions] Our method is quite simple and is not time-consuming, therefore this could be one of the easiest way in daily practice.

P3-082

Effects of biologics (bDMARDs) on bone metabolism in patients with Rheumatoid Arthritis (RA) ~ from data of FIRST registry ~

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Conflict of interest: None

[Objective] The aim of this study is to evaluate the effect of bDMARDs on bone metabolism of RA patients in FIRST registry, which was 2818 RA patients cohort at University of Occupational and Environmental Health, Japan. [Methods] Disease activity and bone mineral density (BMD) of 828 RA patients were evaluated 1 year after first administration (from 2011 to 2016) of bDMARDs. [Results] Although one year treatment of bDMARDs improved RA disease activity, BMD was decreased in both femoral neck (FN) and radial bone. Bisphosphonate (BP) was administered in 235 patients, and the BP group was tended to be suppressed in reduction of BMD compared non-intervention group. However, osteoporosis of the BP group was advanced in both FN and radial bones (ΔT-score FN/radial: non-intervention group: -0.13/-0.20, BP group: -0.07/-0.19). Denosumab was administered in 17 patients, and the BMD of the radial bone was significantly increased in the group (Denosumab group: +0.04/+0.28). Analysis of the predictor of BMD change by logistic regression revealed that low ΔT-score before initiation in FN was detected as the predictor (OR 0.224, 95% CI 0.007-0.448, $p = 0.047$). [Conclusions] Our data suggest that denosumab can suppress the progression of RA-associated osteoporosis.

P3-083

Clinical outcome of rheumatoid arthritis patients who have been treated with denosumab for three consecutive years

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Conflict of interest: None

[Object] The purpose of this study is to clarify the three-year out-

come of denosumab treatment in rheumatoid arthritis (RA) patients. [Methods] Twenty three patients (22 women, a man) with active RA who have been treated with denosumab, anti-RANKL antibody agent for three consecutive years, were analyzed. The mean age of the patients was 65.9 years old. Bone metabolic markers, bone mineral density (BMD) and disease activity of RA were continuously measured. BMD was evaluated by dual x-ray absorptiometry scans of the lumbar spine and femoral neck, and the yearly change of BMD for three years was calculated. [Results] Denosumab treatment markedly reduced both TRAP5b, bone resorption marker and P1NP, bone formation marker. These inhibitory effects were maintained for three years. Denosumab increased BMD in both lumbar spine and femoral neck. The rates of increase in BMD were 9.3% and 5.8% on average in lumbar spine and femoral neck, respectively. On the other hand, treatment of denosumab did not significantly affect the change of RA disease activity, including DAS28-CRP and SDAI. [Conclusion] Administration of denosumab for three consecutive years increase BMD in RA patients, the effects of which are independent of biologic agent treatment and RA disease activity.

P3-084

A prospective, single-center, open-label, randomized-controlled study on drug therapy for the prevention of glucocorticoid-induced osteoporosis in elderly patients with collage vascular diseases. Teriparatide or bisphosphonates?

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Conflict of interest: None

Purpose: To Compare the usefulness of teriparatide (TPTD) and bisphosphonates (BIS) for glucocorticoid-induced osteoporosis (GIO) in elderly patients with collagen vascular tissue diseases (CVD). **Patients:** Fifteen CVD patients who were more than 65 years old and had received or would be treated with glucocorticoid (GC) were enrolled in this study (IRB:682, UMIN:000000222) with a written informed consent from Aug 2013 to Jul 2015. **Methods:** Patients were randomized to receive BIS or TPTD and were followed up for 2 years. Primary endpoint was the rate of vertebral fracture (VFx) and secondary endpoint was increase of lumbar spine and hip bone mineral density (LSBMD, HBMD). **Results:** Patients' profiles were not significantly different between 2 groups except duration of GC. Eight patients were prescribed BIS and 7 received TPTD. Although there was no significant difference in VFx rate, new VFx developed in 4 patients in BIS-group and only 1 in TPTD-group. The change of median LSBMD during 2 years was significantly higher in TPTD-group than in BIS-group (+9.3% vs +5.5%; P=0.031), but that of HBMD was not significantly different between 2 groups (-0.98% in BIS vs +1.4% in TPTD). **Conclusions:** In elderly patients with CVD receiving GC, TPTD might be more useful for the prevention of GIO than BIS.

P3-085

The investigation of the treatment for the glucocorticoid-induced osteoporosis of the rheumatoid arthritis patients in AORA registry

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Conflict of interest: None

Object: With the advent of biological agent, the control of disease activity in rheumatoid arthritis (RA) treatment is becoming definite. However steroid drugs are still one of the therapeutic drug options. Glucocorticoid induced osteoporosis (GIO) is one of the side effect of long-term use of steroid drugs. We investigated the situation of the treatment to GIO listed in the Akita Orthopedic Group on Rheumatoid Arthritis (AORA) registry in 2017. **Methods:** We investigated 645 cases of GIO patients out of 2238 cases in AORA registry in 2017. **Results:** 139 patients were male and 509 patients were female, and mean age was 74 years. Of 645 patients, 436 patients (67.6%) have undergone treatment for GIO. 227 patients underwent bisphosphonate, 32 underwent selective estrogen receptor modulator, 23 underwent teriparatide, 99 underwent denosumab, 207 underwent vitamin D analogues. The ratio of male patients who has not undergone treatment for osteoporosis (61.2%) was significantly higher than that of female ($p < 0.001$, 61.2% vs 24.4%). **Conclusion:** Glucocorticoid induced osteoporosis, elevated fracture risk. We should take care of the treatment of GIO especially in male patient.

P3-086

Analysis of incidence and risk factor of acute injection reaction of Zoledronate

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Conflict of interest: None

Zoledronate is a bisphosphonate (BP) injection drug, recently approved for osteoporosis in Japan. Acute phase reactions (APR) are known as adverse event in early phase after Zoledronate. The incidence of APR under the daily clinical usage has not been known well. We analyzed the incidence of APR in our hospital retrospectively. Three patients were male and 17 were female. Mean age was 65.6 years old. 16 patients had rheumatic disease and two had hematological disorder, and most of them are treated with corticosteroids. Two had breast cancer and received anti-estrogen therapy. Forty % of all patients experienced APR, but they were sustained short duration and all tolerable. APR incidence of Acetoaminophen or NSAIDs pretreatment group is 42.9%, and the incidence of non-pretreatment group is 33.3%. APR of BP naïve group is 50%, and that of BP switcher is 25%. APR incidence of rheumatic disease patients is 43%, hematological disorder is 50%, breast cancer is 0%. Pretreatment of acetoaminophen and NSAIDs is supposed to be a prophylaxis of APR, but the effect is not effective enough, from our study. Although this analysis is a retrospective, small scale and single center analysis, patients should be well informed about APR in advance.

P3-087

Efficacy and complications of Zoledronic acid hydrate in patients with steroidal osteoporosis

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Conflict of interest: None

[Object] The purpose of this study is to analyze the efficacy and the complications of Zoledronic Acid Hydrate (ZAH), a new bisphosphonate (BP), with steroidal osteoporosis. [Methods] We investigated 13 patients of steroidal osteoporosis who treated by conventional BP (cBP), but did not improve bone mineral density (%YAM). We investigated their %YAM, bone metabolism marker, serum electrolyte, renal function, dehydration and side effects such as fever before and after ZAH administration. [Results] These patients were administered PSL, average dose 7.11mg/dL, at the time of ZAH administration. The lumber %YAM of after 1 month of ZAH administration was 73.5% that significantly increased than before administration 70.8% (p=0.04). Both of P1NP and TRACP-5b significantly decreased compared with before and after 1 month of administration (from 19.8ng/mL to 14.4ng/mL, p=0.004, from 263.8mU/dL to 179.1mU/dL, p=0.0005). Although FENa temporarily decreased from before administration 0.92% to 2 weeks later 0.75%, after 1 month it improved to 0.90%. 2 of 13 patients had fever, another 2 had myalgia and arthralgia, 4 had headache and 6 had fatigue. [Conclusions] We concluded that ZAH suppresses the reduction of bone turnover and can improve %YAM that could not improve by cBP from the very early

stage.

P3-088

The effect of concomitant type of vitamin D, biological DMARDs and disease activity for therapeutic effect of denosumab in patients with rheumatoid arthritis with osteoporosis

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Conflict of interest: Yes

[Object] We assessed the effect of the type of vitamin D, bDMARDs use, disease activity on BMD in patients with RA treated denosumab. [Methods] This study included 100 RA patients (96 female, mean age 69.9 ± 9.3 years) treated with denosumab. BMD at the lumbar spine and proximal femoral were evaluated by DXA at baseline and 1 year after treatment. We evaluated the influence of the type of vitamin D, bDMARDs and disease activity for BMD change. [Results] BMD at the lumbar spine, proximal femoral and femoral neck were significantly increased in one years (improvement rate of BMD 6.2%: $p<0.01$, 4.0%: $p<0.01$, 2.2%: $p=0.04$, respectively). There were no significant differences in BMD between 10 patients taking active vitamin D and 71 patients taking native vitamin D (7.7 vs 4.4%: $p=0.55$, 4.3 vs 4.0%: $p=0.83$, 1.4 vs 4.2%: $p=0.52$), between 30 patients with bDMARDs and 57 patients without bDMARDs (6.4 vs 6.2%: $p=0.3$, 2.7 vs 4.5%: $p=0.95$, 1.1 vs 2.5%: $p=0.2$), between 61 patients in remission or low disease activity and 26 patients in moderate or high disease activity (7.2 vs 4.0%: $p=0.25$, 3.3 vs 5.0%: $p=0.87$, 1.6 vs 3.8%: $p=0.98$). [Conclusions] Denosumab improved BMD in patients with RA independently regardless of the type of vitamin D, bDMARDs use, disease activity.

P3-089

Denosumab as the treatment for osteoporosis in rheumatoid arthritis patient (Comparison with non rheumatoid arthritis patient)

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Conflict of interest: None

(Object) We have evaluated rheumatoid arthritis patient (RA) who have been treated with denosumab (dMAB) for osteoporosis (OP) in comparing with non RA (nRA). (Methods) Patients who were treated with dMAB for OP from June 2013 to September 2017 continuously for more than 2 years, were enrolled. Comparing parameter was age at start (AGE@BL), sex distribution (SEX), Survival ratio (SR), steroid induced OP ratio (GIOP), drug naïve ratio (Naïve), bone mineral density (BMD), change of BMD (dBMD), and tartrate-resistant acid phosphatase 5b (TRACP-5b) from start to the last administration. BMD was measured with dual energy X-ray absorptiometry method in lumbar spine (LS), femoral neck (FN), greater trochanter (GT), and whole femur (WF). RA was statistically evaluated comparing for nRA with Mann-Whitney U test. Statistically significant level was set within 5%. (Results) 108 for RA, and 278 patients for nRA were picked up. Parameters what demonstrated significantly were AGE@BL, SEX, GIOP, Naïve, and BMD at baseline in LS and FN, dBMD in each part of femur after fifth administration. The other factors demonstrated no statistical correlation. (Conclusions) dMAB can perform evenly or more for RA than for nRA. Especially, it is suggested to make more effects when more administered.

P3-090

Two cases of focal lateral cortical thickening detected by femur X-ray in patients have long history of bisphosphonates therapy in connective tissue disease

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Conflict of interest: None

Most patients during steroid use have history of bisphosphosnates (BPs) therapy for steroid-induced osteoporosis. A long history of BPs induces atypical femoral fracture (AFF). Before AFF happened, focal lateral cortical thickening (breaking) is found in femur X-ray and the patient feels slight femoral pain. We found two cases of breaking, but they were not reached AFF so far because of adequate therapy. [Case1] 48years old female, SLE from 1995 (PSL7mg, BPs 22years use). She has felt slight femoral pain at long walk for a year. Some clinics have not revealed the reasons. The femur X-ray showed breaking. We diagnosed her as a stage before AFF, stopped BPs and started teriparatide. She could avoid form the AFF. [Case2] 79yeaars old female, dermatomyositis from 2003. (PSL7.5mg, BPs 13 years use). She has felt slight femoral pain and fatigue for several months. The femur X-ray showed breaking. We diagnosed her as a stage before AFF, stopped BPs and started teriparatide. She could avoid form the AFF. [Clinical significance] The risk of the AFF is known to rise by the long history of BPs use. However, many clinicians have not recognized properly. and many cases could be overlooked. Even a minimal symptom, we should assume the AFF and perform the femur X-ray, search the sign of AFF.

P3-091

Cliniclal efficacy of denosumab in patients with osteoporosis between rheumatoid arthritis and primary osteoporosis ; 24 months of follow-up

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Conflict of interest: None

[Objectives] We investigated the efficacy of DMB in rheumatoid arthritis (RA-OP) and primary osteoporosis (P-OP) patients. [Methods] The final study cohort of 72 patients received continuous DMB therapy more than 24 months. 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) and bone turnover markers, PINP and TRACP-5b between RA-OP and P-OP. [Results] The patients included 6 males and 66 females. The mean age was 74.7±8.3 years; the mean disease duration was 8.3±10.3 years; the mean BMI was 20.5±3.1; the mean FRAX was 27.4±14.6%; the mean LS-BMD and TH-BMD was 0.791±0.160 and 0.610±0.085 g/cm^2; the mean P1NP and TRACP-5b was 61.4±33.7μg/l and 583.0±218.9 mU/dL. In the RA-OP (n=39) and P-OP patients (n=33), the rate of decreased PINP and TRACP-5b from baseline to 12 and 24 months were each -32.5% vs -66.6% ($p=0.001$), -42.8% vs -67.8% ($p<0.001$) and -39.6% vs -54.1% ($p=0.045$), -43.4% vs -59.8% ($p=0.012$). The rate of increased LS-BMD and TH-BMD from baseline to 12 and 24 months were each 6.6% vs 7.7% ($p=0.301$), 9.7% vs 11.3% ($p=0.273$) and 3.4% vs 2.4% ($p=0.153$), 5.8% vs 3.5% ($p=0.268$) in the RA-OP and P-OP. [Conclusion] DMB was effective in both RA-OP and P-OP patients for 24 months.

P3-092

Two-years of Denosumab treatment for osteoporosis in Japanese patients with rheumatoid arthritis

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Conflict of interest: Yes

[Object] The aim of this study was to determine the efficacy of two-year Denosumab (DMB) treatment for osteoporosis in Japanese patients with rheumatoid arthritis (RA). [Methods] A retrospective chart review

was conducted of 34 Japanese patients (3 males and 31 females, mean age; 75.5±5.9years) with RA. Patients were administrated DMB (60mg subcutaneously every 6 months) over 2 years, and were measured bone mineral density (BMD) and bone turnover markers (TRACP5b, P1NP and ucOC) every 6 months. [Results] After DMB treatment, lumbar-BMD significantly increased by 3.0±4.4% (P<0.05) change from baseline at 12months. Femoral neck-BMD was delayed in increase by 2.6±4.9% (P<0.05) at 18 months. The bone turnover markers (BTM) were rapidly reduced at 6 months after the treatment (TRACP5b; 273±149 at 0 month, 208±87MU/dl at 6 month, P1NP; 32±21 at 0 month, 21±17ng/ml at 6 month, ucOC; 2.6±2.0 at 0 month, 1.4±0.8ng/ml at 6 month (P<0.05)). [Conclusions] DMB treatment was rapidly effective in increase of BMD and suppression of BTM.

P3-093

Osteoporosis Treatment for the rheumatoid arthritis patients in our hospital

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Conflict of interest: None

[Object] We researched about osteoporosis treatment rateand drug selection for rheumatoid arthritis in our hospital. [Methods] This retrospective study include 113 RA patients. We devided them acording to need to treat osteoporosis or no need as discribed below in detail. 1. Major osteoporotic fracture rate>, 2. Score≧3 at guideline on the management and treatment of Glucocorticoid [Results] 68 patients (60.2%) was need to treatment of osteopolosis, but 41 pateints (68%) was not treated. The drugs for treatment ware bisphosphonate 30 patients (44.1%), denosumab 9 patients (13.2%), alfacalcidole 1 pateint (1.5%), SERM 1 patient (1.5%), teriparatide 0. The reason of bigining treatment ware using of glucocorticoid 17 patients (25%), starting of treatment of RA 2 patients (2.9%), result of DXA 12 patients (17.6%), fracture 4 patients (5.6%), unspecified 12 patient (17.6%). [Conclusions] The treatment of osteopolosis is very important to prevent osteoporotic fracture.

P3-094

Factors associated with bone mass - Nagasaki Island Study in bone -

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Conflict of interest: None

[Object] Several factors associated with Bone mass. Aim of this study was to determine factors associated with bone mass in community-dwering japanease persons. [Methods] We disigned a cross-sectional study in NaIS. Participants were recuruted from in 2014 to in 2016. [Results] Gender Age and BMI were significantly associated with bone mass. A liner regression analysis revealed significant association between drinking status and bone mass. [Conclusions] Life style including drinking would be a candidate as a target to intervention for health promotion.

P3-095

Osteoporosis in RA patients

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Conflict of interest: None

[Object] We examined osteoporosis in RA patients in our hospital. [Methods] 75 RA patients (21 males, 54 females, average age 72, diseased periods 13 years) examined bone mineral density using dual-energy X-ray absorptiometry (DXA) in lumbar and hip and measured serum concentrations of bone-forming marker P1NP and bone resorption marker TRACP-5b. Each of those values were examined with the relationship between steroids, MTX, and biologics. We also investigated the relationship between alendronate and eldecarcitol with the severity of osteoporosis. [Results] In the average of DXA, YAM hip was 80%, YAM spine 101%, age hip 96%, age spine 117%. The oral rate of the steroid in 75 patients was 64%, PSL average 3.0 mg. Each value of DXA, P1NP and TRACP-5b did not relate to the use of steroids, MTX, or biologics. Those data did not even relate to the use of alendronate or eldecarcitol. Daily amounts of steroids did not correlate with each value of DXA, P1NP, or TRACP-5b. A positive correlation was observed between P1NP and TRACP-5b (p<0.000). [Conclusions] A small amount of steroids (average 3 mg) was not related to value of DXA. If a small amount of steroid is required to control RA, to use medicine for osteoporosis was able to prevent to decrease in DXA.

P3-096

Factors that affect influence on bone mineral density gain in lumbar spine

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Conflict of interest: None

(Object) Factors that influence on bone mineral density (BMD) gain in lumbar spine (LS) for osteoporosis (OP) were evaluated from the clinical data. (Methods) Patient who were treated for osteoporosis in our clinic from April 2005 to September 2017, were enrolled. Measurement of BMD was performed with dual energy X-ray absorptiometry method. Patient's BMD was measured at the start of OP drug administration, and finish of the drug. Change of BMD per year was calculated. Influence of change of BMD per year was evaluated. Patient's age, sex, drug classification (DC), drug administration length, drug Naïve, rheumatoid arthritis, previous fracture, glucocorticoid thrown, term length between the two measurement, BMD at the start, were statistically evaluated with multivariate linear regression analysis. Significant level was set within 5%. (Results) 419 cases were picked up. DC demonstrated positive significant correlation, and term length between the two measures, and BMD at the start demonstrated negative significant correlation with BMD gain per year, while the other factors had shown no significant correlation. (Conclusions) In treating OP, if BMD gain of LS is targeted, drug should be considered. Too long term administration of same drug has been suggested to make stagnation risk.

P3-097

Factors that affect influence on bone mineral density gain in proximal femur

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Conflict of interest: None

(Object) Factors that influence on bone mineral density (BMD) gain in proximal femur for osteoporosis (OP) were evaluated from the clinical data. (Methods) Patient who were treated for osteoporosis from April 2005 to September 2017, were enrolled. Measurement of BMD was performed with dual energy X-ray absorptiometry method. Patient's BMD in femoral neck (FN), greater trochanter (GT), and whole femur (WF) were measured at the start of OP drug administration, and finish of the drug. Change of BMD per year for each part was calculated. Influence of BMD gain per year was evaluated. Patient's age, sex, drug classification, drug administration length, drug Naïve, rheumatoid arthritis, previous fracture, glucocorticoid thrown, length between measurements, BMD at the start (BMD@S), were statistically evaluated with multivariate linear regression analysis. Significant level was set within 5%. (Results) 419 cases were picked up. In FN, male, youngness at start, and BMD@S, while in GT, drug Naïve, and BMD@S, and in WF BMD@S demonstrated significant correlation with BMD gain. The other factors demonstrated no correlation. (Conclusions) In treating OP for femur, timing for drug administration and its order is suggested to be important. Female patient has been suggested to make stagnation risk.

P3-098

Relationship between sarcopenia and muscle function analyzed by CHIKARA study

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Conflict of interest: None

[Object] We reported that prevalence of sarcopenia was 28%. However, it was difficult to predict falls by skeletal muscle mass, and we need to evaluate muscle function. We investigated muscle function of rheumatoid arthritis (RA) patients. [Methods] Muscle power, speed, and balance were evaluated by muscle function analyzer (TANITA BM-220) in RA patients. We investigated the relationship between muscle function and history of fall and fracture, locomotive syndrome (locomo), frailty, sarcopenia, body composition, grip strength, DAS28ESR, mHAQ. [Results] 90 from 100 patients entered the CHIKARA study was perfumed muscle function test. Each parameter of muscle function was related with age, history of fall, locomo, frailty, and leg muscle score. However, there was only balance that related with history of fracture (R=0.217, P=0.04). Sarcopenia and skeletal muscle mass did not have significant relation of muscle function. There was negative correlation between DAS28 and power. Steinbroker class and mHAQ have negative correlation of power and speed. [Conclusions] Sarcopenia and skeletal muscle mass did not influence for muscle function (power, speed, and balance). It is interesting that history of fracture had relation of balance, but didn't have that of power and speed.

P3-099

Hypoalbuminemia is a risk factor for osteoporosis in patients with rheumatoid arthritis

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Conflict of interest: None

[Object] To evaluate risk factors for osteoporosis in patients with RA. [Methods] We examined 237 RA patients who were measured bone mineral density. We examined a cross-sectional study on the relationship between each factor of age, gender, disease duration, Steinbrocker classification, RA disease activity, TP, Alb, eGFR in a group of YAM 70% or less (A) and YAM more than 70% (B). [Results] There were 96 cases in group A and 141 cases in group B. The age was 74.3 in group A, 68.3 in group B (P<0.01), Stage was 2.65 in group A, 2.26 in group B (P<0.01), Class was 2.23 in group A, 1.77 in group B (P <0.01), patient VAS was 25.9 in group A, 20.1 in group B (P = 0.02), TP was 7.12 in group A, 7.28 in group B (P=0.01), Alb was 4.04 in group A, 4.25 in group B (P<0.01), eGFR was 62.4 in group A, 70.0 in group B (P<0.01), 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. In multiple logistic regression analysis, Hypoalbuminemia were extracted as independent risk factors with P=0.02 and odds ratio 3.03. [Conclusions] Hypoalbuminemia is a risk factor for osteoporosis in patients with rheumatoid arthritis.

P3-100

TNIIIA2 as a candidate for preventing articular cartilage degeneration

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Conflict of interest: None

[Object] TNIIIA2 is the peptide of tenascin C (TNC). We evaluated the expression of TNIIIA2 in OA cartilage, and the effect of intra-articular injection of TNIIIA2. [Methods] In the study of human cartilage, immunolabeling of TNIIIA2 was performed in OA (n=3) and normal (n=1) cartilage. In the animal experiment, 10μg/ml of TNIIIA2 was injected into the knee joint of mice (group II n=12). The control group had an injection of PBS (group I n=12). We evaluated at 2 and 4 weeks after injection. In the study of OA model mice, 10μg/ml of TNIIIA2 was injected into the knee joint (group IV n=35). The control group had an injection of PBS (group III n=35). We evaluated 2,4,8 and 12 weeks postoperatively. Synovitis was evaluated using synovitis score. Cartilage degeneration was evaluated using Mankin score. [Results] In the study of human cartilage, the expression of TNIIIA2 was observed in the OA cartilage, but not in normal cartilage. In the study of intra-articular injection of mice, there was no difference between both groups. In the study of OA model mice, Mankin scores were higher in group III at 4 and 8 weeks. [Conclusions] TNIIIA2 could prevent articular cartilage degeneration without synovitis.

P3-101

G protein-coupled receptor kinase (GRK)-5 inhibition decrease cartilage degradation in osteoarthritis through suppression of inflammatory response via NFkB signaling

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Conflict of interest: None

[Object] G protein-coupled receptor kinases (GRKs) are defined as the kinases that desensitize G protein-coupled receptors. Among sub families, it was elucidated that GRK-5 promotes inflammatory response through the phosphorylation of IkBa. The object of this study is to reveal the function of GRK-5 as for inflammatory response in pathogenesis of osteoarthritis (OA). [Methods] OA was induced in 12-week-old GRK-5 knock out (KO) and wild type mice for histological analysis. The immature murine chondrocytes were analysed molecular biologically. OA and normal knee joints from human were analysed for expression of GRK-5. OA chondrocytes transfected with small interfering RNAs targeting GRK-5 were also analysed. [Results] GRK-5 KO resulted in prevention of cartilage degradation in OA mice. Expression of IL-6, MMP-13 were significantly decreased in both KO mice and siGRK-5 transfected OA chondrocytes. GRK-5 KO remarkably attenuated nuclear translocation of NFkB after IL-1b stimulation. In human OA cartilage, GRK-5 were more strongly expressed compared to normal. [Conclusions] Our study demonstrates that GRK-5 inhibition decrease cartilage degradation through suppression of inflammatory response via NFkB signaling. This study suggested that GRK-5 is deeply involved in pathogenesis of OA.

P3-102

Elucidation of pain mechanism using mono-iodoacetate-induced osteoarthritis modelof rat hip joints

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Conflict of interest: None

[Object] The purpose of this study was to clarify the local production of proinflammatory cytokines, pain-related sensory innervation of dorsal-root ganglia and spinal changes in the monosodium iodoacetate (MIA) model of osteoarthritis (OA) in rat hips. [Methods] Using 75 6-week-old male Sprague Dawley rats (control group; n=25), 25 μl of sterile saline (sham group; n=25) and 25 μl of sterile saline with 2 mg of MIA (MIA group; n=25) was injected into the right hip joints. [Results] The expression of CGRP-ir in FG-labeled DRG neurons in L4 was significantly higher in the MIA group than in the sham group on days 7, 14, 28, and 42 after injection (P<0.01). There were significantly more FG-labeled GAP-43-ir DRG neurons in L4 in the MIA group than in the sham group on days 28, 42 and 56 days after injection (days 28 and 42: P<0.05, days 56: P<0.01). The number of Iba-1-ir microglia in the ipsilateral dorsal horn was significantly higher than that in the sham and control group after 28 days after the injection. [Conclusions] Pain-related characteristics in the MIA model of OA in rat hips were generated from an inflammatory pain state caused by inflammatory cytokines, and that state will generate grad-

ual neuronal injury, which may give rise to the neuropathic pain state.

P3-103

Iguratimod acts on the osteoarthritis of fingers so as to relieve the digital pain

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Conflict of interest: None

There are many patients to visit rheumatology clinic with the complaint of digital pain due to osteoarthritis of hands including Heberden's and/or Bouchard's nodes. But it's true that rheumatoid picture can be superimposed on them. **[Object]** To evaluate iguratimod's action on digital pain relief in the patients with hand osteoarthritis (hand OA). **[Methods]** To examine visual analogue scale of the pain (pain VAS) (mm) in the fifteen patients with simple hand OA as a final diagnosis, but who were treated under a diagnosis of possible rheumatoid arthritis. **[Results]** In thirteen out of fifteen patients (86%), pain VAS was decreased after administration of iguratimod. After 4 weeks≦,<8 weeks, amelioration of pain VAS was seen significantly (-25.5; $p<0.01$), which is almost as same as that of loxoprofen Na on osteoarthritis shown in the phase 3 trial of celecoxib. Thereafter, amelioration of pain VAS was -25.7 ($p<0.02$) at 8 weeks ≦,<12 weeks, -19.55 ($p<0.1$) at 12 weeks ≦,<24 weeks, -34.4 ($p<0.01$) at 24 weeks ≦,<52 weeks and -31.8 ($p<0.05$) at 52 weeks≦ after administration of iguratimod respectively. **[Conclusions]** Iguratimod is thought to have a remarkable action of pain relief in the patients with hand OA.

P3-104

Systematic review of anatomic variations of knees for total knee arthroplasty

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Conflict of interest: None

[Object] Characteristics of anatomic variations in Asian knees were clarified, and preparation for such knees was summarized. [Methods] A systemic review was conducted. Studies were eligible of inclusion if they featured anatomic variations especially in Asian people. Collectively, 45 studies in English (14 from Japan, 9 from Korea, 8 from China, 6 from India) were reviewed. The characteristics of Asian knees were analyzed, and problems during TKA was assessed when the ordinary technique was applied. Then operative technique to prepare for the variations was summarized. [Results] The characteristics of such knees were anterior and lateral bowing of the femoral shaft and proximal tibia vara with medial shift of the tibial articular surface, and medial torsion of the tibia. In such knees, distal femoral cut perpendicular to the mechanical axis would induce patellofemoral disorder, anterior notch, and/or femorotibial instability in flexion. The proximal tibial cut perpendicular to the mechanical axis would induce varus alignment. Reduction osteotomy is one option to match the anatomical axis of the tibia to the new mechanical axis. [Conclusions] Anatomic variation should be assessed before TKA in each patient in Asia. Operative technique should be modified according to the variations.

P3-105

Relationship between calcium pyrophosphate dihydrate crystal and operated osteoarthritis of the knee -Surgical procedure specific analyses-

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Conflict of interest: None

[Object] To investigate the relationship between CPPD and operated knee OA separated by surgical procedure. [Methods] We operated 584 UKA, TKA and HTO (age 72.9: M/F:106/478) for over Kellgren-Lawrence grade III knee OA. CPPD crystal in joint fluid was elucidated. We evaluated the relationship between CPPD and age, BMI (kg/m^2), CRP, ESR, MMP-3, gender (M/F), osteophyte (OFD: grade1/2/3), FTA (°), and leg alignment (LA: varus/neutral/valgus). [Results] CPPD (+) rate in TKA (34.4%) was significantly higher than that in UKA and HTO (12.3%). There was significant differences between CPPD (+:-) about age (76.6:73.4), BMI (25.1:26.4), gender (13/143:58/240), OFD (40/75/41:154/105/39), LA (119/15/22:230/55/13) in TKA. There were significant differences between CPPD (+:-) about age (77.2:65.8), FTA (185.6:181.7), OFD (6/6/4:87/22/5) in UKA and HTO. There was a significant difference between CPPD (+) patients in both groups about only gender (13/143:4/12). [Conclusions] Higher CPPD (+) rate in TKA might depend on the characteristic differences between both groups, because CPPD (+) rates in both groups were higher in high aged or severe OFD patients. However, gender difference between CPPD (+) patients in both groups was also found. This might suggest that the gender difference in mechanism of CPPD deposition.

P3-106

Calcium pyrophosphate crystal polyarthritis complicated with Paget's disease of bone

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Conflict of interest: None

Calcium pyrophosphate (CPP) crystal polyarthritis is known to present Rheumatoid arthritis (RA)-like polyarthritis. Chondrocalcinosis has been reported to be detected in Paget's disease of bone (PDB). However, few case reports complicated with polyarthritis have been reported. A 81 year-old woman presented intermittent right-sided buttock pain for about 10 years. She also reported one-month history of hand edema and arthralgia. Her MCP, knee and ankle joints were swollen. Laboratory test was consistent with mild inflammation (CRP 1.13mg/dl). She was negative for rheumatoid factor and anti-citrullinated protein antibodies. X-ray of her hands showed chondrocalcinosis within triangular discs of the wrist joints. Ultrasonography revealed synovitis on her wrists and MCP joints. X ray and plain CT detected pagetic bone region of right-sided pelvis, which showed unusual accumulation on FDG-PET. The biopsy discovered increased bone turnover and remodeling, consistent with PDB. Bisphosphonate was continued. The polyarthritis had disappeared for more than a year even without Sulfasalazine. CPP crystal arthritis was clinically diagnosed. We shall be aware of CPP crystal arthritis in the inflamed joints of patients with PDB, possibly associated with increased bone resorption by osteoclasts.

P3-107

Clinical consideration of CPP crystal arthritis

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Conflict of interest: None

[Object] Calcium pyrophosphate deposition (CPPD) disease is an arthropathy caused by CPP crystal deposits in articular tissues. We followed acute CPP crystal arthritis clinically. [Methods] From April 2015 to July 2017, we diagnosed 69 patients with acute arthritis and reviewed retrospectively. We diagnosed 31 patients as CPP crystal arthritis. We excluded gout, crowned dens syndrome, septic arthritis, rheumatoid arthritis, arthritis of unknown cause. There were 8 men and 23 women with a mean age 75 (range 54 to 88) years. Involved site was knee (18), ankle (3), wrist (2), hip (1) and multiple joints (7). [Results] Radiographs and synovial fluid examination detected CPP crystals in 28 patients and 18 patients, respectively. For easily treatable patients, we treated with joint aspiration, joint injection and NSAIDs use in isolation and combination. For hardly treatable patients, we used colchicine. [Conclusions] According to the recent EULAR recommendations for CPPD, the main goals of

CPPD therapy are control of the acute or chronic inflammatory reaction and prevention of further episodes. Mainly, arthrocentesis, joint injection and NSAIDs are effective in acute CPP crystal arthritis but colchicine is effective for intractable and polyarticular arthritis.

P3-108

The predictive factors of rheumatology with systemic lupus erythematousus-cross sectional study

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Conflict of interest: None

Background/Purpose: Recently Treat to target (T2T) was proposed in SLE patients. And Importance od reaching remission is emphasized. However, there have been few reports about the predictive factors of remission with SLE. Thus, the purpose of this study was to describe the predictive factor of remission in patients with SLE. **Methods:** All SLE patients who visited Showa University from 2016 to 2017 were enrolled in this cross-sectional study. Patients with SLE, as defined by the ACR, were included in the study. We describe the predictive factor of remission. The remission was defined as SLEDAI=0 or SLEDAI 2,4 (immunological items are permitted) and medication (PSL≦5mg/day and immunosuppressive drugs) are permitted). The following variables were considered possible predictive factors for the remission and were thus included in the analysis: sex, age, time from onset to treatment, lupus nephritis, neuropsychiatric lupus, lupus serositis. **Results:** 51 patients (27.7%) are in remission. The mean age of the 184 patients was 43 years. The mean SLEDAI was 4. No significant difference was observed in all factors. And no significant difference was observed in multiple regression analysis. **Conclusion:** 51patients (27.7%) are in remission. We cannot describe the predictive factor of remission in patients with SLE.

P3-109

Correlation between irregular menstruation and disease activity of systemic lupus erythematosus: Cross sectional study

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Conflict of interest: None

[Objectives] Systemic lupus erythematosus often occurs to young women of reproductive age. In clinical scene, we often experience, SLE patients having menstrual irregularity before their relapse. Report about correlation between menstrual irregularity and disease activity of SLE is limited, we started this study. [Methods] 74 patients who fulfilled >4 of the American College of Rheumatology (ACR) criteria for the classification of SLE whose age was 20 to 45 and treated at Showa University Hospital were recruited. We defined the menstrual irregularity as deviation from the normal menstruation which is 'flow occur every 25 to 35 days and last three to seven days'. We had questionnaire formed from each patient. Among normal menstruation group and irregular menstruation group we set the primary outcome as SLEDAI. [Results] Irregular menstruation patients were 15 (20.2%). The median score of SLEDAI of the normal group was 2[IQR0-6] and those of irregular group was 5 [IQR2-7]. Adjusted with age BMI, history of treatment with IVCY, present PSL dose, current smoking, and JPSS, there was no significant difference between the both group (p=0.3). [Conclusion] Comparing with SLEDAI, there was no significant difference between the both group. We need the further investingation with longitudinal study.

P3-110

Usage conditions of Hydroxychloroquine for SLE and related disease in our hospital

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Conflict of interest: None

[Object and Methods] We treated 13 female patients, who are 12 SLE and 1 MCTD, with HCQ since January 2016. [Results] Their mean age is 51 years-old and mean disease durations is 16 years. Of 12 SLE, there are one CNS lupus, one lupus panniculitis and five lupus nephritis. They complicated with Anti phospholipid syndrome, Sjogren syndrome, Hemophagocytic syndrome and virus infection such as PVB19 and EBV. Before administration of HCQ, they got treated with mPSL pulse, IVIg, IVCY and PE, then they use PSL, TAC, MZB, MMF for maintenance therapy. Six of thirteen patients continue therapy with HCQ and the rest have been discontinued. On all patients, who are continuing HCQ treatment, we have been able to decrease their steroid dose. One of them become negative of anti-DNA antibody and another is continuing the dose reduction treatment because of eye complication. The cause of discontinuation is brain tumor, compliment level down, exanthema and fatigue. [Conclusions] As previously reported, we conclude HCQ is one of the important medications for SLE and related disease.

P3-111

Examination of the brain Single-Photon-Emission Computed Tomography (SPECT) in systemic lupus erythematosus (SLE)

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Conflict of interest: None

[Object] To identify the characteristics of brain SPECT abnormalities in patients with SLE. [Methods] Patients with SLE who underwent SPECT during Jan 2010 to Oct 2017 were retrospectively evaluated. [Results] Of 82 patients, female 68, mean age 42 years, disease duration 88 months, and neurological symptoms were seen in 56%. Median values were as follows: C3, 67 mg/dl; anti-ds-DNA antibody, 15.3 IU/ml; IgG index, 0.59; and IL-6 levels in cerebrospinal fluid, 2.7 pg/ml. Prednisolone (PSL) was 18.5 mg/day. The ratio of immunosuppressants were azathioprine 13%, tacrolimus (TAC) 37 %, cyclosporine 2%, MMF 5%, mizoribine 10%, MTX 4%, IVCY 15%. The positivity of anti-phospholipid 30%, anti-Sm 29%, anti-RNP 40%, and anti-SS-A was 49%. Sixty-five patients revealed abnormality by SPECT. Compared with the patients with normal SPECT findings, the patients with abnormal findings had significantly lower positivity of anti-SS-A (73.3% vs 43.8%, P=0.048). Multivariate analysis indicated that negativity of anti-SS-A (p=0.001), non-use of TAC (p=0.002), disease duration more than 1 year (p=0.002), presence of neurological symptoms (p=0.03) and over 20 mg/day PSL (p=0.04) were correlated with SPECT abnormalities. [Conclusions] Anti-SS-A is more strongly affected in SPECT findings in SLE patients.

P3-112

Fragmented QRS in patient with Systemic Lupus Erythematosus: Frequency and association with extraneous factor

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Conflict of interest: None

[Object] Cardiovascular disease is an important contributor to mortality in Systemic Lupus Erythematosus (SLE). Fragmented QRS (fQRS) defined as additional spikes within the QRS complex can represent conduction disturbance and a predictor of cardiac events. Even in patient with SLE, it is reported that the prevalence of fQRS appears to be higher than in controls. The purpose of this study was to describe the frequency of fQRS in patient with SLE and association with extraneous factor. [Methods] SLE patients, as defined by ACR, who diagnosed and admitted to Showa University Hospital from 2013 to 2017 were enrolled in this cross-sectional study. The following variables were considered: sex, age, SLEDAI, Anti-dsDNA antibodies, lupus anticoagulant, Anti-SSA antibodies, anticardiolipin antibody, serum complement, CRP, cholesterol, triglyceride, blood pressure, smoking status. [Results] 20 patients were described, and 10 patients had fQRS. Significant difference was observed in SLEDAI between the fQRS (+) and fQRS (-). (fQRS (+): median 20

[12.75-23.25], fQRS (-): median 9[7.5-14.25], p=0.0111) No significant difference was observed in others. [Conclusions] 20 patients were described, and 10 patients had fQRS. Therefore, we state there should be more detailed research to confirm these findings.

P3-113

A therapeutic strategy for attenuating steroid therapy in juvenile-onset SLE

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Conflict of interest: None

OBJECT: Steroid therapy has been used as the first-line treatment for SLE. But it should be reduced and stopped as soon as possible due to apprehensive of adverse effects. We are now trying to reduce dosage of glucocorticoid and terminate it by aggressive application of immunosuppressive drugs. In this study, We investigated clinical futures and courses of treatment with juvenile-onset SLE patients received intensive immunosuppressive therapy. METHOD: Patient background, dosage of glucocorticoid, duration of the steroid therapy and immunosuppressive therapy were assessed in juvenile-onset SLE patients who were treated at our clinic since 2007. RESULTS: A total of 11 juvenile-onset SLE patients was evaluated. 6 cases received initial therapy for induction in our hospital, while others were introduced to our clinic at more than one year after onset. In 10 cases steroid therapy could be terminated because of achievement of remission. In the former 6 cases immunosuppressive drugs were adopted significantly earlier (p=0.04) than in the latter 5 cases with significantly shorter requirement of steroid therapy (p=0.002). CONCLUSION: Application of immunosuppressive therapy in early phase after onset of SLE could shorten duration of steroid therapy with the same outcome at the first 5 year.

P3-114

Analysis of the association between clinical features in patients with systemic lupus erythematosus complicated with brainstem/spinal cord lesion and characteristic in neuromyelitis optica spectrum disorders

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Conflict of interest: None

[Object] Recently, diagnostic criteria for neuromyelitis optica spectrum disorders (NMOSD) has been released. However, there is no certain explanation for NMOSD as one of neuropsychiatric manifestations in systemic lupus erythematosus (NPSLE). The aim is to investigate the relationship between features of SLE patients with brainstem/spinal cord lesion (BSL) and NMOSD. [Methods] We recruited SLE patients who admitted to our hospital due to BSL from January 2014 to October 2017, and compared their clinical data to characteristics of NMOSD. [Results] 6 female patients were enrolled. 1 of 5 patient had the positive result of serum anti-aquaporin-4 antibody. 4 patients manifested longitudinally extensive transverse myelitis as is defined in NMOSD diagnostic criteria, of which 1 patient had cerebral lesion and another patient suddenly died right after image study. Interleukin-6 level in cerebrospinal fluid from 3 patients was 276.4pg/ml, which decreased after treatment along with improvement of symptoms and images. 3 patients were all given combination therapy with an immunosuppressant and corticosteroids, but 2 patients were recurrent. [Conclusions] NMOSD-like manifestation could be a new entity as NPSLE. Further studies are required to reveal the relationship between them.

P3-115

Investigation of improvement of urinary protein in lupus nephritis

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Conflict of interest: None

Objective: To investigate the factors associated with improvement of urinary protein in lupus nephritis. Method: Medical records of patients with hospitalized treatment for lupus nephritis in our department, were analyzed retrospectively. A responsive group in which urinary protein were improved during the immunosuppressive therapy, and a non-responsive group in which the immunosuppressive therapy during hospitalization was insufficient and patients needed additional therapy for treatment of lupus nephritis, were compared and studied. Result: There were 47 subjects in total and 55 cases of hospitalization were analysed. 38 (69.0%) were in the responsive group and 17 (31.0%) in the nonresponsive group. There was no difference in age, gender, anti-dsDNA antibody titer, C3 value, C4 value, positive rate of anti-dsDNA antibody, anti-Sm antibody, anti-SSA antibody and ANCA, and treatment contents in both groups. In the nonresponsive group, the proportion of lupus nephritis mixed type was high and positive rate of anti RNP antibody was low. Conclusion: In the mixed type of lupus nephritis, to improve urinary protein tended to be difficult in initial treatment.

P3-116

The transitional changes about the incidence rate of corticosteroid-induced osteonecrosis in patients with SLE

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Conflict of interest: None

[Object] The purpose of this study was to investigate transitional changes in the incidence of corticosteroid (CS)-associated osteonecrosis (ON) in SLE patients, with a focus on immunosuppressive agent and corticosteroids. [Methods] We retrospectively registered 185 SLE patients with 740 joints, who were newly diagnosed and hospitalized for initial high-dose CS therapy from 1986 to 2015. Immunosuppressive agent, CS dose, age, sex, cause of hospitalization, and incidence of ON were documented. [Results] Based on trends in immunosuppressive agent use, 116 patients treated from 1986 to 1999, before calcineurin inhibitors were introduced, comprised the past group, and 69 patients treated from 2000 to 2015 comprised the recent group. Patient characteristics (age, sex, and cause of hospitalization) were similar between groups. CS doses were significantly lower in the recent group (45.7 mg/day vs 59.0 mg/day, 0.88 mg/day/kg versus 1.16 mg/day/kg). The incidence of ON was significantly lower in the recent group (26.4% vs 41.0%), particularly in the knee (25.4% vs 46.6%). [Conclusions] The incidence of corticosteroid-associated osteonecrosis in SLE patients decreased in association with a decrease in corticosteroid administration after introduction of calcineurin inhibitors.

P3-117

Evaluation of serum levels of soluble interleukin-2 receptor as a biomarker for systemic lupus erythematosus

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Conflict of interest: None

[OBJECTIVE] To elucidate the usefulness of soluble interleukin-2 receptor (sIL-2R) in patients with systemic lupus erythematosus (SLE). [METHODS] We retrospectively reviewed 66 cases with active SLE who hospitalized from 2007 to 2016, and evaluated the correlation between serum sIL-2R titers and the disease activity. Disease activity of SLE was evaluated by SLEDAI and BILAG index. We also examined serum complement (CH50) and anti-dsDNA antibody levels. [RESULTS] Among 66

cases, 55 were females. The mean age was 39.2 ± 16.0 years old. The mean serum sIL-2R titer was 1086.7 ± 821.8 U / ml, anti-dsDNA antibody 189.7 ± 719.2 IU / ml, CH50 32.1 ± 15.6 U / ml, SLEDAI 11.98 ± 6.1, BILAG was 12.39 ± 6.1. In our cases, sIL-2R showed significant correlation with constitutional symptoms ($r = 0.474$, $P < 0.01$), total points ($r = 0.270$, $P < 0.05$) and blood abnormalities ($r = 0.305$, $P < 0.05$) of BILAG. Anti-dsDNA antibody correlated weakly with SLEDAI and musculoskeletal symptoms of BILAG. CH50 correlated weakly with SLEDAI and renal disorder of BILAG. [CONCLUSION] It was suggested that sIL-2R could be a characteristic biomarker reflecting constitutional symptoms in SLE patients.

P3-118

The correlation between disease activity of SLE and anti-DNA antibody titers measured by ELISA, CLEIA and RIA

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Conflict of interest: None

[Object] Anti-ds-DNA antibody titers (DNA titers) are used to evaluate disease activity of SLE, while ELISA often detects low affinity anti-ds-DNA antibodies. CLEIA was recognized as more specific assay as detecting high affinity anti-ds-DNA antibodies. [Methods] We examined 84 SLE cases whose DNA titers measured by ELISA, CLEIA and RIA at same time. In respectively ELISA, CLEIA and RIA, we analyzed the correlation among DNA titers by these three assays with serum complement levels (C3, C4 and CH50), 1 hour erythrocyte sedimentation rate (ESR1h), Immune complex (C1q) and SLE Disease Activity Index (SLEDAI). [Results] In CLEIA, CH50, ESR1h and SLEDAI showed significant correlations (Spearman's rho=0.385, 0.377 and 0.424 respectively). In ELISA, SLEDAI showed a significant correlation (0.427). In RIA, ESR1h and SLEDAI showed significant correlations (0.417 and 0.401 respectively). [Conclusions] Any of CLEIA, ELISA and RIA appeared to be useful as an evaluation marker of disease activity in SLE.

P3-119

Expression of CD64 on monocyte predicts relapse of Systemic lupus erythematosus in five case

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Conflict of interest: None

[Object] Systemic lupus erythematosus (SLE) is a typical chronic disease which often repeats relapses and causes cumulative organ damages during the long-term clinical course. To avoid relapses, biomarkers to predict them are needed. We have reported that expression of CD64 on monocyte (mCD64), a high-affinity receptor for IgG (FcγRI), tightly correlate with the disease activity of SLE. We investigate whether quantitative measurement of mCD64 expression is useful to predict of relapse in SLE. [Methods] The expression of mCD64 was measured quantitatively by using flow cytometry. In The expression of mCD64 were followed in 50 typical SLE patients longitudinally. All patients fulfilled the 1997 American College of Rheumatology classification for SLE. [Results] In most cases, mCD64 expression levels significantly increased before the relapse and decreased in parallel with clinical improvement after treatment. The change preceded to those of the existent biomarker such as complements, anti-DS DNA antibodies and proteinuria [Conclusions] Expression of mCD64 may a useful predictor for relapse in SLE.

P3-120

Monocyte CD64 (Fc gamma Receptor I) for distinguishing exacerbation of lupus nephritis and preeclampsia in two cases of pregnant with systemic lupus erythematosus

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Conflict of interest: None

Background: Distinguishing proteinuria due to lupus nephritis (LN) activity and preeclampsia (PE) during the third trimester of pregnancy is. We report the use of monocyte CD64 (mCD64) as a disease activity biomarker for SLE, where the levels of mCD64 expression was significantly higher in active disease than in inactive disease SLE ($p<0.001$). **CASE 1:** 26-year-old woman at 28 weeks of gestation with a ten-year history of controlled SLE with PSL 10mg presents with high blood pressure and proteinuria. mCD64 level was 33624 molecules/cell, anti-ds DNA antibody was increased, and she presented with hypocomplementemia. We diagnosed LN recurrence and increased PSL to 30mg followed by steroid pulse therapy. mCD64 level decreased to 19748. Vaginal delivery was induced at 36 weeks of gestation. **CASE 2:** 30-year-old woman at 33 weeks of gestation with a ten-year history of controlled SLE with PSL10mg and immunosuppressive agent that presented proteinuria. Additionally, she was also hospitalized for fetal growth restriction. High blood pressure was observed and she was diagnosed with PE. mCD64 level was low at 24087. She had caesarean section at 34 weeks of gestation. **Conclusions:** mCD64 levels may be a useful biomarker for evaluating disease activity of SLE during pregnancy.

P3-121

The aberrant expression of CaMK4 in CD4+ effector T cells in a lupus nephritis patient with thrombotic microangiopathy and diffuse alveolar hemorrhage

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Conflict of interest: None

It has been proposed that the abnormal activity of CaMK4 in T cells is involved in the development of organ disorder of systemic lupus erythematosus (SLE) by promoting the recruitment of pathogenic Th17 cells to target tissues. A previously healthy 19-year-old woman was diagnosed with SLE based on facial erythema, arthralgia, proteinuria, impaired renal function, blood abnormalities, immunological abnormalities, anti-nuclear antibody positive in May, 201X. Her SLEDAI score on admission in late May was 26. Even though we initiated methylprednisolone pulse therapy and mycophenolate mofetil (MMF), the level of her urine protein had exacerbated (20g/gCr). A renal biopsy revealed lupus nephritis IV-G (A)+V. She developed diffuse alveolar hemorrhage (DAH) in addition to thrombotic microangiopathy (TMA). Both TMA and DAH had improved after introducing plasma exchange and IVCY therapy, and the SLEDAI score improved to 4 points on discharge in the middle of August. An increased level of CaMK4 in effector memory T cells in the peripheral blood was observed at the first visit, but its expression was dramatically decreased after 4 cycles of IVCY therapy. This case suggests that assessing the CaMK4 expression of T cells may be useful for predicting multiple organ damage in SLE patients.

P3-122

A mammalian target of rapamycin (mTOR) inhibitor, everolimus ameliorated lupus nephritis in a woman with tuberous sclerosis

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Conflict of interest: None

[Case] A 26-year-old woman presented with bilateral leg edema for three days. She had a history of SLE and tuberous sclerosis (TSC). Her laboratory studies showed hypoalbuminemia, hypercholesterolemia, elevated anti-dsDNA antibody titer and hypocomplementemia. The urinalysis showed massive proteinuria with a lot of WBC casts. Renal biopsy was not performed because of multiple renal angiomyolipomas (AML), which was one of the features of TSC. She was diagnosed with a nephrotic state due to underlying lupus nephritis (LN). Although she had a standard therapy with high-dose corticosteroid, concomitant with immunosuppressive drugs, such as mycophenolate mofetil and tacrolimus, complete remission had not been achieved, leading to steroid-dependent nephrotic syndrome. During the following-up, the AML became larger and had a risk of rupture. She was started to treat with everolimus, an mTOR inhibitor, for the AML. After the treatment of everolimus, the activity of LN was concomitantly ameliorated and we succeeded sparing of corticosteroid. [Discussion] Recently, it has been reported a possible pathogenic association between activation of mTOR and SLE. Taken together, this case suggests a potential of everolimus for the treatment of SLE.

P3-123

Two cases of refractory obstetric antiphospholipid antibody syndrome (APS) treated with pravastatin

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Conflict of interest: None

[Introduction] Recurrent abortion and premature birth with hypertensive disorders of pregnancy (HDP) are major pregnancy complications of APS. More than 20% of obstetric APS patients are resistant to the standard treatment, low-dose aspirin (LDA) and heparin, resulting in a termination of pregnancies. We administered pravastatin to two cases of HDP to improve pregnancy outcomes. [Case 1] A 35-year-old woman with APS and SLE. PSL was increased at 7 weeks gestation due to thrombocytopenia, and she received LDA, heparin and IVIG therapy. She developed HDP at 17 weeks and pravastatin was effective for proteinuria and hypertension. But she had an IUFD at 22 weeks. [Case 2] A 38-year-old woman with APS and SLE. Maternal and fetal courses were stable by receiving LDA, heparin and IVIG except for a mild fetal growth restriction. She developed HDP at 22 weeks and pravastatin was also effective. But later hypertension and renal dysfunction had deteriorated, she delivered a live baby under caesarean section at 23weeks. [Discussion] Recently, several studies demonstrate the efficacy of statins for HDP. We showed that pravastatin treatment temporarily improve APS-related HDP, although final pregnancy outcomes were not necessarily good. We report these cases with some literature review.

P3-124

Two cases of SLE with a decreased frequency of seizure after the administration of hydroxychloroquine

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Conflict of interest: None

We report two cases of SLE with a decreased frequency of seizure after the administration of hydroxychloroquine (HCQ). Case 1 was a 42-year-old woman with a past medical history of epilepsy from age 14 years. At age 29 years SLE was diagnosed. She was treated with HCQ from age 33 years and she stopped HCQ at age 37 years. Thereafter, she experienced dizziness and photophobia. At age 40 years, she experienced a generalized seizure, which has recurred once a month since then. After we began HCQ treatment when the patient was 41 years old, the episodes decreased to once every six months. Case 2 was a 55-year-old woman in whom SLE was diagnosed at age 52 years. Since the age of 54 years she began to experience faintness and clonic seizures. Levetiracetam treatment was begun, but the seizures continued to recur. After we administered HCQ to her at age 55, the convulsions ceased. Discussion: HCQ is known to possibly have the potential to lower the convulsion threshold. However, some studies have reported that HCQ has a protective effect against seizures in SLE patients. We recommend using HCQ without hesitation to treat SLE patients with seizures.

P3-125

A case of lupus nephritis (ISN/RPS Class II) with diffuse podocyte infolding

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Conflict of interest: Yes

A 3X-year old man presenting with proteinuria (2.7g/gCr), leukopenia, a high titer of anti-nuclear antibody, a psotive anti-dsDNA, and hypocomplmentemia, was diagnosed with systemic lupus erythematous. Kidney and bladder ultrasonography revealed hydronephrosis of the left kidney, and thickening of the pelvic and ureter walls. A renal biopsy was perfumed. An immunofluorescence study was conducted which revealed granular deposits of IgM (2+) and IgG (+) were detected in the mesangial areas. Light microscopic findings showed focal segmental mesangial hypercellularity and patchy cell infiltration at the interstium under light microscopy. Those findings were compatible for lupus nephritis (ISN/RPSClass II). However, regarding urinary findings, the severity of morphological findings was descrepant. Diffuse irregular GBM thickening with the infolding of podocytes and microtubules of endothelial cells were observed using electron microscopy. Clinical significance: The morphological findings of our case may lead one to consider that the folding of podocyte was related to lupus podocytopathy.

P3-126

Successful Treatment of Neuropsychiatric Systemic Lupus Erythematosus with Mycophenolate Mofetil

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Conflict of interest: None

A-29-year-old. She was diagnosed systemic lupus erythematosus (SLE) 5 years ago. She was found to have positive LAC. But she was not treated as an outpatient. She miscarried in pregnancy 24 weeks 1 week ago. On admission day she experienced seizure and severe headache. We carried out lumbar puncture and an elevated level of IL-6 in spinal fluid (33.9pg/mL) and level of IL-8 in spinal fluid (1260pg/mL) was found. Laboratory date was hypocomplementemia and positive antinuclear antibody, elevated Anti-Sm antibody and anti-ribosomal p antibodies, anti-ds DNA antibody was negative. We diagnosed Neuropsychiatric systemic lupus erythematosus (NPSLE) complicated by anti-phospholipid antibodies. We did not choose cyclophosphamide because She hoped to bear children. Pulse steroid therapy after treat to prednisolone (PSL) 50mg and mycophenolate mofetil (MMF) 2g. SLEDAI score change 38 to 6, decreased IL-6 (33.9→1.9pg/mL) and IL-8 (1260→54.8pg/mL). her symptoms disappeared completely and PSL dose could be tapered to 35 mg. She was discharged on the 69day of admission. Previous studies have reported that patients with NPSLE were associated with worse

prognosis. The case that succeeded for MMF for NPSLE, we thought that it needed more cases in the treatment results.

P3-127

A case of lupus myelitis with cervical spondylotic myelopathy successfully treated with immunosuppressive therapies

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Conflict of interest: None

[Object] To report a rare case of lupus myelitis (LM) with cervical spondylotic myelopathy (CSM). **[Methods]** We analyzed its clinical course retrospectively. **[Results]** A 58-year-old woman with HBV career had felt girdle sensation in the left abdomen, followed by right monocular blindness and dysuria. She was admitted due to rapid weakness of four limbs. She presented with right monocular blindness, left-side dominant spastic tetraplegia, right-side dominant superficial sensory disturbance below C7, and deep sensory disturbance in the lower limbs with malar rash and head alopecia, and positive Jackson test. Blood tests showed positive anti-dsDNA antibody without pancytopenia, hypocomplementemia, and anti-AQP4/MOG antibody. CSF analysis was normal. Brain MRI showed no abnormal lesions suggesting multiple sclerosis. Cervical MRI showed myelomalacia at C4-5 with atypically enhanced lesion at C5 within disc herniation and OPLL from C4 to C6. FDG PET-CT showed marked uptake in the same lesion, indicative of LM. Administration of PSL and AZT after IVMP resolved neurological deficits rapidly. **[Conclusions]** LM might mainly cause neurological deficits because of atypically enhanced MRI lesions with marked FDG uptake and good response to immunosuppressive therapies, although CSM coexisted.

P3-128

Extra-renal manifestation in SLE patients with lower serological indices

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Conflict of interest: None

Case 1: 52year-old man with 4-year history of SLE. He was diagnosed as having lupus enterocolitis when he complained about abdominal pain, vomit and diarrhea. None of the pancytopenia, hypocomplementemia or anti dsDNA antibody was noted. Case 2: 47year-old female with 4-year history of SLE. She was diagnosed as having lupus cystitis when she complained about abdominal pain and vomit. None of the pancytopenia, hypocomplementemia or anti dsDNA antibody was noted. Case 3: 44year-old female with 13-year history of SLE. Computed tomography exhibited the rupture of right gastroepiploic artery. Pancytopenia and hypocomplementemia were not found but she had a positive anti-dsDNA antibody titer. was noted. Discussion: The prevalence of hypocomplementemia and hemotocytopenia in patients with lupus enterocolitis were 88% and 40-50%, respectively. Most patients with lupus cystitis were accompanied by anti-dsDNA antibody. Rupture of arteries with SLE was known not to exhibit higher activity for serological tests. In fact, three patients in our presentation demonstrated lower lupus activity by serological tests. Scores of SLEDAI-2K-30 days in case 1,2 and 3 were 16,0 and 12, respectively. These cases reaffirm the significance of clinical manifestation other than serological tests.

P3-129

Anti-cardiolipin antibody turned to be negative through the treatment of syphilis in a patient with systemic lupus erythematosus

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Conflict of interest: None

[Patient] 33-year-old woman [Clinical course] She was diagnosed as SLE on the basis of photosensitivity, butterfly rush, hypocomplementemia, ANA and anti-DNA antibody positivity, and decreasing of WBC in X-1. She was also diagnosed as Sjögren syndrome. Because no organs were disordered severely, she was observed with no treatment. In X January, an aphthous ulcer with pain appeared on her upper lip. It disappeeared in a month, but another one appeared in March. Erythema punctatum in her palm appeared. Antiherpes agents and vitamin pills weren't effective. Because RPR and TPHA were positive, we diagnosed them as syphilis and medicated her amoxicillin. They disappeared smoothly. Both Lupus anticoagulant (LAC) and Anti-cardiolipin antibody (aCL) were positive previously, but only aCL turned to be negative. She had neither thrombosis or repeated miscarriages. aCL-β2GPI was negative. [Discussion] We considered that her aCL was false positive by syphilis, but we haven't denied that she have also antiphospholipid syndrome (APS) yet because LAC is positive. Recently, the number of the patients with syphilis is increasing. We report this case, since there is some possibility of suffrering to diagnose and treat SLE or APS in the patients with syphilis in the future.

P3-130

A case of protein-losing gastroenteropathy in association with systemic lupus erythematosus (SLE)

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Conflict of interest: None

A 57 year-old woman admitted to our hospital because of diarrhea, systemic edema and weight gain. Laboratory tests showed hypoalbuminemia, positive ANA and anti-ds-DNA antibody, and low serum levels of complement. She was strongly suspected systemic lupus erythematosus (SLE). She had about 5 kg weight gain, systemic edema, and pleural effusion and ascites in CT. Protein-losing gastroenteropathy was diagnosed by α1-antitrypsin clearance test. Esophagogastroduodenoscopy and colonoscopy showed no macroscopic abnormal findings. Pathological findings showed deposits of immunoglobulin and complement in submucosal interstitium and capillary by immunofluorescence, and led to a diagnosis of protein-losing gastroenteropathy in association with SLE. Intravenous prednisolone (80 mg/day) after m-PSL pulse therapy was administrated. Rapidly, diarrhea disappeared, urine volume increased, and her general status improved. Levels of anti DNA antibody decreased, levels of serum albumin improved from 1.3 g/dl to 2.6 g/dl, and she was discharged from the hospital. We experienced a case of protein-losing gastroenteropathy in association with SLE. She was not satisfied ACR criteria and SLICC criteria. α1 antitrypsin clearance test and pathological findings by immunofluorescence were useful for diagnosis.

P3-131

Prolonged acute generalized exanthematous pustulosis by hydroxychloroquine

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Conflict of interest: None

Acute generalized exanthematous pustulosis (AGEP) is uncommon cutaneous eruption characterized by acute, extensive, nonfollicular, sterile pustules accompanied by widespread erythema, fever, and leukocytosis. We report a case of AGEP after HCQ administration. The patient continued to cutaneous eruptions that waxed and waned for 56 days. 43-year-old woman was diagnosed as a case of systemic lupus erythematous and was prescribed prednisolone 20mg/day and famotidine 20mg/day. After one month, HCQ 200mg/day was added on because of lupus nephritis. 25 days after starting HCQ treatment, she developed a pustular exanthema that gradually spread on the trunk over the next 48 hours. Morphologically, she had innumerable 1-2 mm pustules with confluent erythema on the abdomen and the back, extending to the arms and legs. A biopsy demonstrated subcorneal pustular dermatosis consistent with AGEP. She was treated with steroid pulse therapy and oral predonisolone was taperd to 30mg daily. She showed waxing and waning of the erythe-

ma and pruritus. At 56 days after AGEP onset, the eruption had resolved. Drug lymphocyte stimulation test of HCQ and famotidine were negative. HCQ has a particularly long half-time. Therefore, it is possible that resolution of HCQ-induced AGEP may take a long time.

P3-132

Our selected cases of systemic lupus erythematosus effectively treated with hydroxychloroquine

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Conflict of interest: None

[Case 1] 32-year-old woman. She was diagnosed with systemic lupus erythematosus (SLE) in 2000. Although her disease has been in stable condition, lupus-related erythema on her upper extremities and trunk continued. She was then treated with hydroxychloroquine (HCQ) from August 2016. [Case 2] 35-year-old woman. She was diagnosed with SLE in 2001. Since she developed facial erythema and skin lesions on her elbows and knees from February 2017, she was given HCQ. [Case 3] 43-year-old woman. She was diagnosed with SLE in 2001. Since her erythema has worsened from 2012 despite treatment with tacrolimus and mizoribine (MZR), administration of HCQ was started. [Case 4] 46-year-old woman. She was diagnosed with SLE in 1998 and was followed with low dose prednisolone (PSL). There was a sudden decrease in platelet count to 30,000/μL on April 2017, despite treatment with PSL and MZR, and HCQ was administered to her. [Results] HCQ was effective for skin lesions and thrombocytopenia of our lupus patients. We also evaluated efficacy of HCQ in 40 patients with SLE (4 males, 36 females) who have been treated with HCQ more than 3 months between October 2015 and September 2017. [Conclusions] HCQ appears to be effective for various types of lupus skin lesions and a part of hematological disorders.

P3-133

The usefulness of repeated renal biopsy in a patient with lupus nephritis

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Conflict of interest: None

A 17-year-old female presented to our hospital because of high fever, malar rash, oral ulcers and arthralgia. She was diagnosed as systemic lupus erythematosus. Although her manifestations improved by prednisolone (PSL) of 20 mg/day, her proteinuria gradually increased. We used PSL 50 mg/day and performed renal biopsy. It revealed diffuse segmental lupus glomerulonephritis, ISN/RPS IV-S (A). The following day of the renal biopsy, she developed severe acute pancreatitis. She was transferred to the university hospital for intensive treatment including methylprednisolone pulse therapy and subsequent PSL 60 mg/day. It took her 5 months to discharge due to lung and abdominal abscess. PSL was tapered but it is difficult to reduce PSL less than 7 mg/day because of hypocomplementemia. When she was presented to us again at the age of 26, proteinuria (0.5 mg/day) and slightly positive anti-DNA antibodies were remained and complement levels were normalized. Second renal biopsy showed ISN/RPS class III (A/C) nephritis. We used multi-target therapy with mizoribine, tacrolimus and high dose prednisolone, and her serological data were improved completely. 2 years later, third renal biopsy revealed that C3 and C1q were negative by immunofluorescence study.

P3-134

A case of secondary antiphospholipid syndrome occurring after hepatectomy in a patient with autoimmune hepatitis

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Conflict of interest: None

We report here a rare case of secondary antiphospholipid syndrome (APS) that developed after hepatectomy in a patient with autoimmune hepatitis (AIH). The patient was a 66-year-old woman diagnosed with AIH, who underwent a hepatectomy because of hepatocelluar carcinoma. In the perioperative period, all tests including blood coagulation tests showed normal values. However, the patient suffered from acute abdominal pain on postoperative day 38. The positive aPL and prolongation of the activated partial thromboplastin time were also noted. Doppler ultrasound and computed tomography showed portal vein thrombosis and massive ascites. Based on the diagnosis of secondary APS, we immediately began the combination of thrombolytic and anticoagulation therapy. Portal vein thrombosis revealed complete resolution of the thrombi after treatment. As secondary APS is a rare adverse event after hepatectomy in a patient with AIH, physicians must be vigilant in identifying the occurrence of secondary APS in patients with autoimmune disease because early detection can decrease the severity and prevent mortality.

P3-135

A case of left ventricular apical thrombus in a patient with anti-phospholipid antibody negative systemic lupus erythematosus

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Conflict of interest: None

[Case] A 34-years-old man, who was diagnosed systemic lupus erythematosus (SLE) by some signs of malar r ush, immunologic disorder and renal disorder as lupus nephritis (ISN/RPS V) 10 years ago at the previous hospital. The doctor treated him with prednisolone (PSL) 30 mg/day. Pulse of steroid and cyclophosphamide was administered. However he stopped taking medication 3 years ago. Then he visited our hospital with complains of hip pain and leg edema. He admitted to our hospital because of flare-ups. ECG showed ST-segment elevation and abnormal Q wave in leads V2-4. Echocardiography revealed cardio function decline (EF 45%), the apex dyskinesia and an apical thrombus in the left ventricular. Coronary angiography showed 99% stenosis of the left anterior descending branch. He received percutaneous coronary intervention and dual antiplatelet therapy. After that, he received medication for care of SLE. By echocardiography after 3 months, the size of thrombus didn't change remarkably, wall motion improved slightly (EF 55%). [Conclusion] An increased prevalence of cardiovascular disease is present among patients with SLE. We report a case of left ventricular apical thrombus in a patient with anti-phospholipid antibody negative SLE.

P3-136

A case of systemic lupus erythematosus with dysuria caused by meningitis secondary to hand, foot, and mouth disease

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Conflict of interest: None

[Case] A 41-year-old man with a 1.5-year history of lupus nephritis presented to our emergency department with the complaint of incomplete voiding and dysuria for 1 day. Four months prior, complete remission of lupus had been achieved and predonine was discontinued. He remained on mycophenolate mofetil and hydroxychloroquine. Seven days prior to admission, he was diagnosed with hand, foot, and mouth disease (HFMD), but had no significant neurological abnormalities. The laboratory data included normal complement and anti-DNA antibody levels. Abdominal ultrasound revealed mild prostatic enlargement and bladder distension. Cerebrospinal fluid (CSF) revealed a cell count of 201/μL, with 100% mononuclear cells. Dysuria caused by central nervous system lupus could not be ruled out, even though lupus activity was stable. We

diagnosed dysuria caused by meningitis secondary to HFMD. On hospital day 2, intravenous acyclovir and immunoglobulin were initiated. On hospital day 5, herpes simplex virus-polymerase chain reaction testing of CSF was negative. By hospital day 9, dysuria had improved and he was discharged from the hospital. [Discussion] Dysuria caused by viral meningitis in a patient with systemic lupus erythematosus is rare. We report this case and a literature review.

P3-137

A case of systemic lupus erythematosus and secondary antiphospholipid antibody syndrome combined with Libman-Sacks endocarditis

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Conflict of interest: None

We report a case of 50s-year-old man, he occured Raynaud's symptoms in X-1 year and right-toe ulcers in X-8 year. He was treated with a vasodilator and an antiplatelet drug by previous doctor. After that, ulceration was observed in the right foot joint, and a skin graft surgery was performed. However, in March X, heart failure due to mitral valve regurgitation and hyperthyroidism occured and visit to the previous doctor, and pancytopenia and autoantivodies positive were recognized. He was admitted to our hospital. We diagnosed SLE with APS from complement reduciton, positive anti-Sm antibody, pancytopenia, positive anti-phopholipid antibodies. We found vegetation at the antrior leaflet of the mitral valve by that we diagnosed Libman-Sacks endocarditis associated with SLE. We treated SLE with prednisolone, cyclophophamide, mycophenolate mofetil, Hydroxychloroquine and aspirin and warfarin, so we found complement normalization and blood cell recovery, but vegetation did not shrink. Opportunities to experience Libman-Sacks endocarditis are rare. We will report this by adding litterarture considerations.

P3-138

Case report: Pancytopenia in late onset SLE

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Conflict of interest: None

A 90-year-old man was referred to our hospital in October 20XX-1 because of prolonged anemia. Laboratory data revealed positive test for Coombs and hemolytic anemia, he was diagnosed as AIHA. Treatment with PSL 20 mg/day was started, and his laboratory data recovered. He was referred to our hospital because of leukopenia in August 20XX. His laboratory data showed pancytopenia (WBC 800 /μl, Hb 9.5 mg/dl, Plt 113000 /μl), and positive test for ANA, anti-DNA, lupus anticoagulant (LAC). He was diagnosed as SLE, and treatment with PSL 25 mg/day was started. After the treatment, his laboratory data recovered. SLE is an autoimmune disease that predominantly affects 20-40 years females and shows clinical features such as nephropathy, cutaneous manifestations, vasculitis, neuropsychiatric symptoms. But features of LO-SLE patients in over the age of 50 years tend to have a more insidious onset of disease, and less frequently show typical symptoms. Our data indicated that elderly patients should be considered the diagnosis not only hematologic malignancies such as MDS but also autoimmune disease such as SLE.

P3-139

Co-presentation of facioscapulohumeral muscular dystrophy and myositis related to systemic lupus erythematosus

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Conflict of interest: None

Introduction: Facioscapulohumeral muscular dystrophy (FSHD) is an autosomal dominant muscular dystrophy which mainly affects face, shoulder blades and upper arms. We report a case of a woman with FSHD complicated by myositis of systemic lupus erythematosus (SLE). Case report: A 54-year-old female with FSHD from the age of 15 years old was diagnosed with idiopathic thrombocytopenic purpura at 38 years old. After the patient developed pulmonary embolism, the diagnosis was changed to SLE and antiphospholipid syndrome based on serology test. 2 months after rituximab and hydroxychloroquine was started for thrombocytopenia, the patient suddenly reported muscle weakness. The serum creatine kinase (CK) level was slightly high. The muscle biopsy showed features of FSHD and perivascular inflammation. As myositis related to SLE, prednisolone was increased to 20 mg/day (0.4 mg/kg/day) from 2mg/day, which increased her muscle strength and decreased the CK level. Discussion: This is the first description of a patient co-presenting with muscular dystrophy and SLE and also with congenital muscle disease and myositis of SLE. In case of muscle symptoms which are incompatible with natural history of muscle disease in the background, further neuromuscular investigations may be appropriate.

P3-140

A case report: effect of plasmaphresis to prevent systemic lupus erythematosus relapse during pregnancy

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Conflict of interest: None

A 41-year-old woman, She was diagnosed with systemic lupus erythematosus (SLE) from anti-nuclear antibody positive, anti-DNA antibody positive, low complementation, proteinuria, fever, erythema when she was 24 years old. Anti SSA antibody was detected when she had parotitis in 28 years old. Her first pregnancy, at the age of 29, fetal congenital herat block was detected at 23 weeks' gestation. SLE was relapsed at the same time. Her fetus died on the fifth day after birth although he underwent pacemaker implantation. In her second pregnancy, 31 years old, she was treated with plasmaphresis (double filtration plasmapheresis: DFPP) once a week from 6 weeks' gestation. She was able to give birth without SLE relapse. She stopped DFPP after birth, but SLE was relapsed in 32 years old. Therefore prednisolone was increased 30mg/day and she underwent DFPP again. Afterwards, tacrolimus was combined. In her third pregnancy, 39 years old, she underwent DFPP during the pregnancy. Her fetus was intrauterine growth restriction, so she was performed caesarean section at 38 weeks' gestation. SLE wasn't relapsed during the pregnancy. [Clinical Significance] Plasmaphresis can be safely administered even during pregnancy, and its effectiveness is expected in the future.

P3-141

A case of giant lumbar lupus erythematosus profundus successfully treated with a combined use of systemic corticosteroid, immunosuppressant, and hydroxychloroquine

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Conflict of interest: None

A 42-year-old woman who had been diagnosed as systemic lupus erythematosus and treated for two years with oral prednisolone (PSL) presented with a palm-sized ulceration on the lumbar skin. It occurred during tapering of PSL 0.5 mg/kg to 0.3 mg/kg and progressed to deep-seated ulceration with pocket formation, extending to the underlying fascia. Topical treatment and an additional oral cyclosporine 1 mg/kg/day

were less effective. The skin pathology showed atrophic epidermis with hydropic degeneration of the basal layer, and lymphocytic infiltration and mucin deposition into the dermal periappendages, without any features of malignancy and no evidence for T cell receptor gene rearrangement. We made a diagnosis of lupus erythematosus profundus (LEP), and started oral PSL 1 mg/kg and cyclosporine 2 mg/kg, but the lesion did not change. We added alternate day administration of hydroxychloroquine (200 mg/400 mg), enable to form favorable granulation tissue within two weeks. Debridement of the necrotic tissue and subsequent split-thickness skin grafting achieved the ulcer healing. She remained lesion-free at one-year of follow up. We discuss the unusual clinical phenotype of LEP, concerning the pathogenesis and updated treatment approach including anti-malaria agent.

P3-142

A case in which rituximab was successful for refractory swallowing dysfunction caused by dermatomyositis

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Conflict of interest: None

[Case report] 76-year-old man [CC] Eruption, Swallowing dysfunction, and Muscle weakness In March 2015, A 76-year-old man developed dermatomyositis (anti-Tif1-γ antibody positive). And at the same time, swallowing dysfunction appeared. He was treated with steroids (PSL1mg/kg), and IVIG, but none were ineffective on swallowing dysfunction. He repeatedly hospitalized for aspiration pneumonia many times, and the stomach tube was inserted frequently. In February 2016, IVIG course7 was ineffective and introduced rituximab. (375mg/m2/w, 4 courses) As a result, his swallowing dysfunction improved, and the stomach tube was pulled out. Also, aspiration pneumonia never repeats. [Discussion] Some of the inflammatory myopathy may cause steroid resistant swallowing dysfunction and treatment options are limited. Swallowing dysfunction in this case was IVIG ineffective and difficult to treat, but remarkably improved with rituximab. There are few reports that rituximab has improved swallowing dysfunction with dermatomyositis, because it is a valuable case, we report it.

P3-143

Two cases of steroid-resistant and anti-SRP antibody-positive polymyositis (PM) treated with intravenous immunoglobulin (IVIG)

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Conflict of interest: None

Introduction Patient with anti-SRP antibody-positive PM is thought severe muscle weakness. It needs multiple immunosuppressive treatments, because of resistance to steroid therapy. We have experienced two cases in which steroid and immunosuppressive treatment was resistant and IVIG was effective. Case 1 She was 44 years old with difficulty of walking, swallowing, high creatine kinase (CK) titer (20,100 U/L), anti-SRP antibody positive, and finding of necrotic muscle disease in the biopsy. Despite treated with steroid pulse, prednisolone (PSL) 50 mg/day and methotrexate, she couldn't stand. But adding IVIG, her muscular strength improved till so much that she could walk and eat herself. Case 2 He was 53 years old with muscle weakness, high CK titer (9,089 U/L) and anti-SRP antibody positive, and finding of necrotic muscle disease in the biopsy. After treated with steroid pulse, PSL 60 mg/day and azathioprine, the CK titer was't normalize, and his symptoms repeated exacerbation easily. Adding IVIG, his muscle strength and CK titer has improved. Clinical Significance Two cases had multiple prognostic factors. Case of anti-SRP antibody positive PM with plural prognostic factors should be treated with early IVIG, because immunosuppressive therapy may be also resistance as with steroid.

P3-144

A case of anti-SRP antibody positive refractory necrotizing myositis-treated with DFPP

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Conflict of interest: None

Background: Anti-SRP antibody positive myositis is often refractory to steroid therapy, and there is not established treatment yet. Case: A 38-year-old woman was admitted to our department due to muscle weakness. She had been well until 2 months before admission (1 month after giving birth to 1st child), when difficulty to raise arms and to stand up appeared. One day before admission, CK elevation (7000IU/L) was pointed and admitted to our department. Muscle biopsy showed immune-mediated necrotizing myopathy, and diagnosis of anti-SRP antibody positive myositis was made. Although PSL 60mg (1mg/kg) and Tac were administered, CK remained remarkably high (>3000IU/L) after 2 weeks. Methylprednisolone pulse and IVIg were added, then she once recovered from weakness. However, recurrence was occurred in about one month and she was admitted again. The state of disease was refractory to repeats of methylprednisolone pulse and IVIg. We tried treatment with double filtration plasmasis (DFPP), referring to some case reports. After DFPP was performed, muscle weakness was improved and she has kept condition able to walk by herself. Here, we report this rare case with some literature review.

P3-145

Successful combination therapy with mycophenolate mofetil (MMF) and tacrolimus (TAC) for anti-MDA5-antibody associated interstitial pneumonia: A case report and review of the literature

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Conflict of interest: None

We herein report a case of 73 years old Japanese woman with anti-MDA5-associated rapidly progressive interstitial pneumonia. She suffered exanthema, joint pain, and dyspnea on exertion in November last year. She visited her doctor's office, but her symtoms didn't recover and referred to our hospital. She had Gottron palpues and palmar Gottron sign and didn't have muscle weakness. Her computed tomography (CT) revealed subpleural reticulation. We diagnosed her as clinically amyopathic dermatomyositis (CADM) with interstitial pneumonia. She didn't have hypoxemia, but had anti-MDA5-antibody (>150 index), whence we administered prednisolone, cyclosporine A (CYA), and intravenous pulse cyclophosphamide (IVCY). CYA later induced liver dysfunction, was switched to TAC. Instead of three times IVCY, she got exagerrated nail erythema, elevation of ferritin level, and new consolidation on CT scan appeared. We recognized IVCY resistant CADM, and switched IVCY to MMF. Then interstitial pneumonia improved, and ferritin level and titer of anti-MDA5-antibody decreased. In conclusion, anti-MDA5-antibody positive patients frequently develop threatment-resistant rapidly progressive interstitial pneumonia. Our report suggests combination therapy with MMF and TAC can be an effective therapy in case of IVCY resistant.

P3-146

A case of the antiNXP2 antibody-positive dermatomyositis complicated with cervical cancer

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Conflict of interest: None

Case was 44 years old woman. Chief complaint was muscle weakness. She had exanthema with itching to posterior region of neck and forearms from March 201X. Then she visited a family doctor, because she detected a myalgia of legs in April. She had an increased myogenic enzyme and was introduced to Gifu Municipal Hospital in May. In the

physical examination she had heliotrope rash, Gottron's papule and mmuscle weakness at deltoid, biceps of upper extremity and biceps femoris muscles. She showed a graspache of biceps and gastrocnemius muscles. Laboratory data indicated CK 2,201IU/L and LDH 575IU/L, and negative AntiARS Ab, antiMDA-5 Ab, antiMi-2 Ab, antiTIF1γ Ab were observed. Cervical cancer was detected becaue of irregular genital bleeding. Finally, she was diagnosed as cervical cancer with dermatomyositis. Before surgery mini-steroid pulse therapy was done, but muscle weakness and progression of dysphagia were gradually increased. Panhysterectomy with adnexectomy was undergone maintained with prednisolone (PSL) 20mg treatment. However, vessels permeations in the pelvic cavity were found out. Finally, she has been becoming a bedridden ADL. The antiNXP2 Ab was sometimes found in dermatomyositis in the children and dermatomyositis complicated with malignant tumors in adult.

P3-147

Anti-ARS antibody-positive dermatomyositis complicated by rapid progressive interstitial pneumonia: A case report

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Conflict of interest: None

[Case]: An 84-year-old man presented to our hospital with dyspnea. Chest radiograph showed a slight degree of consolidation throughout both lower lung fields, and he was diagnosed with bacterial pneumonitis. Despite administration of antibiotic for 2 weeks, he did not show recovery of his respiration failure. Chest CT showed diffuse ground-glass-opacities throughout both lung fields, and he was diagnosed with rapid progressive interstitial pneumonia (RPIP). His anti-ARS antibody was positive. He showed a heliotrope rash, forehead and periungual erythema, as well as upper and lower extremity muscle weakness. His serum levels of muscle enzymes were within reference range. EMG showed myogenic conversion. A biopsy performed on an affected muscle specimen revealed cellular infiltration, and he was diagnosed with dermatomyositis. Steroid pulse therapy, prednisolone (60 mg/ day) and tacrolimus (2 mg/ day) were initiated and led to gradual improvement in his respiration failure. [Conclusion]: Dermatomyositis can often be complicated by IP. While anti-ARS antibody-positive IP frequently shows a subacute or chronic course, anti-MDA-5 antibody-positive IP shows an acute course. Clinicians should be aware that anti-ARS antibody-positive dermatomyositis rarely occurs in association with RPIP.

P3-148

Efficacy of steroid and intravenous immunoglobulin treatments for anti-HMGCR necrotizing myopathy

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Conflict of interest: None

A case is a 38 years-old woman. She was referred to our hospital because of pain of both legs and decrease in swallowing force. MRI showed abnormal signs in infraspinatus muscle, subscapularis, inside and outside closing muscle, quadriceps muscle and biceps femoris. Electromyogram showed myogenic changes in left deltoid muscle and left quadriceps muscle. Muscle weakness of trunk and dysphagia were found. Anti-HMGCR antibody was detected. Histology of muscle was characterized by necrosis and regeneration of muscle fibers. She was diagnosed as anti-HMGCR necrotizing myopathy. She was treated with prednisolone following the methylprednisolone pulse. Administration of intravenous immunoglobulin (IVIG) and intravenous methylprednisolone pulse therapy were repeatedly performed, because her serum creatine levels were not fully improved. After IVIG treatments, serum creatine kinase levels were markedly decreased. [Clinical Significance] Anti-HMHCR antibodies were initially reported as a disease marker of statin-associated myopathy, however, this patient has not been treated with such medications. This case indicated that administration of IVIG and methylprednisolone pulse therapy show excellent therapeutic effects for anti-HMGCR-related necrotizing myopathy, as previously reported.

P3-149

A case of developing anti-MDA-5 antibody positive dermatomyositis after allogeneic peripheral blood stem cell transplantation

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Conflict of interest: None

A 56 - year - old man. In April 2016, remission was achieved after allogeneic peripheral blood stem cell transplantation for the treatment of chronic myelogenous leukemia (explosive crisis). Liver dysfunction appeared in June, the same year, it was diagnosed as cGVHD, improved by high dose steroid therapy. After that, the steroid gradually decreased, stopped the steroid in August 2017. In September of the same year, polyarthritis, skin rash, interstitial pneumonia appeared. Heliotrope eruption, Gottron's signs admitted. Due to worsing of interstitial pneumonia, He was hospitalized on October of the same year, and treated with intensive regimen of combined immunosuppressive therapy, but he was died. Because he had previously undergone bone marrow transplantation, bone marrow function was decreased and myelosuppression by cyclophosphamide was highly advanced. Therefore, it was suggested that the failure to administer a sufficient amount of immunosuppressive agent may have affected the treatment.

P3-150

A case of dermatomyositis associated with anti-TIF1-gamma antibody and anti-Mi-2 antibody

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Conflict of interest: None

[Case] A 42-year-old man. In February 201X, anterior resection was performed for rectal cancer, and slight increase in CK value was observed after surgery. In mid-April, lifting of upper limbs became difficult after postoperative chemotherapy. In mid-May, the CK value rose to 20000 IU/L. He was consulted to our department suspected of dermatomyositis in July. Diagnosis of dermatomyositis was easy from typical rash, muscle weakness, arthritis, electromyogram change, blood test findings, and so forth. Prednisolone and tacrolimus, high-dose intravenous gamma-globulin therapy led him to remission. Although anti-TIF1-γ antibody and anti-Mi-2 antibody measured at the time of diagnosis were positive, re-examination after 3 months was negative only for anti-TIF1-γ antibody. [Conclusion] The anti-TIF1-γ antibody and anti-Mi-2 antibody test is widely used as a diagnostic aid for dermatomyositis. These test have the possibility of theoretically becoming double positive, but there is no report that one side has become negative after both are positive.

P3-151

A case of statin-naive anti-HMGCR-positive myopathy with extramuscular manifestations

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Conflict of interest: None

(Case) A 67-year-old man was sent to a general hospital with nonproductive cough and abnormal chest X ray. Chest CT scan showed interstitial lung disease and blood test revealed high level of CK and LDH. He came to our hospital for further evaluation under suspision of polymyositis. After biopsy from left semimembrane muscle, the initiation therapy was started of methyl predonisolone pulse followed by 60mg of predonisolone. As echocardiogram showed diffuse low cardiac function and high-sensitive cadiac troponin T was positive, he underwent cardiac muscle biopsy. Small infilteration of inflammatory cells and pathy lesions of degenerative necrosis, hemorrhage and fibrosis were seen. Furthermore, the biopsy from lower limb suggested necrotizing autoimmune myopathy showing monocyte infilterations with HE staining and MAC deposition and HLA-ABC expression on myofibrotic membrane in immunostaining. Anti-HMGCR antibody turned out to be positive. (Clinical value) Extramuscular involvement is infrequent in anti-HMGCR-positive myopathy. His lung and cardiac manifestations associated with myopathy got better after immunosuppressive therapy. We report this case with a slight literature consideration.

P3-152

Myositis specific antibodies-negative dermatomyositis developed into complete atrioventricular block with myocarditis and chronic intestinal pseudo-obstruction : a case report

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Conflict of interest: None

A 77-year old woman was admitted to our hospital 2 years ago, because of asymptomatic elevated myogenic enzyme, Raynaud's phenomenon and skin pigmentation around the chest and abdomen. Then she began to suffer from nausea, uncomfortable bowel distention and constipation, without mechanical obstruction, was treated conservatively. Interstitial pneumonia and Hashimoto-disease were detected. Heliotrope rash and muscle weakness appeared this year, as well as cardiomegaly and abnormal ECG were also observed. Two weeks later she was hospitalized for heart failure of complete atrioventricular block, to insert a cardiac pacemaker. EMG and muscle biopsy confirmed dermatomyositis. Cardiac positron emission tomography allowed to identify myocarditis. No myositis specific antibodies were detected, only anti SS-A antibody was positive. She was treated with prednisolone at a daily dose of 40mg. However, muscle weakness was not improved and her serum levels of myogenic enzymes were not normalized. Heart failure and chronic intestinal pseudo-obstruction were repeated. The combination therapy of prednisolone and tacrolimus, twice intravenous immunoglobulin showed good response to myositis. We report here a rare case of dermatomyositis with myocarditis and chronic intestinal pseudo-obstruction.

P3-153

A case of anti-PL7 antibody positive dermatomyositis with interstitial pneumonia and dysphagia

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Conflict of interest: None

[Case] 70-year-old man [Chief complaint] muscle weakness [Present illness] He consulted a doctor about dyspnea and cough one year ago. He was diagnosed as interstitial pneumonia and treated with 40mg/day of prednisolone which was tapered to 12.5 mg/day. The symptoms of muscle weakness and muscle pain emerged three weeks prior to his admission, when he presented with muscle weakness of the trunk, trunk rush and dysphagia. Laboratory examination revealed the elevation of muscle enzymes, CRP and KL-6, and that anti-PL7 antibody was positive. Chest CT showed that ground glass opacity of both bottoms of lung field were stable. MRI of upper arm showed that both sides of biceps brachii had a high signal on STIR. Muscle biopsy revealed no infiltration of inflammatory cells but the expression of MHC class I around some muscle bundles. He was diagnosed as dermatomyositis and treated with 70mg (1mg/kg)/ day of prednisolone added with 4 mg/day of tacrolimus, however his dysphagia got worse. So we added high-dose intravenous immunoglobulin for five days and dysphagia improved garadually two weeks after that. [Consideration] We report this case with effectiveness of the combination of prednisolone, tacrolimus and intravenous immunoglobulin therapy.

P3-154

The case of polymyositis complicated with bent spine syndrome

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Conflict of interest: None

[Case] The case is 78 years old woman. In March 20XX, She was diagnosed with lung adenocarcinoma and performed radical surgery. From this time she was aware of standing, walking disorders and bending forward posture. 4 month later she came to our department because of the elevation of serum myogenic enzymes. In physical examinations, her proximal muscles were weak and her bend forward was reversible in supine position. MRI-FLAIR showed muscles were high intensity around pelvis and paraspinal muscles. Autoantibodies were positive of anti-PL-12, anti-SRP and anti-SS-A antibody in ELISA. Muscle biopsy from quadriceps revealed lymphocyte infiltration around muscle fibers. We diagnosed polymyositis (PM) complicated with bent spine syndrome (BSS) and started treatment with high-dose glucocorticoid and tacrolimus. During the treatment, her BSS, serum CK level were improved and discharged to home. [Discussion] This is a rare case of PM presenting complicated autoantibodies with BSS. BSS should be differentiated from diverse diseases like degenerative, endocrine and autoimmune diseases. Especially like this case complicated with BSS and intricate autoantibodies, biopsy from paraspinal muscles or plural different muscles should be considered for detailed diagnosis.

P3-155

A case of dermatomyositis with positive anti-TIF1 antibody complicated with malignant lymphoma and gastric cancer

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Conflict of interest: None

Male, 70 years old had erythema appeared in the forehead part from January 201X. He visited a family doctor and was introduced to dermatologist in Gifu Municipal Hospital. After treatment with anti-allergic drug and glucocorticoid, erythema repeatedly disappeared and diagnosed as erythroderma. In March, because swelling at the lower left cervical portion was gradually increased, he was introduced to our department on May 16th. Dermatomyositis was suggested due to Heliotrope rash and Gottron's papule. Laboratory data indicated that increased CK 809 IU/L, and soluble IL-2R 1,810 U/mL and positive anti-TIF1-γ antibody were observed. PET-CT scanning showed high FDG accumulation in the upper left internal deep-neck lymph node (SUVmax 31.9). Histological finding from the lymph node biopsy proved diffuse large B-cell lymphoma (DLBCL). Upper endoscopic finding showed the ulceration of upper gastric body. Biopsy specimens indicated the signet ring cell carcinoma. Finally he was diagnosed as dermatomyositis with malignant lymphoma and gastric cancer. Three courses of R-CHOP and radiation therapy for DLBCL and gastrectomy for gastric cancer had been treated. The titer of anti-TIF1-γ antibody gradually decreased to the normal range without recurrence and metastasis.

P3-156

A Case of Anti-Centromere Antibody Positive Dermatomyositis

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Conflict of interest: None

A 77-year-old female. She was visiting a practitioner for hyperlipidemia, hypertension, taking rosuvastatin, and telmisartan for a long period of time. Pain in both upper extremities appeared on August 3, X, and she visited the same practitioner on August 6. Drug rhabdomyolysis was suspected and rosuvastatin was discontinued because blood test revealed creatine kinase as high as 2055 U/L, but at the time of reconsideration pain continued mainly at the upper arms and thighs, with no improvement in blood test data. So myositis was suspected and on August 22nd she visited our department and got hospitalized on the same day for the purpose of scrutiny and treatment. Heliotrope rash, Gottlon's signs, muscle weakness in the proximal muscles of the upper and lower limbs, muscle grasping pain, elevation of serum myogenic enzymes, electromyographic changes indicative of myositis, systemic inflammatory findings was confirmed, she was diagnosed as dermatomyositis. For autoantibodies related to rheumatic diseases, only antinuclear antibodies (Discrete) and anti centromere antibodies were positive, all others were negative. This case seems to be atypical for dermatomyositis, who is positive for anti-centromere antibody, so I report it.

P3-157

The efficacy of the combination therapy of IVIG and MMF for the refractory ILD in anti-MDA5-positive CADM

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Conflict of interest: None

[Objective] Consensus of the management of interstitial lung disease (ILD) with anti-MDA5 antibody-positive clinically amyopathic dermatomyositis (CADM) has not been established. We report 2 cases with anti-MDA5-positive CADM, the progression of which ILDs was successfully suppressed by intravenous immunoglobulins (IVIG) and MMF after multi-targetting immunosuppressive therapies. [Result] Case 1: 63-year-old female was diagnosed with CADM by skin rash, elevated anti-MDA5 and the presence of ILD. Because steroid pulse therapy followed by PSL 60mg/day with TAC and additional 3kurs of IVCY were not effective for the continuous exacerbation of ILDs, IVIG and MMF were treated. Case 2: 62-year-old female was diagnosed with CADM by skin rash, anti-MDA5 positivity, and the presence of ILD. After treatment with high dose of corticosteroids in combination with AZP, CyA or TAC, ILD continuously progressed. Because 4kurs of IVCY was not effective, IVIG and MMF were adminstered. In both cases, followed CT images showed no new grandglass opacity, and titers of anti-MDA5 and ferritin were significantly decreased. [Conclusion] Our cases suggested the efficacy of the combination therapy of IVIG and MMF for the refractory ILD in anti-MDA5-positive CADM.

P3-158

A case of anti-MDA5-positive rapidly progressive interstitial lung disease which rescued by aggressive immunosuppressive therapy although poor compliance of medication and smoking habit made it relapse

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Conflict of interest: None

A 51-years-old female had first admitted to our hospital with a high fever, myalgia, proximal muscle weakness, heliotrope rash and Gottron's sign in June 2015. Hypoxemia and rapid progressive interstitial lung disease (RP-ILD) with high titers of anti - MDA 5 antibody and serum ferritin were observed. We administered high-dose of prednisolone (PSL) and oral cyclophosphamide (CPA) for her dermatomyositis (DM) and she achieved a complete remission. From November 2016, she was maintained only with daily 5mg of PSL and 100mg of azathioprine (AZA). In February 2017, she has presented myalgia and erythema on her forearms, face and precordium. Her serum levels of CK, ferritin and anti-MDA 5 antibody titers were increased. ILD was also deteriorated by chest CT and considering her condition, we diagnosed as recurrence of RP-ILD with DM and hospitalized again in February 18. Withdrawal of PSL, AZA and smoking habit seemed to be the causes of relapse. She was started on methyl-PSL pulse, oral CPA and cyclosporine and successfully responded to those treatment. Anti-MDA 5 antibody-positive RP-ILD is rarely relapsed after remission. In this case, we successfully saved her again by aggressive immunosuppressive therapy although poor compliance of medication and smoking habit made RP-ILD relapse.

P3-159

A case of anti-MDA 5 antibody positive dermatomyositis with new onset interstitial lung disease during immunosuppressive therapy

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Conflict of interest: None

A 64-year-old woman was admitted to our hospital with proximal muscle weakness and erythema on her fingers in 2017 May. She was diagnosed with anti-MDA5 antibody positive dermatomyositis (DM). Respiratory symptoms were not observed and chest CT did not show the interstitial lung disease (ILD). A small invasive shadow was found in the lingular segment of left lung, and non tuberculous mycobacteriosis (NTM) was suspected. On day 10, a fever and arthritis deteriorated. Her serum levels of CK and ferritin were increased. Although we administered high-dose of prednisolone (PSL) and intravascular cyclophosphamide, chest CT showed the appearing of the ILD. On day 30, cavitary lesions appeared in the left upper lobes and deteriorated. Treatment for NTM and hemoperfusion was initiated but ILD deteriorated rapidly. On day 41, cyclosporine was additionally administered. However, she died on day 97 despite aggressive immunosuppressive therapy. In this case, we couldn't stop the progress of the RP-ILD by aggressive immunosuppressive therapy although ILD was not observed on admission. Treatment of anti-MDA5-positive dermatomyositis without ILD has been not established. We report this case with some literature review.

P3-160

A case of anti melanoma differentiation-associated gene 5 (anti-MDA5) antibody positive dermatomyositis with elevation of ferritin, that was difficult to decide whether the cause was drug eruption or disease progression

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Conflict of interest: None

(Case) A 70-year-old woman showed one month history of dry eye and dry mouth. At the visit, she had reversed Gottron's signs, nail-fold capillary change, bilateral fine crackles. Her blood test showed KL-6 818 U/ml, ferritin 822ng/ml, Antinuclear antibody was 1:40, anti MDA-5 antibody was positive (more than 150 unit; cut off:32 unit). Her chest CT scan showed interstitial lung disease. That is why we diagnosed as dermatomyositis and started prednisolone 50mg every other day, tacrolimus, mizoribine as "Multi-target therapy". On the day 51, she had systemic rash. She also had the elevation of serum ferritin level. Her respiratory symptom didn't change and KL-6 had been decreasing, so we diagnosed drug-induced rash. Stopping bactrim started just a few days before, her rash subsided. During her treatment period, she didn't have any deterioration of the interstitial lung disease. Her KL-6 and ferritin maximum level was 1356 U/ml and 7119 ng/ml, which decreased to 876 U/ml, and 693 ng/ml respectively. (Clinical significance) We experienced the case of anti-MDA5 antibody positive dermatomyositis treated with "Multi-target therapy". It is said that the elevation of ferritin is associated with their

prognosis. Drug allergy can mimic the worsening of dermatomyositis.

P3-161

A case of carotidynia mimicking giant cell arteritis

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Conflict of interest: None

A 59-year-old-man was admitted to a hospital for syncope while running on January, 20XX. He was diagnosed with angina and underwent coronary artery stenting. He was referred to our hospital on February, 20XX for a persistent fever over 38 degrees Celsius and elevated serum levels of CRP after the coronary angioplasty. FDG-PET/CT scan showed an accumulation of FDG in thoracic and abdominal aortae. Although the accumulation pattern was atypical, we performed the biopsy of temporal artery for a possibility of giant cell arteritis. Three days later, he developed pain in his left neck. CT scan revealed an area around the carotid artery with increased density which suggested panniculitis. We diagnosed the patient as having carotidynia. His neck pain spontaneously subsided along with the CT finding. The fever and CRP levels also normalized without treatment. The biopsy was negative for arteritis/periarteritis and the FDG accumulation in aortae was considered due to atherosclerosis. Carotidynia is a self-limiting, idiopathic clinical syndrome characterized by acute unilateral neck pain and tenderness in the carotid artery originally described by Fay in 1927. Our case, which mimicked giant cell arteritis, will be discussed with some literature review.

P3-162

A case of good response of TNF inhibitor to a woman with elderly onset Crohn's disease and giant cell arteritis

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Conflict of interest: None

An 80-year-old woman presented with headache and neck stiffness. She had a history of Crohn's disease (CD) and received prednisolone (PSL). As her blood samples showed a C-reactive protein level of 9.9 mg/dL, she was hospitalized. With no signs of infection and malignancy, she was diagnosed as having giant cell arteritis (GCA) according to the American College of Rheumatology criteria. She took 30 mg PSL, and her symptoms vanished. The PSL dose was tapered. Five months later, she experienced stomachache, bloody stool, headache, and neck stiffness. The first two symptoms were due to the flare of CD; and the latter ones, the flare of GCA. We tried adalimumab (ADA) therapy for the CD. All the symptoms disappeared promptly. Thus, we think that the ADA therapy was effective not only for CD but also for GCA. Inflammatory bowel disease and vasculitis sometimes co-occur. However, coincidence of CD and GCA is not reported. Besides, the effectiveness of TNF inhibitor is said to be limited in vasculitis and only some case reports are available. We believe this case is useful in suggesting the possibility of TNF inhibitor therapy in the treatment of large vessel vasculitis.

P3-163

A case of giant cell arteritis and three cases of Takayasu arteritis which achieved remission maintenance with anti-IL-6 receptor antibody Tocilizumab

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Conflict of interest: None

[Introduction] In November 2016, subcutaneous injection of Tocilizumab (TCZ) was approved for refractory Takayasu arteritis (TA) and Giant cell arteritis (GCA). We report 4 cases of refractory large vessel vasculitis which were successfully maintained remission with TCZ. [Case report] (Case 1) A 16-year-old woman who developed cerebral infarction of left internal carotid artery was diagnosed as TA. Although she was initially treated with 30mg per day of prednisolone (PSL), elevated inflammatory markers were observed on PSL13mg per day and methotrexate (MTX). Additional treatment of 3 types of anti-TNF-inhibitor (TNF-I) could not improve her inflammatory markers, low fever and loss of appetite, which improved after switching to intravenous TCZ. (Case 2) A 17-year-old woman who developed neck pain and fever was diagnosed as TA. Although she was initially treated with 30mg per day of PSL, she relapsed during tapering of PSL. Although 2 types of TNF-I failed to control disease, subcutaneous injection of TCZ was administered, successfully maintained remission. [Conclusion] Including above two cases, we described three patients with TA and one with GCA who showed a good response to TCZ in even refractory patients to other immunosuppressive agents or biologic treatment.

P3-164

Investigation of Picture Diagnoses of Temporal Arteritis occurred GCA

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Conflict of interest: None

[Object] A temporal artery biopsy and PET-CT had been useful for diagnosis of Giant cell arthritis (GCA), while these methods were difficult to examine, because of highly invasiveness and limitation for establishment. We investigate the possibility of usefulness for blood ultrasonography and 3DCTA. [Methods] We estimate GCA patients in our hospital about the difference for characteristic of clinical and serum test and picture images. We are examining blood ultrasonography for all newly polymyalgia rheumatic (PMR) diagnosed cases, and examining 3DCTA, PET-CT and biopsy of temporal artery for the cases which are doubtful with GCA. We will prove the usefulness for diagnosis methods of blood ultrasonography and 3DCTA which are low invasiveness. [Results] Stenosis and stoppage of blood vessels were detected by 3DCTA, and also they were improved by 3DCTA after immunosuppressive therapy. So that we propose 3DCTA for temporal artery is useful for diagnosis and judgment of treatment effect. Although comparison with MRA, PET-CT and blood ultrasonography for diagnosis of GCA had been reported, it had been rarely reported with 3DCTA. [Conclusions] We propose that ultrasonography and 3DCTA are useful method for diagnosis of GCA.

P3-165

Utility of ultrasound to diagnose giant cell arteritis with chronic renal failure: a case report

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Conflict of interest: None

A 82-year-old woman with type 2 diabetes was admitted to our hospital suffering from 3-month history of pain in both shoulder and hip, and elevated inflammatory markers. We diagnosed her as polyarthritis rheumatica since musculoskeletal ultrasound revealed bursitis and tenosynovitis in shoulders. Furthermore, we considered concomitance of giant cell arteritis (GCA) because she experienced jaw claudication 6 months before. As contrast-enhanced computed tomography (CT) was contraindicated by her renal dysfunction due to diabetes, we performed vascular ultrasound examination instead. An increase in wall thickness was observed in common carotid arteries, subclavian arteries, and axillary arteries. [18F]-fluorodeoxyglucose positron emission tomography-CT also confirmed high uptake in the same arteries. Active GCA was suggested and prednisolone 40mg/day was initiated. She had no findings and symptoms

in temporal arteries. Following predonisolone treatment, all the clinical features and wall thickness in vascular ultrasound were significantly improved. Vascular ultrasound examination is useful and helpful to diagnose GCA especially in patients who are contraindicated to contrast-enhanced computed tomography (CT).

P3-166

A case of giant cell arteritis with generalized granuloma annulare

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Conflict of interest: None

We report a case of giant cell arteritis (GCA) with preceding granuloma annulare (GGA). A 80-year-old man presented with asymptomatic general erythematous papules 1 year ago. A skin biopsy was performed and diagnosed as GGA. He was aware of fever and ocular pain 2 months ago, but MRI revealed no abnormal signals. He presented with jaw claudication, headache, general malaise, and loss of vision from 10 days ago. He was admitted to our hospital because of sudden bilateral blindness. Ophthalmologist diagnosed biocular retinal central artery occlusion. He was treated with intravenous urokinase and hyperbaric oxygen, but improvement in visual acuity was poor. Laboratory findings showed an inflammation (C-reactive protein 15 mg/dl, the erythrocyte sedimentation rat 90 mm/1h). His bilateral superficial temporal arteries were dilated with tenderness. US and CT showed the wall thickening and luminal narrowing of them. So a diagnosis of GCA was made. There were no clinical signs of polymyalgia rheumatica. Oral corticosteroid (PSL30 mg/day) was started and his symptoms without visual acuity were immediately improved. There were no recurrence for 6 months. The association of GGA and GCA is unclear, but the histological has been reported. We considered present case is precious.

P3-167

Development of giant cell arteritis during the course of erythema nodosum

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Conflict of interest: None

A 78-year-old woman was admitted to our hospital with a one-month history of fever, chest pain, and headaches. Eighteen months prior to her admission, she developed painful nodular skin lesions on the bilateral lower legs. Biopsies from skin lesions showed septal panniculitis with perivascular inflammatory lymphocytic infiltrate suggestive of erythema nodosum (EN). No diseases associated with EN were identified. She was treated with colchicine. CRP ranged between 2.8 and 11.5mg/dl until this visit. The laboratory findings revealed a white blood cell count of 12.9×10^9/l, a hemoglobin level of 7.5g/dl, a CRP level of 24.2mg/dl, and an erythrocyte sedimentation rate of 140mm/hr. Rheumatoid factor, antinuclear antibodies, MPO-ANCA, and PR3-ANCA were all negative. MRI revealed clear wall thickening of the ascending aorta, aortic arch, brachiocephalic trunk, common carotid artery, and left subclavian artery. FDG-PET/CT showed FDG uptake in the walls of the proximal carotids and subclavian arteries. These results were consistent with the diagnostic criteria of GCA. Induction therapy with prednisolone at 20mg/day resulted in rapid improvements in her symptoms and inflammation. Physicians need to consider GCA as one of the causes of idiopathic EN with recurrent inflammatory markers.

P3-168

Temporal arteritis in the elderly manifesting flu-like symptoms

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Conflict of interest: None

An elderly female has suffered flu-like symptoms such as fever, headache, polyarthralgia and anorexia. She had past history of ovarian cysts, salivary gland tumor and type-2 diabetes treated with insulin. Laboratory data showed a seronegative arthritis with highly active inflammation as follows: WBC:15900/μl (Nt 83.2%, Ly 7.5%), CRP:26.6 mg/dl, RF:3 IU/ml, anti-CCP antibody:0.6 U/ml, ANA:x40, MPO-ANCA:1.0 U/ml, PR3-ANCA:1.0 U/ml: and urinary WBC:1~4/HPF.A whole-body CTscan found no particular abnormality, and respiratory and urinary infections were excluded. As a condition of FUO, the patient was admitted for the examination. Since a painful stiffness with bilateral temporal arteries was found, biopsy of right temporal artery was performed. The pathological finding, showing the thickened intima of the artery with calcification of vascular media and infiltration of neutrophils around the artery, was diagnostic for the temporal arteritis. Prednisolone was administered and the symptoms have improved for 4 weeks. Regarding temporal arteritis, manifestation of the respiratory symptoms such as dry cough and sore throat were reported to be ~9%. The temporal arteritis should be considered in the patients with elderly-onset FUO accompanying respiratory symptoms.

P3-169

A case of Giant Cell Arthritis successfully treated by Tocilizumab

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Conflict of interest: None

[Background] The efficacy of steroid or MTX to treat GCA is sometimes insufficient. We experienced a case of GCA treated well by Tocilizumab. [Case] A 82-year-old Japanese man diagnosed as GCA was treated with steroid and MTX, but did not keep remission when the dose of steroid was tapered less than 10mg/day. [Course] After TCZ was initiated, he was able to keep remission even after steroid and MTX was off. [Conclusion] TCZ was effective for the treatment of our case.

P3-170

A case of cerebral infarction associated with giant cell arthritis

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Conflict of interest: None

An 80-year-old female was admitted to our hospital because of fatigue and bilateral lower limb pain, which had sustained for 2 month, in March 2017. She had a history of polymyalgia rheumatica and been treated with prednisolone (PSL). PSL had been discontinued in 2016. She showed an inflammatory reaction rise with blood test and aortic wall thickening by contrast CT examination. She was diagnosed with giant cell arthritis (GCA). After treatment with PSL, the symptoms improved, but she presented left hemiplegia. Head MRI showed a high signal area in the right frontal lobe and caudate nucleus. She was diagnosed with acute cerebral infarction. Carotid ultrasonography, echocardiography and head MRA examination revealed no aberrations, hence, it is probable that her cerebral infarction was associated with GCA. It is reported that 3-4% GCA patients are complicated with cerebrovascular events, most of which are caused by occlusions of extracranial vessels. There are only a few reports of intracranial blood vessel related to GCA patients. In this case, no aberrations were found in the extracranial vessels, and cerebral infarction occurred in the region of the anterior cerebral artery. We discuss the pathogenesis and characteristics of cerebral infarctions associated with GCA.

P3-171

Extracranial involvement with the ascending aorta extending to the common iliac arteries in a case of giant cell arteritis

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Conflict of interest: None

Giant cell arthritis (GCA) typically involves the temporal arteries, but can involve extracranial vessel described in 10 to 15% of cases. We report a case of a 68-year-old female with GCA who has extensive extracranial lesions having the aortic arch extending to the common iliac arteries. She was admitted with a 4-week history of fever and fatigue. She had developed headache, jaw claudication, and sore throat in 1 week before admission. The brain MRI with gadolinium showed a thickened wall of the ascending aorta extending to internal carotid arteries and the temporal artery. The contrast-enhanced CT indicated a contrasting effect of diseased arterial walls involving the ascending aorta extending to the common iliac arteries. The temporal artery biopsy revealed perivascular and intestinal lymphocytic infiltrates with giant cells. She was commenced on high-dose prednisolone (60 mg daily), and her symptoms resolved completely on the 2nd day of treatment. The MRI after 12 weeks of the steroid therapy showed complete resolution of temporal GCA and no evidence of other vasculitis. This case with extensive extracranial arteries was successfully treated with steroid therapy and the progression of vasculitis occasionally leading to the aneurysm and dissection could be suppressed.

P3-172

Development of granulomatosis with polyangiitis in patient with dermatomyositis

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Conflict of interest: None

A 59-year-old man was referred to respiratory department of our hospital for further evaluation of interstitial pneumonia (IP). He was diagnosed with clinically amyopathic dermatomyositis, based on Gottron's sign, no elevation in creatine phosphokinase, positivity for anti-Jo-1 antibodies. He did not receive treatment, because disease activity was considered low. At that time, myeloperoxidase-antineutrophil cytoplasmic antibodies (MPO-ANCA) was positive but he had no symptom of vasculitis. After three years, he was referred to our department due to elevation of C-reatctive protein (CRP) and MPO-ANCA. He presented with sinusitis, repeated bloody nasal discharge, dry cough, hearing loss and otitis media. Thus, we diagnosed him with granulomatosis with polyangiitis (GPA). We started treatment with 50 mg of prednisolone orally and rituximab therapy. As a result, cough disappeared and hearing loss was improved. CRP levels decreased into normal range, and MPO-ANCA titer also decreased gradually. Chest computed tomography showed improvement of IP. To our knowledge, this is the first case report of GPA associated with DM.

P3-173

The efficacy and safety of rituximab on relapsing granulomatosis with polyangitis

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Conflict of interest: None

[Object] To evaluate the efficacy andsafety of rituximab (RTX) in patients with relapsing granulomatosis with polyangiitis (GPA) in our hospital. [Methods] Five patients with GPA were administrated with RTX. Three of five patients were refractory to cyclophosphamide treatment. Two patients discontinued cyclophosphamide due to adverse events. Rituximab (RTX) of 375mg/m2 was administered once weekly for consecutive 4weeks in principle. [Results] We recruited 5 relapsing GPA cases (1 males and 4 females). The average age was 60.8-years old. 2 patients treated with RTX administration achieved remission for twelve months. One patient acknowledged the improvement of the clinical symptoms including recurrent epistaxis and ear fullness, whereas bronchial stenosis was not improved. Two patients were now under course of observation. No adverse events were observed in all five patients. [Conclusions] RTX was efficient for patients with relapsing GPA, who were refractory to CY treatment. No adverse events were observed in all cases, thus suggesting its efficacy and safety for treating with GPA.

P3-174

B cell repopulation after rituximab treatment help to predict the relapse in a case of Wegener's granulomatosis

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Conflict of interest: None

We report a case of a 67-year-old man with Wegener's granulomatosis (WG) complicated with repeat rhinorrhagia and lung granulomas. He was diagnosed with WG in 2008, and treated with PSL (1mg/kg) and cyclophosphamide (CY). Although he did not have a complete remission and long-term use of CY and he switched to MTX, he also had several relapses after MTX treatment. Then he was started rituximab (RTX) treatment on relapse in August 2015. RTX was effective and peripheral B cell counts decreased to 0/mm^3. After 12 months from RTX treatment, due to slightly elevation of ANCA titers and B cells (33/mm^3) we added on RTX for maintenance treatment. One week later, he had pancytopenia and was withdrawn RTX and MTX. After the recovery of cell count, he was retreated with MTX6mg/w. Although in May 2017 only B cells elevated (157/mm^3) without symptom and elevation of ANCA titers, he had a relapse and retreated with RTX in August 2017. [Clinical Implication] In this case, peripheral B cell repopulation was more important indicator of relapse of WG than ANCA. Recently, RTX has been shown to be effective in AAV maintenance therapy, but an optimal RTX treatment schedule is unknown. B cell repopulation has to be taken into account when designing RTX retreatment schedules on RTX maintenance therapy.

P3-175

Granulomatosis with polyangitis complicated with central diabetes insipidus

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Conflict of interest: None

An 82-year-old man was admitted to our hospital with fever, otitis media, sinusitis, and diabetes insipidus. He was positive for PR3-ANCA. The results of hypertonic salt solution and desmopressin tests were consistent with central diabetes insipidus. He was diagnosed with granulomatosis with polyangiitis (GPA) and central diabetes insipidus. Treatment with high-dose glucocorticoid, rituximab, and desmopressin improved the otitis media, sinusitis, and central diabetes insipidus. He did not develop polyuria even after stopping desmopressin, suggesting that pituitary involvement of GPA caused diabetes insipidus in this patient. Pituitary dysfunction is a rare manifestation that occurs in only 1% of patients with GPA. Only 54 patients with GPA and such involvement have been described in the literature. The median age at diagnosis of pituitary dysfunction is 38.6 years and females predominate. This case report describes pituitary dysfunction in an elderly male patient with GPA.

P3-176

The pulmonary nocardiosis was discrimination difficult to the ambulatory patient of Granulomatosis with polyangiitis: A case report and review of the leterature

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Conflict of interest: None

68 old man. He was the ambulatory patient of Granulomatosis with polyangiitis (GPA). His symptm was respiratory distress and bloody sputum, pedal edema. The cause of emergency hospitalization was a low-grade fever and high value of inflammatory response. He was tested using computed tomography of emergency. It was the result of pulmonary infiltrative shadow. At late date, we wondered the alveolar hemorrhage and tested using bronchoscopy. Nocardia sp was detected in bronchoalveolar lavage fluid. Nocardia sp was treated by Imipenem/colastatin (IPM/CS) and Linezolid (LZD). Treatment period needed a half year. There was a reduction in Pulmonary infiltrative shadows and he was discharged from hospital. This experience teaches us a renewed recognition of consequence with the pulmonary nocardiosis.

P3-177

A case of granulomatosis with polyangiitis accompanied by hemophagocytic syndrome who successfully treated with rituximab

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Conflict of interest: None

A 57-year old female was admitted to our hospital due to organizing pneumonia refractory to the treatment with prednisone (0.6-1 mg/kg). She newly developed headache, nasal discharge and bleeding, and then was clinically diagnosed with granulomatosis with polyangiitis (GPA) according to the imaging findings of hypertrophic pachymeningitis and sinusitis and MPO-ANCA positivity. Despite the treatment with high dose of steroid including steroid pulse and intravenous cyclophosphamide, her rhinosinusitis and lung lesions deteriorated. In addition, she developed high grade fever with laboratory findings of liver dysfunction, high serum level of LDH and soluble IL-2R, and hyperferritinemia. CT revealed splenomegaly and hemophagocytosis was evident in bone marrow. CMV antigenemia was negative, whereas peripheral EBV-DNA slightly increased. The diagnosis of GPA was confirmed by nasal biopsy revealing necrotizing angiitis and no evidence of malignant lymphoma. Based on the diagnosis of secondary hemophagocytic syndrome (HPS) caused by GPA or by re-activation of EBV, rituximab (RTX) was introduced. RTX therapy induced remission of GPA as well as HPS. This is the first case of GPA accompanied by HPS, a rare but life-threatening complication with GPA, that was successfully treated with RTX.

P3-178

A case report suspected of large-vessel involvement in granulomatosis with polyangiitis

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Conflict of interest: None

[Case] A 38-year-old man. Nasal bleeding worsened over the course of 6 months, bloody stool, abdominal pain, and diarrhea from 1 month before. He was admitted to a doctor and colonoscopy showed aphthous colitis. The fever persisted and he was transferred to the gastroenterology unit of our university hospital under suspicion of ulcerative colitis (UC). The colonoscopy did not reveal typical findings of UC. He had swelling of the bilateral neck, cusp and root of nose, and left eyelid. Ophthalmologic examination pointed out left scleritis. Infections such as syphilis were denied. He was transferred to our department under suspicion of vasculitis because of vessel wall thickening of the internal and external carotid artery in the contrast CT, increase in CRP, and PR3-ANCA positive. From the above findings, we suspected granulomatosis with polyangiitis (GPA), giant cell arteritis (GCA), Takayasu arteritis (TAK) and relapsing polychondritis (RP). We started oral prednisolone 70 mg per day, and clinical symptoms improved promptly. We kept the possibility of TAK (Type I) in mind because it has been reported scleritis as a complication from GCA and TAK. Finally, we judged that diagnosis was large-vessel involvement in GPA since the PR3-ANCA positive cases in GCA and TAK are rare.

P3-179

A case of Granulomatosis with polyangiitis (GPA) leading to diagnosis by ocular conjunctival biopsy

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Conflict of interest: None

[Case] We describe a case of Granulomatosis with polyangiitis (GPA) leading to diagnosis by ocular conjunctival biopsy. A 73-year-old man. He was consulting respiratory department internal medicine and ophthalmology because of coughing and uncomfortable feeling of eyes. Although an abnormal shadow on chest radiograph and palpebral conjunctiva ulcer were found, the cause is unknown. We performed ocular conjunctival biopsy and identified granuloma with giant cells. This case suggests that ocular conjunctival biopsy is useful for diagnosis of GPA.

P3-180

Intestinal perforation in a patient with granulomatosis with polyangiitis

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Conflict of interest: None

A 45-year-old man presented with polyarthralgia and left chest pain, which had developed 2 months earlier. CT of the chest showed infiltrations and multiple nodules in both lung fields. He was admitted due to fever, general fatigue, hearing loss, and dyspnea. CRP was 22.78 mg/dl, creatinine was 1.07 mg/dl, and PR3-ANCA was >350 IU/ml. Granulomatosis with polyangiitis (GPA) was suspected due to cavitation of lung nodules, hearing loss, and microhematuria. Glucocorticoid pulse therapy was started followed by prednisolone (1mg/kg/day). Skin biopsy from a toe revealed leukocytoclastic vasculitis. Intravenous cyclophosphamide (IYCY) pulse therapy (500 mg/m^2) was added. On the fifth day from the admission, abdominal pain suddenly developed. On laparotomy, two perforations were found in the small intestine. Histopathological examination of the resected bowels also revealed vasculitis of medium sized arteries. After 3 doses of IVCY, renal dysfunction continued, while his hearing impairment did not recover in both ears. Intestinal perforation is a common complication in patients with vasculitis syndrome, while it is relatively rare in patients with GPA. However, we should always keep in mind that intestinal perforation can occur even in patients with GPA.

P3-181

A case of granulomatosis with polyangiitis diagnosed by surgical biopsy in which initially pulmonary infection was suspected

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Conflict of interest: None

A 68-age-old woman visited our hospital because of exertional dyspnea. She had been diagnosed as having microscoipe polyangiitis with interstitial pneumonia 4 years before admission and treated successfully with steroid and mizoribine. In September 2016, she had a fever, began to feel exertional dyspnea that gradually worsened. In February 2017, new nodular shadows were found on thoracic CT, and she was admitted to our hospital. Initially her fever appeared to respond to the treatment with antibiotics, but it occurred repeatedly and serum CRP levels stayed elevated since multiple cultures of sputa and bronchoscopiecal examination failed to identify the pathogenic microorganism, surgical lung biopsy

was performed, and granulomatosis with polyangiitis (GPA) was suspected because of existence of vasculitis with granuloma. When prednisolone was increased to 30mg/day, fever subsided and CRP became negative. We present here a suspected case of GPA with pulmonary nodules and intersitial pneumonia diagnosed by lung biopsy.

P3-182

A case of systemic lupus erythematosus complicated with MPO-ANCA-positive pauci-immune crescentic glomerulonephritis

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Conflict of interest: None

We experienced a 48-year old woman of systemic lupus erythematosus (SLE) with rapidly progressive glomerulonephritis (RPGN). At 16 years old, she had malar rash, polyarthralgia, lymphocytopenia, proteinuria, and positive antinuclear and anti-DNA antibodies (Abs) and was diagnosed as having SLE. She received steroid pulse, cyclosporine and daily oral cyclophosphamide (CPA), and then low dose of betamethasone was continued as maintenance therapy. Because fever and polyarthralgia were observed at 48 years old, daily betamethasone dose was increased. High-grade fever with CRP protein elevation (11.84 mg/dl), however, developed with anti-DNA Ab elevation. In addition, after admission to our hospital, high titer of MPO-anti-neutrophil cytoplasmic Abs (ANCA) and RPGN (Cr. 0.26 to 1.26 mg/dl) with hematuria, proteinuria and granular casts were found and a renal biopsy demonstrated pauci-immune crescent GN. For these findings, she was diagnosed as having active SLE and ANCA-associated GN overlap. She was treated with high dose of prednisolone and intravenous CPA and obtained remission. Although MPO-ANCA were sometimes observed in sera from SLE patients, pauci-immune GN in patients with SLE has been rarely reported. In the presentation, we show this case with some literature review.

P3-183

A case of microscopic polyangitis (MPA) involving temporal artery

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Conflict of interest: None

A 69-year-old male patient was admitted to our hospital, presenting with leg pain, paresthesia of the toes and dry cough in the last 4 months. He also complained of jaw claudication for 1 month. Laboratory examination showed elevated levels of serum C-reactive protein (8.76 mg/dL) and MPO-ANCA (276 U/mL). With CT scan, interstitial pneumonia was identified in the lungs. Deep tendon reflexes were attenuated in the legs, and nerve conduction study revealed axonopathy. Headache and enlargement of temporal artery were present, and high-intensity area around temporal artery was observed on gadolinium-enhanced MRI (T1). Temporal artery biopsy showed that the temporal artery was intact, but adjacent small and medium arteries had inflammatory cell infiltration, disruption of internal elastic membrane and luminal obstruction. A contrast-enhanced CT scan did not show any large vessel involvements. Diagnosed of MPA was made and prednisolone and rituximab was administrated, which resulted in remission of the disease. Clinical Significance: ANCA-associated vasculitis rarely causes similar cranial symptoms with giant cell arteritis (GCA) by implicating arteries branching from cranial large arteries. Temporal artery biopsy is considered to be useful to differentiate GCA.

P3-184

A case of microscopic polyangiitis with multiple hepatic arterial micro-aneurysms

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Conflict of interest: None

An 89-year-old woman was presented to our hospital because of a three-week history of fever and numbness in lower limbs. Laboratory studies showed elevated levels of CRP, creatinine, MPO-ANCA, and the presence of microhematuria and proteinuria. Nerve conduction studies of lower limbs revealed mononeuritis multiplex. Diagnosis of MPA was made. After admission, the patient suddenly complained of severe abdominal pain. Abdominal CT showed hepatic hemorrhage in segment 4. Hepatic angiography disclosed the extravasation and multiple micro-aneurysms. We successfully performed TAE, and initiated methylprednisolone pulse therapy, followed by oral prednisolone. One week later, sudden hemoptysis occurred. Chest CT revealed diffuse alveolar hemorrhage. Additional treatment with rituximab was administered, and remission was achieved. Hepatic aneurysm formation is very rare in MPA. Only two cases with hepatic aneurysms in MPA have been reported, one of which was died because of their ruptures. The rupture of hepatic aneurysms in MPA is rare but lethal so that should be kept in mind. Of note, induction with rituximab was effective and safe in this case although the patient was very advanced age and had life-threatening diseases, including the ruptured hepatic aneurysm.

P3-185

Coincidence of IgG4-related neuropathy and MPO-ANCA-positive microscopic polyangitis presenting polyneuropathy

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Conflict of interest: None

<Case> A 70-year-old man was admitted for polyneuropathy. He felt numbness of both lower legs, 8 months before admission. Dorsiflexion of the feet was gradually impaired. Numbness in both hands developed, 3 weeks before. On admission, livedo reticularis and hypoesthesia in bilateral lower legs was noted. Mild myasthenia was present (MMT (R/L) bi5/5, tri5/5, apb3/4, ip4/4, ham4/4, quad4/4, ant.tib1/1, gastro5/5.). Laboratory findings include ESR 84 mm/h, CRP 5.6 mg/dl, ANA×40 (H.Sp), MPO-ANCA 255 IU, and IgG4 356mg/dl. No abnormal finding was seen by chest X ray and urine analysis. A skin biopsy revealed leukocytoclastic vasculitis, leading to the diagnosis of AAV. Sural nerve biopsy, however, disclosed no fibrinoid necrosis in the blood vessels. Instead, fibrosis around the nerve and numerous plasma cells (IgG4/IgG positive cell: 55%) invasion, indicating coexistence of IgG4-related neuropathy. <Discussion> Coincidence of these two diseases suggest at least some parts of peripheral neuropathy commonly occurred in AAV are related to IgG4-RD. Recently, IgG4RD cases combined with GPA, MPA, or EGPA have been reported. Concurrence of IgG4-related neuropathy and AAV in this case is valuable for consideration of the mechanism of their neuropathy.

P3-186

A case of microscopic polyangiitis with hypertrophic pachymeningitis

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Conflict of interest: None

It is comparatively rare that microscopic polyangiitis complicating hypertrophic pachymeningitis.A 63-year old male who received treatment for MPA descrived headache and auditory disturbance. His lavoratory deta of MPO-ANCA in condition to have become negative. But, as a re-

sult of exammination of head MRI, he had a diagnosis of hypertrophic pachymeningits. He was treated for MPA and hypertrophic meningitis with the dosage of Rituximab, was going well recovered.

P3-187

Efficacy of low dose Rituximab and rapid steroid tapering in the induction therapy of microscopic polyangaitis

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Conflict of interest: None

[Objectives] The dose of rituximab (RTX) in ANCA-associated vasculitis (AAV) is commonly 375mg/m2 × 4, as well as in lymphoma. However, the optimal dose of RTX to AAV has not been established. We investigated the efficacy and safety of low-dose RTX in induction therapy of AAV. [Cases] Four consecutive patients (mean age 73) with microscopic polyangiitis (MPA) were treated for their Interstitial lung disease (3), nephritis (3) and peripheral neuropathy (1). The mean BVAS score were 9.3 at baseline. RTX 500 mg was administered × 3 in 1 patient, × 2 in 2, and 500 mg × 1 in 1. The mean initial dose of PSL was 38.3mg. One relapsed case was added RTX without increasing PSL. [Results] The average observation periods were 14.7 months. Remission had been maintained in all cases. Three patients were able to discontinue PSL within 8 months. No other immunosuppressants were used, a single administration of RTX was added in 2 cases (8 and 12 months later) for the maintenance therapy. There were no serious adverse events observed. [Conclusion] Low-dose RTX therapy for MPA seems effective, safe and cost-saving for the treatment of MPA.

P3-188

A case of optic neuritis with microscopic polyangiitis

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Conflict of interest: None

[Case] A 81-year-old woman appeared with proteinuria (±~1+) and hematuria (1+~2+) since about 5 years ago. Her proteinuria (2+) and hematuria (3+) got worse 3 months ago and urinalysis showed high level of urinary protein (3.77g/gCr) 2 months ago. She complained headache and prescribed NSAIDs for 1 month. She was diagnosed as microscopic polyangiitis (MPA) because of high MPO-ANCA (121.0U/ml). She hospitalized for kidney biopsy. Magnetic resonance imaging (MRI) showed no specific findings including hypertrophic scleritis. She gradually felt worse of headache and suddenly appeared left visual impairment on day 7. She was diagnosed with optic neuritis from the findings of vision test, flicher inspection, visual field inspection and orbital MRI. She started steroid pulse therapy and intermittent pulse intravenous cyclophosphamide therapy, and resulted to improve all of these manifestations dramatically. She discharged on day 32. Pathological finding of kidney biopsy was pauci - immune - type necrotizing glomerulonephritis. [Clinical significance] Optic nerve neuropathy is rare manifestation of MPA. In addition, it is mostly caused by hypertrophic scleritis. Optic neuritis is extremely rare presentation of visual loss associated with MPA patients.

P3-189

MPA with liver homorhage

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Conflict of interest: None

[Case] A-66-year old woman with fever and edema of legs for 2 weeks had been diagnosed cellulitis and received antibiotics for 2 weeks at the previous hospital. But the clinical manifestations didn't improve, and muscle wasting and sensory disorder appeared. On admission to our hospital, acute renal failure, proteinuria, hematuria, axonal pattern of nerve conduction studies, positive serology for MPO-ANCA was admitted. And abdominal CT revealed extravasation in the liver. Although abdominal ultarasonography revealed the suspicious findings of hepatic aneurysm, angiography wasn't performed because of kidney failure. On hospital day 2, we diagnosed the patient microscopic polyangitis (MPA) and started pulse methylprednisolone. After start of therapy, fever and glomerulonephritis improved. And liver hemorrhage became smaller. Three months after the start of therapy, lung CT scan revealed interstitial pneumonia which wasn't revealed on admission because of pleural effusion. [Discussion] The major cause of liver hemorhage and hepatic aneurysm with vasculitis is polyarteritis nodosa. In this patient, although the lacks of the biopsy and angiopraphy, we diagnosed the patient MPA because of pulmonary involvement and glomerulonephritis. We report MPA with liver homorhage which is very rare.

P3-190

Gastrocnemius muscle necrosis in microscopic polyangiitis

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Conflict of interest: Yes

A 59-year-old man presented with bilateral lower leg pain of 1 month duration. The pain was more severe in the left leg, with associated swelling of the lower aspect of the leg. No other abnormalities were detected on further physical examination. Blood tests showed C-reactive protein of 15.5 mg/dL and leukocyte count of 10.3×10^9/L (neutrophil count 8.4×10^9/L). Creatine kinase was slightly elevated at 237 IU/L. PR3-ANCA was positive with a titre of 241 U/mL. Magnetic resonance imaging showed diffuse oedema in the gastrocnemius muscle. Biopsy of the left gastrocnemius muscle revealed an infarct-like muscle necrosis with small-vessel vasculitis. No granuloma was observed. We made a diagnosis of microscopic polyangiitis. The patient was successfully treated with prednisolone 50 mg/day and intravenous cyclophosphamide, followed by methotrexate. Clinical significance: The skeletal muscle of the lower limbs can be affected by small- to medium-sized vessel vasculitis. Our case is uncommon in that the muscle biopsy revealed ischaemic infarct-like necrosis, which has been described as being rare in this disease. More cases reporting skeletal muscle vasculitis are needed to better understand the histopathologic findings in this disease.

P3-191

A case of hypertrophic pachymeningitis related with MPO-ANCA-associated vasculitis

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Conflict of interest: None

Case: 63 years old male. Chief complaint: Headache. Present illness: He was diagnosed as MPO-ANCA-associated vasculitis when he was 57 years old. When remission was maintained with 3mg/day of prednisolone and 300mg of mizoribin every other day for one year, he had a headache. Brain contrast CT showed thickening of the dural membrane from the right middle cranial fossa to the cerebellum tent, MRI revealed thickening of the meningeal membrane in the right middle cranial fossa, cerebellar tent, cerebellar hemisphere, and we diagnosed as hypertrophic pachymeningitis. Ga scintigraphy also showed abnormal accumulation consistent with the lesions. Right trigeminal neuropathy occurred, so we increased prednisolone to 55 mg/day, and it improved the symptoms and MRI image. Discussion: It is reported that ANCA-associated vasculitis developing hypertrophic pachymeningitis are often MPO-ANCA-associated GPA. It is reported that titer of ANCA increases with the onset of hypertrophic pachymeningitis. In this case, hypertrophic pachymeningitis occurred without the elevation of titer of MPO-ANCA. When headache or cranial nerve impairment occurs during the course of MPO-ANCA-associated vasculitis, even if titer of MPO-ANCA is low, we should consider the possibility of hypertrophic pachymeningitis.

P3-192

Clinical characteristics and survival in Japanese patients with microscopic polyangiitis having interstitial lung disease

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Conflict of interest: None

[Object] To analyze clinical characteristics and survival of microscopic polyangiitis (MPA) patients with interstitial lung disease (ILD). [Methods] We retrospectively investigated 124 Japanese patients with ANCA-associated vasculitis who admitted to our University hospital from 2006 through 2014. Of 124 patients, 76 (61%) were MPA. All performed chest CT for the diagnosis of ILD. We analyzed clinical characteristics, survival, and causes of death in 76 MPA patients (n =44) with and without ILD (n =32). [Results] The median age [IQR] in patients with ILD and without ILD was 71 [64-77], and 70 [59-78], respectively. The median follow-up period [IQR] was 64 [33-92] months. The frequencies of alveolar hemorrhage, and emphysema were not significantly different between the two groups. Patients with ILD had lower survival than those without ILD (P = 0.049) with 7-year survival of 58% and 85%, respectively. Out of 22 patients who died, 17 (77%) had MPA with ILD. The most common cause of death in patients with ILD was infection (31%). [Conclusions] The survival in MPA patients with ILD was lower than in those without ILD. Therapeutic strategies with less potential risk for infection and more intensive prevention for infection may improve the survival in MPA patients with ILD.

P3-193

Clinical Characteristics of Pulmonary Limited Vasculitis (PLV)

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Conflict of interest: None

[Object] To identify the clinical characterisctics of ANCA positive interstitial pneumonia (IP). [Methods] 27 subjects with ANCA positive IP diagnosed in our hospital were retrospectively studied. In patients with ANCA positive IP without any other organ involvement was defined as pulmonary limited vasculitis (PLV). We divided into two groups that developed MPA during the course (Group A) and those who did not develop MPA (Group B). The clinical characteristics, radiological findings and prognosis were compared among these two groups. In addition, physical and laboratory and radiological findings and prognosis between before and at the onset of MPA development in group A were compared. [Results] In Group A, CRP was increased at the onset of MPA development (1.9±3.6 mg/dl→6.7±5.3mg/dl P=0.002). Body weight (BW) was decreased at the onset of MPA development (57.7±12.3kg→53.4±10.6kg P=0.007). Body temperature was higher at the onset of MPA development (36.7±0.6°C→37.2±0.8°C P = 0.032). The prognosis of group A and B was not significant differences. Therefore, the prognosis in PLV was poor irrespective of MPA development. [Conclusions] ANCA-positive IP had poor prognosis regardless of MPA development. CRP and fever elevation, BW loss, may be a predictor of MPA development.

P3-194

A case of Microscopic polyangitis (MPA) as rapidly progressive glomerulonephritis (RPGN) with Certolizumab Pegl (CZP) for rheumatoid arthritis (RA)

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Conflict of interest: None

[Case] A 88-year-old man was diagnosed with RA 2 years ago. He was positive for rheumatoid factor, anti-CCP antibody, and MPO-ANCA (4.5 U/mL). His computed tomographic scanning showed mild honeycomb lung along the diaphragm. He was treated with prednisolone (PSL) and iguratimod, but so stiffness persisted, etanercept was added. His Biological agent was replaced by golimumab and CZP (200mg/4 weeks) a year ago. He was negative for serum HBs antigen, but found to be HBV-DNA positive, so treated with entecavir. Serum creatinine (Cre) level was 0.8 ~ 1.1 mg/dL. A month ago, his data got worse: serum Cre 1.4 mg/dL, urine blood (3+), urine protein (2+). His serum Cre showed 5.9 mg/dL after a month, so he was admitted as RPGN. He was found to be elevated MPO-ANCA (29.9 IU/mL). The renal biopsy showed necrotizing crescentic glomerulonephritis, so he was diagnosed with MPA. After he was treated with methylpredonisolone 500mg/day for three days, he was treated from PSL 40mg/day (0.8mg/kg), and his renal function was improved: serum Cre level was 3.6mg/dL after a month. [Clinical significance] We discuss about that onset of ANCA-associated angitis is affected by treatments with anti-tumor necrosis factor-α antibody with literature review.

P3-195

Microscopic polyangitis in an elderly patient on maintenance hemodialysis

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Conflict of interest: None

Case report: 78 year-old man admitted for high fever and weakness in the lower limb. He has been undergoing maintenance hemodialysis (HD) caused by gouty kidney disease for seven years. After initiation of HD, cognitive impairment gradually became exacerbated and then physical activity was reduced. He was diagnosed as microscopic polyangitis (MPA) with mononeuropathy multiplex and elevation of MPO-ANCA (200 EU). Because of poor physical and cognitive conditions, it was difficult to be treated with the corticosteroid therapy, and he was managed with the palliative treatment. **Summary:** The MPA patients who developed on maintenance HD have been rarely reported. We would report this case with literature review of the development of MPA on chronic HD.

P3-196

A case of idiopathic cytopenia of undetermined significance (ICUS) in the course of treatment of microscopic polyangiitis complicated with diffuse alveolar hemorrhage

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Conflict of interest: None

A 91 year old female underwent to fixation surgery of left femoral neck fracture. Four months later, she suffered from fever and hypoxemia and transferred to our hospital. Diffuse ground glass appearance were observed in X-ray and CT scan, and MPO-ANCA was positive. Microscopic polyangitis (MPA) complicated with interstitial pneumonia was diagnosed and she was treated with glucocorticoid pulse therapy. However, anemia and thrombocytopenia getting worsen, she was transferred to a tertiary care center. Bronchoscopy was performed and diffuse alveolar hemorrhage was diagnosed. She was treated with additional glucocorticoid pulse therapy, once plasmapheresis followed by prednisolone (PSL) at 30 mg/day (1 mg/kg/day) and got improvement of inflammation and pulmonary damages. However, cytopenia did not improve and transfusion was necessary. MDS was suspected and bone marrow aspiration was done. Chromosomal abnormalities of 47, XX, +8 were detected, but there is no dysplasia of marrow or peripheral cells, which led to the diagnosis of idiopathic cytopenia of undetermined significance (ICUS). Although cytopenia sustained thereafter, PSL was tapered carefully to 7 mg/day. In cases of cytopenia in elderly MPA patients, ICUS should be considered as a differential diagnosis.

P3-197

Therapeutic outcomes in patients with elderly-onset microscopic polyangitis

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Conflict of interest: None

[Object] To investigate therapeutic outcomes of the immunosuppressive therapy in patients with elderly-onset microscopic polyangitis (MPA) with regard to efficacy and adverse effects. [Methods] We retrospectively studied medical records of MPA patients with onset age of 65 or older who were admitted to our hospital between April 2016 and October 2017. [Results] Six patients were enrolled in this study (1 man and 5 women, onset age: 75.8 ± 5.7 years, BVAS: 13.3 ± 6.3). All of the patients showed upper respiratory infection-like symptoms prior to the onset of MPA with elevated levels of serum MPO-ANCA (119.3 ± 86.8 IU/L). Clinical manifestations consisted of renal involvement in 4 patients, pulmonary involvement in 3, and purpura and peripheral nerve impairment in 2 each. Oral prednisolone was used for treatment in all of the patients. Methylprednisolone pulse therapy and intravenous cyclophosphamide was performed in 5 and 1 patient, respectively. Five patients achieved complete or partial remission after treatment, but one died of infection. [Conclusions] Intensive immunosuppressive therapy should actively be considered as a potent therapeutic option requiring care of infection even in patients with elderly-onset MPA in order to avoid irreversible damage of vital organs.

P3-198

Rate of renal function deterioration in IgG4-related tubulointerstitial nephritis

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Conflict of interest: None

[Object] We investigated the renal function (RF) deterioration rate in patients (pts) with IgG4-related tubulointerstitial nephritis (IgG4-TIN), leading to clarification of the divergence of the deterioration rate of RF, identifying the factors affecting the deterioration rate, and confirming the influence of the deterioration rate on final RF. [Methods] We analyzed 18 pts with IgG4-TIN. Based on the rate of RF deterioration using estimated glomerular filtration rate (eGFR) before starting steroid therapy, we divided them into a slowly deteriorating group (Group A) (deterioration rate < 4 ml/min/1.73m^2/month) (n=8), and rapidly deteriorating one (Group B) (deterioration rate ≧ 4) (n=10), and compared various clinical features during the clinical course in them. [Results] In 7 pts, the deterioration rate of eGFR was less than 2, while in 10 pts it exceeded 4. Steroid was effective in all, and average recovery of eGFR after therapy was 17.4. In group A, recovery of eGFR was less than that in group B (6.4 vs. 26.3, P = 0.001). Hypocomplementemia was more frequent in group A than group B (P = 0.032). [Conclusions] Regarding the RF deterioration rate before therapy, there are two groups, i.e. rapidly and slowly deteriorating groups. The former shows less recovery of RF after therapy.

P3-199

A case of IgG4RD successfully treated with Azathioprine (solo)

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Conflict of interest: None

The male patient with diabetes in his seventies admitted to our hospital due to thalamic infarction. During admission, gastric cancer was discovered, and dissected by endoscopically. Since then, he was followed up by three departments (gastroenterology, neurology, and endocrinology). In 2010, when he admitted again for the control of diabetes, swelling submandibular lymph nodes was pointed out. In the same year, he noticed skin lesion in his cheek, and multiple lymphadenopathies was suspicious for malignant lymphoma. Skin lesion was biopsied and the histological findings was diagnosed to be those of IgG4RD together with high value of serum IgG4 level. His third admission in 2016 was because of recurrence of gastric cancer, pre-operative examination disclosed enlargement of pancreas head which seemed due to IgG4RD. Operative procedure was performed in success. At that time, his cheek swelling became remarkable, so we recommended treatment with Steroids, but he denied it, concerning of AE of the drugs because having diabetes. So we again proposed the therapy with solo Azathioprine. He accepted the treatment only small dose of azathioprine, which was very effective to his condition.

P3-200

Two cases of membranous nephropathy and tuburointerstitial nephritis with nephrotic syndrome and high serum IgG4 level. IgG4 related kidney disease or lupus nephritis or both?

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Conflict of interest: Yes

[Case 1] A 64-year-old female with RA and bronchial asthma admitted in our hospital because of nephrotic syndrome (NS). She presented with butterfly erythema, hypocomplementemia, hemolytic anemia, thrombocytopenia, increased serum IgG and IgG4, positive antinuclear and anti-dsDNA antibody. Renal biopsy revealed membranous nephropathy (MN) and tubulointerstitial nephritis (TIN) with infiltration of plasma cell in which an IgG4+/IgG+ ratio was 20%. We diagnosed lupus membranous nephritis with TIN and started prednisolone (PSL). She had complete remission after 6 month. [Case 2] A 73-year-old male admitted in our hospital because of NS and renal insufficiency. He presented with hypocomplementemia, increased serum IgG and IgG4, positive antinuclear and anti-dsDNA antibody, swelling of parotid and submandibular glands. MN and TIN were shown with infiltration of plasma cell in which an IgG4+/IgG+ ratio was 50%. We diagnosed IgG4 related kidney disease and started PSL. His eGFR immediately recovered. [Clinical relevance] We presented two cases of MN and TIN with NS, high serum IgG4 level, hypocomplementemia, positive antinuclear and anti-dsDNA antibody. Based on current diagnostic criteria, it is difficult to strictly distinguish IgG4 related kidney disease or lupus nephritis or both.

P3-201

Characteristics of IgG4-Related Disease with Lymphadenopathy

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Conflict of interest: None

[Object] Lymphadenopathy is a common manifestation in IgG4-related disease (IgG4-RD). We examine the characteristics of IgG4-RD with lymphadenopathy. [Methods] We analyzed 44 patients suspected of IgG4-RD. All cases underwent FDG-PET, and laboratory data were collected from their medical records retrospectively. [Results] 44 patients were divided into 3 groups (IgG4-RD with lymphadenopathy (Group A): 28, IgG4-RD without lymphadenopathy (Group B): 8, non IgG4-RD who showed abnormal accumulation of FDG in lymph nodes and high serum IgG4 levels (Group C): 8). Relapse rate after treatment was higher in Group A than in Group B. In Group A, patients who had multiple lymph node regions had higher eosinophil/leukocyte ratio, serum IgG4 levels and maximum standardized uptake value in FDG-PET than those with single lymph node lesion. In addition, Group A had a greater number of lymph node lesions and the size of lymph nodes was smaller compared to Group C. [Conclusions] In Group A, the relapse rate was higher than in

Group B. It is suggested that lymph node involvement may be related to disease activity. According to FDG-PET/CT findings, the size and distribution of lymph nodes were useful to distinguish IgG4-RD and other diseases.

P3-202

4 cases of IgG4-related disease that received Rituximab administration

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Conflict of interest: None

<Introduction> Rituximab is sometime used for patients with corticosteroid refractory IgG4-related disease (IgG4-RD). We report four cases of IgG4-RD treated with Rituximab. <Case 1> A 63 y/o man with right submandibular mass, pancreatitis, and autoimmune hemolytic anemia, and his serum IgG4 was 1,260 mg/dL. Because 30mg/day of prednisolone (PSL) was insufficient, he received rituximab treatment, then showed improvement.<Case 2> A 40 y/o woman with IgG4-Mikulicz disease (MD), showed improvement by PSL at once, however arthralgia and regaining of serum IgG4 occurred. Rituximab was administered, then symptoms were improved. <Case 3> A 30 y/o man had IgG4-MD and paranasal sinus lesion, and his serum IgG4 was 731 mg/dL. Because of poor adherence of PSL, the disease activity of IgG4-RD was not controlled, then he was administrated rituximab and showed improvement.<Case 4> A 55 y/o man presented right upper jaw mass, and his serum IgG4 was 196 mg/dL. The upper jaw mass did not respond to rituximab as well as PSL and cyclophosphamide treatment. As a result of re-examination, his diagnosis was altered to inflammatory pseudotumor. <Discussion> If the diagnosis of IgG4-RD is correct, rituximab treatment should be effective even in the severe refractory cases.

P3-203

A case of autoimmune pancreatitis complicated by splenic artery aneurysm

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Conflict of interest: Yes

A 65-year-old man was referred to our clinic with swelling of bilateral salivary glands. Serum IgG4 level was 540 mg/dl, and histopathological findings of the right submandibular gland revealed a dense lymphoplasmacytic infiltrate and storiform fibrosis with increased IgG4-positive plasma cells (IgG4/IgG ratio 67%). Contrast-enhanced computed tomography (CT) showed diffuse enlargement of the pancreas with capsule-like rim. A diagnosis of IgG4-associated sialadenitis and autoimmune pancreatitis (AIP) was made. The patient did not have any abdominal complaints and jaundice, and then he was followed by careful observation. One year later, follow-up enhanced CT identified newly formed aneurysm of splenic artery (11 mm in diameter). PET-CT images showed diffusely increased FDG uptake of pancreas. No tracer uptake was seen in the aneurysm, indicating that it was likely to be pseudoaneurysm. Coil embolization were performed for prevention of rupture of this aneurysm, and he was then started on prednisolone 70 mg/day. Clinical significance: Vascular complications in acute or chronic pancreatitis are well recognized. However, there are no published reports of AIP developing splenic artery aneurysm. We should recognize artery aneurysm as a potentially fatal complication of AIP.

P3-204

Clinical evaluation of 5 cases with IgG4-related kidney disease (IgG4-RKD) diagnosed by renal biopsy

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Conflict of interest: None

[Objectives] We report the clinical and laboratory characteristics of 5 cases with IgG4-related kidney disease (IgG4-RKD). [Methods] We retrospectively reviewed 5 cases diagnosed with IgG4-RKD by renal biopsy in our hospital between 2011 and 2017. [Patient characteristics] Among 5 cases,4 were males. Baseline characteristics of the 5 IgG4-RKD were: Age:71 years (median), Cr:0.92mg/dl, eGFR:60ml/m/1.73m^2, CystatinC:1.88mg/l, IgG:4035mg/dl, IgG4:1600mg/dl, All cases were positive upon hypocomplementemia. Among 5 cases,2 cases were positive upon Urine protein. Among 5 cases,1 case was positive upon occult hematuria. Urine β_2MG:497ng/ml, Urine NAG:9.4 IU/l, Among 5 cases,4 cases with abnormal kidney lesions that showed with echo or CT findings. Pathological findings obtained by renal biopsy revealed IgG4-RKD in all cases. All patients presented with multiple organ involvement (median:3 organs). [Result] Prednisolone (PSL) was used in 4 cases and the mean initial dose was 0.45mg/kg/day. In a case with hypophysitis and membranous nephropathy was treated with methyl-PSL pulse. One patient refused PSL treatment. After treatment, serum IgG4/IgG level and renal function improved. [Conclusion] IgG4-RKD was treated successfully with PSL in 4 cases. We report these cases with literature review for IgG4-RKD.

P3-205

To evaluate the therapeutic effect of glucocorticoid to IgG4-related vascular lesions

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Conflict of interest: None

[Object] To evaluate the therapeutic effect of prednisolone (PSL) to IgG4-related vascular lesions. [Methods] Enrolled in this study were five patients who fulfilled the Comprehensive diagnostic criteria for IgG4-RD 2011. Clinical data, computed tomographic findings, and serum IgG4 (sIgG4) level before and after treatment were retrospectively investigated. [Results] All patients were male. The average age at the diagnosis was 68.6 ± 5.9 (SD) yo. PSL were administered in all patients and average initial dose was 32.4±4.0mg/day. All arterial walls of the lesions were thickened and the average thickness decreased from 11.1 ± 3.3 mm to 8.7 ± 3.6 mm in 2 months after treatment. The improvement rate was 26.9 ± 20.0%. The average sIgG4 level was 498.6 ± 555.4 mg / dl and decreased to 294.2 ± 346.9 mg / dl in 2 months. The decrease rate was 42.9 ± 12.1%. The average length of the lesion was 108.0 ± 67.9 mm and decreased to 97.0 ± 65.9 mm in 2 months. The improvement rate was 12.4 ± 10.0%. The average width of the lesion was 40.9 ± 17.0 mm and decreased to 37.4 ± 16.7 mm in 2 months. The improvement rate was 9.8 ± 4.4%. [Conclusion] For IgG4-related vascular lesions, the arterial wall thickening and sIgG4 level may be improved soon after PSL treatment.

P3-206

A case of IgG4-related disease associated with severe olfaction disorder

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Conflict of interest: None

<Case> A 47-year-old woman developed severe olfaction disorder since August 20XX. At same time, swollen upper eyelid, which suggested

swollen lachrymal glands on MRI, was revealed. The specimens from lachrymal gland showed storiform fibrosis with IgG4-positive plasma cells infiltration, indicating IgG4-related disease (IgG4RD). PET/CT demonstrated high FDG uptake in bilateral lachrymal grands, sinonasal, nasal cavity and lymph nodes. Laboratory findings showed increased levels of serum IgG4 (206mg/dL), IgG (1346mg/dL) and IgE (1043mg/dL). We possibly considered IgG4 related nasal and sinonasal lesions, because swollen lachrymal grand and olfaction disorder appeared at same period. The specimens from swollen nasal mucosa revealed lymphoid follicle formation with IgG4-positive plasma cells infiltration. Therefore, we finally diagnosed with IgG4RD. Oral prednisolone 0.6mg/kg was initiated. Then, swollen lachrymal grand, nasal and sinonasal lesions with olfaction disorder were immediately improved. <Discussion> IgG4RD associated with nasal and sinonasal lesions have recently reported, and a half of cases possibly develop olfaction disorder. Olfaction disorder is required to treat because of leading deterioration of QOL. We discuss about pathophysiology and mechanism with literature.

P3-207

Glucocorticoid treatment of neutropenia associated with IgG4-related disease

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Conflict of interest: None

A 76-year-old woman was admitted to our hospital with high fever and neutropenia (white blood cells, 2000/μL; neutrophils, 200/μL). She had been diagnosed seven years previously with IgG4-related disease (IgG4-RD) based on bilateral lacrimal and bilateral submandibular gland enlargement, elevated IgG4, and biopsy findings, and glucocorticoid treatment had been successful. At the time of admission for febrile neutropenia, she had retroperitoneal fibrosis, a thickened pituitary stalk, and lung involvement under oral treatment with 5 mg/day of prednisolone (PSL). The cause of the neutropenia remained obscure despite a detailed physical examination, microbiological assays, imaging studies, and other laboratory testing including a bone marrow survey. Neutropenia persisted regardless of antimicrobial therapy and the discontinuation of all drugs except the 5 mg/day of PSL. Thus, we diagnosed the neutropenia as a complication of IgG4-RD and increased the PSL dose to 40 mg/day, which rapidly improved the neutropenia. Several published studies have associated neutropenia as well as various other conditions as complications of IgG4-RD. This case report describes a successful outcome of glucocorticoid treatment for neutropenia associated with IgG4-related disease.

P3-208

A case of IgG4-related disease of the unilateral urethra mimicking urethral cancer

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Conflict of interest: None

[Case] A 73-year-old man was diagnosed with left hydronephrosis by an urologist a year before admission to our hospital. Thickening of left ureteral epithelium was found by CT, which was considered to be a malignancy. He underwent left nephrectomy and ureterectomy. Pathological examination, however, revealed no malignant cells in the tissues but numerous infiltration of IgG4 positive plasma cells. As serum IgG4 was elevated (225mg/ml), this case satisfied Japanese IgG4 related disease comprehensive diagnostic criteria 2011 (Definite). Without any findings of involvement of right kidney and urethra, glucocorticoid was not employed. As serum creatinine increased gradually to 2.38 mg/dl in the next 6 months, IgG4-related nephropathy of the residual kidney was suspected. After 40 mg of PSL (0.75 mg/kg) was started, serum creatinine improved to 1.69 mg/dl. [Discussion] In IgG4 related diseases, tumorous lesions usually appear symmetrically. In case a tumor appears on only one side as this patient, we would have difficulty in distinguishing it from a malignant tumor. This rare case is important, suggesting that we should consider possible unilateral IgG4RD.

P3-209

Hyperviscosity retionopathy in a patient with IgG4-related disease

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Conflict of interest: None

A 73-year-old man was admitted to our hospital for blurred vision, serum levels of polyclonal immunoglobulin G (IgG), including IgG4 was elevated. Upper abdominal computed tomography showed a diffuse pancreatic swelling, dilatation of the main pancreatic duct, lymphadenopathy, and multiple renal nodular lesions. The funduscopic findings are soft exudates and distention or tortuosity of the retinal veins. Review of the renal biopsies with immunohistochemical staining for IgG4-positive plasma cells confirmed IgG4-related disease (IgG4-RD). The patient was administered 40 mg prednisolone daily. After treatment with a steroid, the patient showed a good clinical, biochemical response. Hyperviscosity syndrome is mainly associated with primary macroglobulinemia and multiple myeloma. However, hyperviscosity syndrome has been described in autoimmune disease such as Sjögren's syndrome and systemic lupus erythematosus. Seven published cases of hyperviscosity syndrome in IgG4-RD were reviewed, only two of those have visual disfunctions. As this case report has demonstrated, hyperviscosity syndrome should be considered in patients who present polyclonal hypergammaglobulinemia and visual disfunctions in IgG4-RD.

P3-210

Examination of the useful clinical finding for initial differentiation of EoRA and PMR

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Conflict of interest: None

[Object] The clinical manifestations of elderly onset rheumatoid arthritis (EoRA) are often accompanied by difficulty in differentiation with polymyalgia rheumatica (PMR). Of course, we know well that imaging such as MSUS and FGP-PET is very useful for the differential diagnosis of both diseases. However, they need time and expense. And then, we examined it to look for the simple and easy differential method of both diseases. [Methods] We examined 193 patients 60 years or older who were diagnosed as RA or PMR between 2014 and 2017. In those patients, the number of RA with RF (-) & ACPA (-) and PMR was 50 and 27, respectively.. We classified EoRA with ACPA (-) & RF (-) and PMR as group E and group P, and analyzed for related factors in both groups. [Results] We recognized the statically significant differences in SDAI ($p<.05$), DAS-28ESR ($p<.05$), swollen joints count (66 joints) ($p<.05$) and tenderness joints count (68joints) ($p<.05$), but we did not show significant differences in their onset age, CRP, ESR, MMP-3, HAQDI at 1st diagnosed day. [Conclusions] For the useful initial differentiation without using imaging analysis of EoRA and PMR, we recommend that we should perform the assessment of the composite measure and joint findings at their 1ST visit.

P3-211

A case of Golimumab effective seronegative arthritis with severe synovitis in biratelal ankle and subtalar joint

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Conflict of interest: None

[Object] we report our experience of golimumab responsive seronegative arthritis with severe synovitis of bilaateral ankle joint and subtalar joint, along with some literature review. [Results] A 51-year-old woman presented at our hospital with pain and swelling in right ancle that had persisted for 6 months and. Without anothor arthritis, lung lesions, renal failure, skin lesions, and hyperproteinemia, Labodate showed mild elevation in CRP and RF, ACPA, ANA are renagive. Plain ancle X-ray showed slightry erosion in lateral gutterof ankle. MRI finding showed hypertrophied synovium around ankle and subteler joint. Pathological examination showed synovitis with neutrophil infiltration. These findings suggested seronegative RA, PSL5mg/day is effective. 6 months later, biratelal ankle and subtaler sinovitis tended to increase, started MTX and effective at 14mg/w but showed progressive joint damage of ankle and subtalar. Because the sympton to exacerbation 9 months later, Golimumab started and effective. Swelling and dark redness were almost disappeared. [Discussion] Initial, The clinical and laboratory findings led to a diagnosis of seronegative RA and anti-rheumatic-drugs are effective. But sever synovium and dark redness findings led us to suspect sarcoid arthritis.

P3-212

Diagnosis of "RS3PE syndrome" Often Turns to Rheumatoid Arthritis in Daily Clinical Setting

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Conflict of interest: None

[Object] Acute-onset seronegative polyarthralgia in the elderly is often a clinical challenge for diagnosis and happens to be diagnosed correctly later in the clinical course. We reviewed the cases with peripheral edema and who fulfilled the classification of RS3PE syndrome at initial presentation to determine their final diagnosis. [Methods] Patients fulfilled the criteria by Olive for RS3PE syndrome who attended the clinic between 2009 and 2017 were evaluated retrospectively by medical chart review. [Results] Total of 15 patients fulfilled the criteria for RS3PE syndrome were evaluated. All patients were both RF and ACPA negative, and 10/15 patients were clinically diagnosed as RS3PE syndrome, whereas 6/10 patients also fulfilled the criteria for polymyalgia rheumatica by Healey, and further 5/10 fulfilled the 1987 classification for rheumatoid arthritis (RA), respectively. In 2/10 patients initially diagnosed as RS3PE syndrome, crystal-related inflammatory arthritis was detected, and 4/10 patients were finally diagnosed as RA during follow-up, applying careful monitoring by imaging studies such as ultrasound and conventional radiography. [Conclusions] Patients with initial diagnosis of "RS3PE syndrome" should be carefully monitored during follow-up to confirm the diagnosis.

P3-213

A case with RA using Biological products developed Fibromyalgia later

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Conflict of interest: None

Object A case of RA using Biorogical products could be developed to FibromyalgiaA clinical study on Fibromyalgia during follow-up observation of about 5 years using Biorogical products for rheumatoid arthritis. Case33 years old women, the other hospital diagnosed as rheumatoid arthritis (RA), Biorogical products was started to be administered. First agent is Infliximab, Secondaly Shinponi was choiceed. Because DAS 28-CRP is 5.9, this showed the RA activity could not be improved. As a result of joint pain and joint swelling showed a tendency to improve, and the DAS 28-CRP value decreased to 2.45. However, symptoms of fibromyalgia was observed. ACR Diagnosis criteria showed <WPI 10, SS 6.>, so Fibromyalgia was diagnosed. Pt's symptomatic improvement was observed as a result of useing medical drugs against fibromyalgia such as SSRI + muscle relaxant and fibromyalgia. conclusions Developing or complicating fibromyalgia in RA are considered to be less frequent. But this case of RA can be on set of FM during RA treatment usingBiological products.

P3-214

The acute pyrophosphate calcium crystal-related arthritic (pseudogout) clinical features which we diagnosed our hospital

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Conflict of interest: None

[Object] Pseudogout is an acute arthritic disorder that is common in elderly people. We assessed clinical features of patients with pseudogout in our hospital. [Methods] Patients who visited our hospital between August 2015 and October 2017 were collected. We defined the case with arthritic findings and findings calcified by an imaging study [X-ray, CT, US] or pyrophosphate calcium (CPPD) findings by an examination for synovial fluid (SF) as pseudogout. [Results] 19 males and 32 females were collected. Outpatients were 35, and inpatients were 16 patients. The mean age 89.2 years, mean CRP 11.52 mg/dl (n=41). Monoarthritis in 31, polyarthritis in 20, affected joints are; knee 38, wrist 8, cubital 8, cervical vertebrae 7, shoulder 7, ankle 4. Among 44 imaging studies, 40 had any findings suggesting pseudogout. Among 29 cases who were performed puncture of a joint, CPPD crystal was positive in 28. 20 Patients were positive for both imaging and SF. NSAIDs was used in 46, steroids joint injection in 4, oral steroids in 2, miscellaneous in 2. [Conclusions] Pseudogout is common in the area with many elderly people. Joint puncture and imaging studies were useful for diagnosis of Pseudogout.

P3-215

Study of 5 cases of relapsing polychondritis

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Conflict of interest: None

[Objectives] Relapsing polychondritis (RP) is a chronic inflammatory disease, characterized by inflammation of cartilage and joints. Mainly treated with high dose steroids, immunosuppressive drugs are also used for refractory cases. The present study aimed to clarify the clinical features of RP. [Methods] 5 cases of RP patients that admitted to our hospital from 2012 to 2017 were analyzed retrospectively. We investigated clinical characteristics and treatments. [Results] The median age of disease onset was 48±15 years old. All case had auricular symptoms. 4 cases had airway symptoms. The average of serum ferritin levels before treatment was elevated to 447 ± 416 ng/dL, especially high in cases with airway symptoms. High dose steroids were used in all cases, and MTX was combined in 3 cases with airway symptoms for initial therapy. 2 of the 4 cases with airway symptoms recurred, and one case without airway symptoms did not recur. 1 of 2 cases treated with steroids alone recurred, and 1 of 3 cases treated with steroids and MTX recurred. [Conclusions] These results indicate that elevation of serum ferritin levels is associated with presence of airway symptoms of RP. In addition, recurrence may relate to presence of airway symptoms and steroid monotherapy.

P3-216

A case of relapsing polychondritis complicated with polyarthritis, uveitis and aseptic meningitis

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Conflict of interest: None

A 67-years-old man was diagnosed as aseptic meningitis at six months before admission to our hospital. He had painful and swollen hands at 3 months after the episode and he was diagnosed as pseudo four and treated with prednisolone for 2 months. He subsequently developed visual impairment and was diagnosed as uveitis and introduced to our hospital. On physical examination, He had swollen joint on the right thumb MP and the left thumb MP and second finger PIP. He also had a deformation of his right auricle. C-reactive protein and erythrocyte sedimentation ratio were increased, but anti nuclear antibody, rheumatoid factor, anti citrullinated peptide antibody and ANCA were all negative. In imaging studies, we recognized the ground glass opacity around the right bronchus, and degeneration of atlantoaxial joint. The biopsy of his right auricle showed lymphocytic infiltration on auricular cartilage. He was diagnosed as relapsing polychondritis.

P3-217

A rare case of relapsing polychondritis associated with psoriasis vulgaris

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Conflict of interest: None

A 58-year-old Japanese male with 15 year history of psoriasis vulgaris was admitted to our hospital presenting fatigue, ear pain and eye ball pain. Physical examination revealed elevated levels of CRP (4.38mg/dL) and positive anti-type 2 collagen antibody. PET-CT showed FDG accumulation in the right ear and nose. The biopsy specimen of the auricle demonstrated a dense inflammatory mixed cell infiltration in the deep dermis over the auricular cartilage. We diagnosed him as relapsing polycondritis associated with psoriasis vulgaris. Steroid pulse therapy was administrated, followed by oral PSL 40mg daily. His symptoms were improved immediately without recurrence. Almost one-third of the cases with relapsing polycondritis had been reported to be associated with other autoimmune diseases as well as psoriasisvulgaris. However, there are few reported case with the association of relapsing polycondritis and psoriasis vulgaris. Here, we report the rare case of relapsing polychondritis associated with psoriasis vulgaris.

P3-218

Organizing pneumonia associated multicentric reticulohistocytosis: A case report

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Conflict of interest: None

[Case] A 67 year old female, who had papula and arthralgia and had diagnosed as multicentric reticulohistiocytosis (MRH) by the biopsy of the papula 17 years before, has been under good control with MTX (11mg/w) and PSL (7mg/d). She presented with cough and computed tomography (CT) of the chest showed a new consolidation with air bronchogram on the right upper lobe. We performed bronchofiberscopy and transbronchial lung biopsy (TBLB). We ruled out infecition by the finding of bronchoalveolar lavage fluid (BALF). Because the image of chest CT was not consistent with MRH, we diagnosed it as drug induced OP and increased PSL up to 17.5 mg (0.5 mg/kg/d). The consolidation improved, however TBLB showed some agglomeration of histiocytes. [Discussion] There are few case reports about MRH patient with OP. One report described a pathology of OP associated with MRH, which showed lymphoid cell infiltration and intra-alveolar organizations. In our case TBLB showed the cluster of histiocytes in intra-alveolar space, which means the association of MRH itself with OP pattern of lung infiltration. The problems is that the histiocyte like cells are not similar to the histiocytes in the biopsy of papula. It is better to confirm the histiocyte like cells are in intra-alveolar or not clearly.

P3-219

A case of TAFRO syndrome successfully treated with tocilizumab

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Conflict of interest: None

Object: TAFRO syndrome (T-syn) is a rare disorder of unknown etiology, which is often mortal with no established standard therapy. We present the case of T-syn ameliorated by tocilizumab (TCZ). Case: A 72-year-old female was referred to our hospital for leg edema and fever. Thrombocytopenia and elevated serum level of CRP were observed in the blood examination. Pleural effusion, ascites and multiple lymphadenopathies were revealed in the computed tomography. Plasma cell proliferation and angiogenesis were histologically observed in the samples of lymph node biopsy. We diagnosed her as T-syn, then initiated prednisolone (PSL) accompanied by TCZ. After that, clinical improvement was obtained and she was transferred to another hospital. 4 months later, thrombocytopenia recurred and she was readmitted. Anaphylactic reaction occurred at the fifth TCZ injection, we discontinued TCZ and increased the PSL dose. For persisting low platelet count, we tried cyclosporine or eltrombopag combined with PSL, only resulted in no remarkable effect. Discussion: T-syn is characterized by high serum level of IL-6. For this immune dysregulated disorder, TCZ may suppress the hyper-activated response. Conclusion: It is conceivable that in some cases, TCZ is effective for the steroid resistant T-syn.

P3-220

A case of TAFRO syndrome complicated with seronegative rheumatoid arthritis

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Conflict of interest: None

Case: A 78-year-old Japanese female. She was diagnosed as having rheumatoid arthritis (RA) (RF-, CCP-, stage4, class2) about thirty yeas ago and was treated with bucillamine, etanercept, abatacept and golymumab. She was admitted to our hospital because of bilateral axillary lymphadenopathy, anasarca and kidney failure. Histological examination of lymph node revealed no neoplastic proliferation or inflitration of IgG4-positive plasma cell, but germinal center atrophy and hyperplastic lymph node follicle, which was compatible with hyaline-vascular type of Castleman's disease. She was diagosed as TAFRO syndrome by 2015 classification criteria because of thrombocytopenia, pleural and peritoneal effusion, splenomegaly, myelofibrosis and elevation of serum IL-6 and ALP, followed by corticosteroid therapy. Laboratory data showed HIV-negative, HHV-8 (PCR) below detection sensitivity, anti-SS-A positive and elebation of VEGF. We report this as a rare case of TAFRO syndrome complicated with RA.

P3-221

A case of the diabetic nephropathy which was similar to TAFRO syndrome with the clinical condition of the autoimmune hepatitis

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Conflict of interest: None

[Case] An 80-year-old woman had type 1 DM. She visited our hospital for gastroenterology consultation on April 20XX. She showed elevated hepatobiliary enzyme levels as follows: AST, 700 IU/L; ALT, 483 IU/L; ALP, 2314 IU/L. After 2 months, she was referred to our department because of proteinuria, large volumes of ascites and generalized edema. Fever, generalized edema, thrombocytopenia, renal dysfunction, anemia, and lymphadenopathy led us to suspect TAFRO syndrome. Renal biopsy revealed diabetic nephropathy. Intravenous (IV) 20-mg/day furosemide did not improve the edema. IV tocilizumab 480 mg/day once every 2

weeks improved the overall bodily condition. The ascites and edema disappeared. Her AST/ALT and ALP levels decreased to 50 and 400 IU/L, Owing to repeated mild increases in AST/ALT and ALP levels even after a few days of treatment, a gastroenterology consultation was conducted. Liver biopsy revealed “possible autoimmune hepatitis.” The levels of anti-LKM-1 antibodies were high. Internal use of 15-mg/day predonine gradually improved her liver function. On the 89th day, her AST/ALT level decreased to 30 IU/L. Follow-up examinations were continued. [Conclusion] We present a rare case of diabetic nephropathy presenting with clinical symptoms of TAFRO syndrome and autoimmune hepatitis.

P3-222

A case of Haemophilus parainfluenzae septic arthritis

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Conflict of interest: None

An 84-year-old Japanese female with 15 year history of diabetes mellitus was admitted to our hospital presenting high fever and polyarthralgia. One month before admission, she had high fever and jaw pain. Subsequently, polyarthralgia of bilateral shoulder joints and knee joints occurred. PSL 5mg daily was started and her symptoms improved partially. However, elevated CRP levels continued and her symptoms relapsed. On admission, laboratory examination revealed elevated levels of CRP (4.0mg/dL). Autoantibodies including RF, ANA, ACPA, etc. were all negative. Gallium scintigraphy showed gallium accumulation in the jaw, shoulder and hip joints. Cultures of sputum specimen showed Haemophilus parainfluenzae. We diagnosed her as septic arthritis caused by Haemophilus parainfluenzae. ABPC was administrated, and her symptoms were improved immediately without relapse. There have been only few reported cases of Haemophilus parainfluenzae septic arthritis. Here, we report a case with Haemophilus parainfluenzae septic arthritis in diabetes mellitus.

P3-223

A case of bone sarcoidosis leading to diagnosis triggered by left knee pain

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Conflict of interest: None

[Case] 31-year-old man. [Main complaint] Left knee pain. [Current medical history] X-Year acknowledged from December in Year, June X visiting a near orthopedic surgery. MRI revealed multiple nodules on the left knee and CT with lymphadenopathy, so it was introduced to our department for the purpose of scrutiny. [Elapsed] Arthralgia of the left knee joint and right thumb index MP joint at the time of admission, swelling of the left cervical and supraclavicular lymph nodes, and multiple subcutaneous nodules on the bilateral upper arm extension side. Blood test revealed high accumulation of FDG in ACE, sIL-2R high value, chest X-ray with bilateral hilar lymphadenopathy, and PET-CT in upper and lower limbs including hilar and left knee multiple nodules. There was no malignant findings by aspiration cytodiagnosis of the cervical lymph node, and diagnosis was diagnosed as sarcoidosis because we obtained findings of non - bovine granuloma by subcutaneous nodule skin biopsy. Introduction of prednisolone 30 mg/day. Clinical Significance] Because sarcoidosis patients who consult with bone / joint pain of unknown origin as the main complaint exist, it is considered to be a suggestive case in considering the distinction of joint pain patients.

P3-224

Ultrasonographic findings of sarcoid arthritis -tenosynovitis of the wrist joints-

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Conflict of interest: None

<Case>A 56-year-old woman visited our hospital because of polyarthralgia and skin eruptions. Two months before, she began having finger joints pain and swollen forarm and lower legs. While these symptoms exacerbated gradually, skin eruption appeared in both legs and the trunk. As skin biopsy of the right leg revealed non-caseous granulomas, she was reffered by a dermatologist to our medical center. She was given a diagnosis of sarcoidosis according to the Japanese diagnostic standard and guideline for sarcoidosis 2015, because of skin and joints lesions and pathological findings. Ultrasonography of joints showed tenosynovitis without inflammation of the synovial membrane that lines the joint capsle. 15mg of PSL ameliorated not only arthralgia but edema in a few days. Laboratory findings include WBC 7390 /μl, Alb 3.6 g/dl, Ca 10.0 mg/dl, CRP 1.4 mg/dl, MMP-3 280 mg/ml, ACE 5.8 U/I, ANA negative, RF negative, anti-CCP antibody negative, ELISPOT negative, sIL2-R 284 U/ml. <Discussion>Sarcoidosis with arthritis at onset is often reported overseas, but is rare in Japan. There are few reports of ultrasonographic findings of sarcoid arthritis so far. This case is valuable, showing tenosynovitis predominantly of extensor muscle in the wrist joints as described in the literature.

P3-225

Ustekinumab holiday in patients with psoriasis arthritis

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Conflict of interest: None

[Object] Ustekinumab in patients with psoriatis arthritis is very efficacy. How about stopping ustekinumab after low disease activiy? [Methods] Retrospectively, we evaluated the disease activity after stopping ustekinumab under low disease activity in patients with psoriatic arthritis. [Results] We checked 4 cases. 3 cases after stopping unstekinumab is good for disease activity. Only 1 case got worse in 2 months after stopping it. [Conclusions] Stopping ustekinumab under control disease activity in patients with psoriatis arthritis is effective so far.

P3-226

A case of plaque psoriasis in which drug-induced interstitial pneumonia was exacerbated with adalimumab and secukinumab

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Conflict of interest: None

In November 20XX a 55-year-old man was diagnosed with plaque psoriasis, and ADA was started. In screening prior to the start of ADA, KL-6 was high at 725 U/ml. However, no abnormalities were seen on chest CT and so treatment with ADA was started. KL-6 gradually increased during treatment with ADA, reaching 3629 U/mL in May 20XX+4. CT findings also appeared in the right lower lobe, and ADA was discontinued in May of that year. In August, the plaque psoriasis treatment was changed to secukinumab. After the change, exacerbation of the CT manifestations were still seen in both lower lobes, and in March of 20XX+6 secukinumab was also discontinued. Reduction of the CT findings were seen after the discontinuation of secukinumab, and he was diagnosed with interstitial pneumonia associated with biological therapy.

Interstitial pneumonia is an uncommon complication of plaque psoriasis, but rare cases of pneumonia from drugs are reported. The ADA used with this patient was 0.7%, and the secukinumab was 0.04%, both of which have been reported. We thought that in this case immune balance abnormalities caused the drug-induced pneumonia. When drug-induced interstitial pneumonia occurs, there may be a risk of exacerbation even with changes to biologics that are considered to be low risk.

P3-227

Two cases of amyloidosis in collagen vascular disease patients, in which contribution of chronic Pseudomonas. aeruginosa infection for development and/or exacerbation of amyloidosis was suspected

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Conflict of interest: None

Case 1: a 64 year-old female. In 1994, she was diagnosed with rheumatoid arthritis (RA). In 2014, she was diagnosed with intestinal AA amyloidosis along with glomerulonephritis and cardiac hypertrophy. In July 2015, tocilizumab (TCZ) was started, and her RA and glomerulonephritis followed a stable course afterward. In July 2017, she developed *P. aeruginosa* pneumonia, and TCZ had to be discontinued for nearly two months, leading to progression of renal dysfunction, without apparent exacerbation of RA. Case 2: a 70 year-old female. In 2006, she was diagnosed with microscopic polyangitis (MPA). After treatment, her MPA followed a stable course with low dose steroid. However, she started to repeatedly develop *P. aeruginosa* pneumonia. Eradication of *P. aeruginosa* was difficult, and she had persistently elevated CRP, without apparent signs of MPA exacerbation. In Sept 2017, she developed heart failure, and was subsequently diagnosed with cardiac AA amyloidosis. AA amyloidosis results from chronic inflammation, and can complicate chronic infections such as tuberculosis. Our cases suggest that even when CVD's are sufficiently controlled, chronic infections, such as *P. aeruginosa* infection, that complicate them may contribute to development and/or progression of amyloidosis.

P3-228

HLA-DRB1 and DQB1 alleles in Japanese Type 1 Autoimmune Hepatitis: the predisposing role of the DR4/DR8 heterozygous genotype

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Conflict of interest: None

[Object] Autoimmune hepatitis (AIH) is a chronic progressive liver disease and shares some clinical features with systemic lupus erythematosus. Many studies including a recent genome-wide association study showed the genetic association of AIH with genes located within human leukocyte antigen (HLA) region. Here, we conducted an *HLA* association study in order to find *HLA* alleles or haplotypes predisposing or protective for Japanese AIH. [Methods]*HLA-DRB1* and *DQB1* genotyping of type 1 AIH patients and healthy controls was performed. [Results] The predisposing association of *DRB1*04:01*, *DRB1*04:05,* and *DQB1*04:01* and the protective association of *DRB1*13:02* with Japanese AIH were confirmed. An association of the DR4/DR8 heterozygous genotype with Japanese AIH was identified for the first time (P=3.12×10^{-9}, OR 3.52, 95% CI 2.34-5.29). Susceptible diplotypes were *DRB1*04:05-DQB1*04:01/DRB1*08:02-DQB1*03:02* (P=0.0004, OR 24.77, 95% CI 1.45-424.31) and *DRB1*04:05-DQB1*04:01/DRB1*08:03-DQB1*06:01* (P=1.18×10^{-6}, OR 10.64, 95% CI 3.19-35.46). [Conclusions] The important roles of specific combinations of *DRB1* and *DQB1* alleles or haplotypes in the pathogenesis of type 1 AIH were suggested.

P3-229

A case of eosinophilic fasciitis in which ultrasound was useful for diagnosis

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Conflict of interest: None

Case: A 72-year-old woman had knee flection restriction in March, and finger flexion restriction and enlargement of the palmar side of the whole upper limbs in April 2017. The symptoms gradually progressed, with 6 kg weight loss over 3 months. She was referred and admitted to our department in June. There was no joint tenderness or swelling. Orange-peel-like appearance (±) and groove sign (+) were noted. Ultrasonography showed thickening of the antebrachial fascia with blood flow signal and tendon sheath synovitis. On suspicion of eosinophilic fasciitis, contrast-enhanced magnetic resonance imaging (MRI) was performed, which showed findings consistent with fasciitis. The definite diagnosis was established with skin biopsy. She was started on prednisolone 45 mg and showed improvement, although partial sclerotic change remained. **Discussion:** Eosinophilic fasciitis is characterized by plate-like sclerotic skin with symmetrical distribution in the limbs, and joint motion restriction. MRI and biopsy are recommended to establish a definite diagnosis. Joint ultrasound has been recently used for the diagnosis of diseases such as rheumatoid arthritis. It is also likely useful for the screening of eosinophilic fasciitis.

P3-230

A case of paraneoplastic syndrome presenting pectoralis muscle pain preceding gastric carcinoma

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Conflict of interest: None

A 76-year-old woman had superficial pectoralis muscle pain, and later myalgia of the shoulder, upper arm, and femur. She had elevated C-reactive protein (CRP) level (2.65 mg/dL) but mormal creatine kinase level. Anti-ARS antibody was negative, and no malignancy was detected. Polymyalgia rheumatica (PMR) was suspected at first. The myalgia was improved with 15 mg of prednisolone (PSL), but tapering the PSL dose to < 9 mg was difficult because of recurrence. Several immunosuppressants were discontinued because of adverse effects. Biopsy of the femoris muscles revealed no specific findings such as vasculitis or myositis. The electromyogram and ultrasonogram of the joints were normal. She did not meet the diagnostic criteria for PMR or myositis. After the PSL dose was increased to 20 mg, the myalgia improved. Reevaluation for malignancy revealed, early-stage gastric cancer. The myalgia was eliminated after argon plasma coagulation (APC) for the cancer. Five months later, the cancer relapsed and myalgia recurred. However, after re-APC, the myalgia improved and only low-dose PSL was needed. Paraneoplastic syndrome was suspected. As reports of pectoralis muscle pain are rare, this case brings an awareness of the importance of repeated examination for malignancy in unidentified myalgia.

P3-231

A case of Weber-Christian disease in which myelodysplastic syndrome was suspected from bone marrow tests and which was difficult to distinguish from bone marrow failure-induced infection

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gy, Juntendo University Hospital

Conflict of interest: None

A 76-year-old man had developed fever and a mass in the right neck 4 months prior to admission, which improved with antibiotic treatment. Three weeks prior to admission he developed a fever. On admission, he had fever and swelling with pain in the right chest and around both scapulae. Although the symptoms improved after around 5 days, during 56-day subsequent hospitalization the patient again developed fever and elevated inflammatory response three times and subcutaneous swelling twice. As mild leukopenia was present, bone marrow tests were carried out, and chromosome tests revealed trisomy 8. We considered that patient to be suffering from repeated bacterial infections associated with a leukocyte functional disorder similar to MDS. However, biopsy of the subcutaneous masses revealed panniculitis with neutrophil infiltration, and because the masses appeared at the same time as the fevers, Weber-Christian disease (WCD) was diagnosed. Colchicine therapy was not insufficient effect. Steroid therapy with prednisolone was also started. There was no subsequent reappearance of the fever or mass, and the patient was discharged. We here report our treatment of a patient with trisomy 8 who repeatedly developed fever who was not diagnosed with MDS but rather with WCD.

P3-232

4 cases of rheumatoid arthritis with myelosuppression induced by methotrexate

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Conflict of interest: None

We report 4 cases of rheumatoid arthritis (RA) with severe myelosuppression induced by methotrexate (MTX). Case 1 is a 78-year-old woman with 6-year history of RA. She was prescribed MTX10mg/week. She had cytopenia (WBC600/μL, Hb9.1g/dl) on admission. Case 2 is a 76-year-old woman with 26-year history of RA. She was prescribed MTX12mg/week. She had cytopenia (WBC300/μL, Hb6.4g/dl, Plt11000/μL) on admission. Case 3 is a 76-year-old woman with 10-year history of RA. She was prescribed MTX6mg/week. She had cytopenia (WBC2000/μL, Hb6.1g/dl) on admission. 3 cases were treated with folinic acid and G-CSF. Case 2 was received blood transfusion. Cytopenia in Case 1-3 was improved after 4-10 days. Case 4 is a 68-year-old woman with 30-year history of RA. She was prescribed MTX8mg/week. She was admitted to our hospital because of a fever, pneumonia and cytopenia (WBC200/μL, Hb4.4g/dl, Plt47000/μL). She was treated with folinic acid, G-CSF and antibiotics. Her leukoenia was improved after 6 days, but pneumonia was worsened. She died after 10 days. Myelosuppression is one of important side effect of MTX. We report characteristics, clinical courses and an autopsy result in 4 cases.

P3-233

A case of rheumatoid arthritis accompanying acute myeloid leukemia

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Conflict of interest: None

A 78-year-old man diagnosed with rheumatoid arthritis (RA) ten years ago. He had been treated with methotrexate (MTX) and low dose prednisolone from that time. When the patient had taken MTX after 10 years, a blood test showed thrombocytopenia. MTX was then stopped to be administered because of suspicion that MTX induced cytopenia. However, the pletelets count was no change. Complete blood count showed a white blood cell count at 5.2×10^9/L, hemoglobin at 12.5g/dL and low pletelets at 39×10^9/L. Bone mallow examination showed myeloblast proliferation (80%) and chromosomal abnormality with trisomy 8. Therefore, He was diagnosed as acute myeloid leukemia (AML). This case is an interesting case in considering association with RA, MTX and AML.

P3-234

One case of the pancytopenia in the RA patient who experienced it in our House

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Dr. Medical Corporation Yamaguchi's Office

Conflict of interest: None

[Object] Report a case of the pancytopenia in the rheumatoid arthritis patient who experienced it in our House [Methods] It was a diagnosis with the asthmatic bronchitis not pneumonia for pneumonia of fever, a cough symptom in 69-year-old female patient MTX6mg/ week of stage-2class3 and patients in the Golimumab50mg/ moon dosage in other Houses in August, 2017 for MTX history of treatment eight years for rheumatoid arthritis onset eight years. After lightness, I gave September and MTX, Golimumab in August and quitted it among Golimumabin October and gave only MTX. [Results] Acute pancytopenia was caused and introduced me to other Houses, and Pan-cytopenia was completely relieved by folic acid supplement afterwards one week later. [Conclusions] The pancytopenia is caused for various causes, and the case to be angry at like this patient for MTX happens quite often, but it seems with a cause, and an abnormality rise of the blood concentration of MTX by the cancellation of Golimumab which is the antiTNF α antibody preparation which I used together with MTX just examines the cure for case, the for way of a case similar again including document retrieval as well as one of the past.

P3-235

A case of SLE-associated type B insulin resistance syndrome successfully treated with immunosuppressive therapy

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Conflict of interest: None

A 39-year-old female complained of general malaise. Based on chilblains like erythema, pancytopenia, hematuria, proteinuria, anti-dsDNA antibody, and hypocomplementemia, she was diagnosed with SLE, and treated with PSL 50 mg/day and MMF 1000mg/day. Although there was no history of diabetes mellitus, she showed severe hyperglycemia and treated with insulin up to 400 units/day. Based on anti-insulin receptor antibody, a diagnosis of type B insulin resistance syndrome was made. High dose insulin, oral hypoglycemic agent and liraglutide were used to lower blood glucose, and immunosuppressive therapy was continued to remit both SLE and type B insulin resistance syndrome. After TAC 1.5mg/day was added, hypocomplementemia gradually improved. Hyperglycemia also improved after 6 weeks of therapy. Finally, insulin therapy became unnecessary after 8 weeks of therapy. [Discussion] There are several reports that the type B insulin resistance syndrome is treated with corticosteroid, immunosuppressant, plasmapheresis, and rituximab. A response of this disease to immunosuppressive therapy may be associated with a response of underlying disease. So, evaluation of severity and activity of underlying disease and choice of an appropriate therapy are most important.

P3-236

Glucose intolerance in patients with rheumatic diseases during immunosuppressive therapy

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Conflict of interest: None

[Object] We performed a retrospective study to analyse risk factors affecting on rheumatic diseases about glucose intolerance. **[Methods]** We enrolled 35 patients with rheumatic diseases and divided into two groups on the basis of the value of HbA_1C (NGSP) 6.2%. **[Results]** (1) No statistical significances were observed in rheumatic disease duration; age; sex; PSL use; serum urate and triglyceride; and BMI between patients with glucose intolerance (n=14) and tolerance (n=21), but the former had longer intolerant periods (p=0.018). (2) Intolerance group was worse in

blood pressure, total cholesterol and CRP (p=0.040, p=0.004, p=0.020, respectively). (3) Multiple regression analysis by means of stepwise methods showed significant factors. (4) Higher creatinine levels correlated with between more values of BMI and worsen glucose tolerance (p=0.013). (5) Mizoribine was administered over 40% in both groups. **[Conclusions]** Glucose intolerance is supposed to affect on inflammatory processes in rheumatic diseases during immunosuppressive therapy, especially via effects on renal function as shown in the present study. In the levels of serum glucose, mizoribine without relationship in its mode of action and hydroxychloroquine with effect of decrease, would be suggested as therapeutic options.

P3-237

The correlation of the fibromyalgia activity and the parameters of rheumatoid arthritis in the RA patients with fibromyalgia

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Conflict of interest: None

[Object] We researched the factors showing correlation between the change of activity rheumatoid arthritis (RA) and of fibromyalgia (FM). [Methods] The objects were the RA patients using Biologics in Matsubara Mayflower Hospital. RA activity was accessed by RF, CRP, TJC, SJC, PtGA, PhGA, SDAI and PainVAS. FM activity were by TJC in ACR1990 FM criteria, FAS31 (ACR2010). And, we used FIM for ADL and CES-D for depression self-assessment. RA patients were assessed in 0 and 6 months both RA and FM activity. We researched the correlation between FM activity change and RA activity change. [Results] The change of TJC in ACR1990 FM criteria has correlation with the change of DAS, SDAI, TJC, PhGA, WPI, PtGA and PainVAS. These correlation coefficients were 0.496, 0.433, 0.406, 0.265, 0.228, 0.218. The change of FAS31 has correlation with the change of PtGA, CES-D, SDAI, DAS. The correlation coefficients were 0.314, 0.265, 0.238, 0.218. [Conclusions] The change of FM activity were affected by the different RA factors using ACR1990 FM criteria and ACR2010 FM criteria.

P3-238

Three cases of Pulmonary Arterial Hypertension with Connective Tissue Disease

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Conflict of interest: None

<Case 1> A 35-years-old female with MCTD, RA. After birth through two-times abortion, palpitation and dyspnea presented. She was diagnosed with SLE and pulmonary arterial hypertension (PAH), and treated with immunosuppressive therapy and pulmonary vasodilator. <Case 2> A 6-years-old female with spinal bifida. She was diagnosed with SLE in 2012, and treated with low-dose glucocorticoid and MMF after high-dose glucocorticoid and IVCY. In January, 2017, she developed fatigue and pedal edema, and she was diagnosed with PAH using echocardiography and heart catheterization study. Immunosuppressive therapy and pulmonary vasodilator were introduced. <Case 3> A 67-years-old female who was diagnosed with systematic sclerosis with digital ulcer and interstitial pneumonia. ERA was introduced because of steroid-resistant digital ulcer. She stopped taking ERA while both knees bone necrosis treatment. In April, 2017, exertional shortness of breath, slight fever presented. Then she was diagnosed with PAH and treated with Immunosuppressive therapy and pulmonary vasodilator PAH is one of the most important complications for connective tissue disease because of treatment-resistant and poor prognosis. Early diagnosis and appropriate treatment are fundamental for PAH treatment.

P3-239

A case of common variable immunodeficiency which progressed during the course of MCTD

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Conflict of interest: None

A 65-year-old woman visited our hospital in December, 2016, because of progressive decrease in IgG level. 37 years previously, she was diagnosed with malignant lymphoma. 26 years previously, she was diagnosed with MCTD. Therapy with prednisolone resulted in remission and it continued under maintenance dose of 5 mg. However, her IgG level progressively decreased and she was presented to our hospital. Serum IgG level was 398 mg/dl. Because her serum IgA level was undetectable in 2000, (IgG: 2820 mg/dl), a diagnosis of common variable immunodeficiency (CVID), which progressed from isolated IgA deficiency, was made. In June, 2017, she was admitted to our hospital because of pneumonia (IgG: 302 mg/dl). She was treated with antibiotics and intravenous IgG (400 mg/kg), with favorable response. Administration of IgG was continued every 4 weeks and IgG level is maintained over 600 mg/dl, and the patient is doing well. CVID is one of the immunodeficiency syndromes, which involves impaired B-cell differentiation. Autoimmune diseases affect about 20% of CVID and in some patients, and the autoimmunity may be found before the diagnosis of CVID. Rheumatologist should be aware of the existence of CVID which could progresses during the course of rheumatologic diseases.

P3-240

Clinical features of pneumatosis cystoides intestinalis in rheumatic diseases

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Conflict of interest: None

OBJECTIVE: Pneumatosis cystoides intestinalis (PCI) is defined as the presence of gas in the bowel wall. This unusual pathology can arise due to surgical emergencies, intestinal ischemia, and nonsurgical causes. We aimed to determine the clinical features of PCI in patients with rheumatic diseases. METHOD: This retrospective study included 18 patients (average age, 69.8 years; male, n=10) with PCI at our center between April 2011 and July 2017. RESULTS: Six, five, three, and two patients had microscopic polyangitis, rheumatoid arthritis, systemic sclerosis, and systemic lupus erythematosus or dermatomyositis/polymyositis, respectively. Among 16 patients with lung involvement, 10 and three had interstitial pneumonia and alveolar hemorrhage, respectively. Fifteen of them were treated with corticosteroid. Four patients had acute abdominal complaints such as bowel necrosis and peritonitis. Eleven out of twelve patients who were treated with a high concentration of oxygen immediately improved. CONCLUSIONS: Patients with lung complications or who are under corticosteroid therapy are more likely to develop PCI. Breathing high concentrations of oxygen might improve PCI.

P3-241

A case report of lymphoproliferative disorders (LPD) with rheumatoid arthritis (RA) suspected as bone metastasis

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Conflict of interest: None

The patient is a 72-year-old woman suffered from RA for 25 years and sustained remission by tacrolimus (TAC) 1mg/day. In addition, she was a HBV carrier and treated by TACE+RFA for developed HCC in 2013. In February 2017, liver MRI revealed high signal at the ribs and vertebra which suggested bone metastases. Added PET-CT showed FDG accumulation at the multiple bones and ileocecum. Therefore, it was diagnosed inoperable state of cecal cancer (CC) with multiple bone metastases (cStageIV). Total colonscopy revealed type 2 advanced CC, but the size was just 30mm and no metastatic symptoms such as ALP elevation and bone pain were observed. So, bone lesions were unlikely to be caused by CC. Then the rib biopsy was performed and consequently the diagnosis was marginal zone lymphoma. We thought the lesions were

LPD due to TAC and stopped the drug. The CC was restaged as cStageII and laparoscopic auxiliary ileocecal resection with lymph node dissection was performed in May. When PET-CT was reexamined in August, bone lesions mostly disappeared, and there was no finding that suspected metastasis or recurrence of CC. [Disussion] When malignant tumors are observed while using an immunosuppressant such as MTX or TAC, it is necessary to be conscious of LPD and positively perform tissue biopsy.

P3-242

A rare case of coexistence of ulcerative colitis (UC) and rheumatoid arthritis (RA), in which colitis occurred 26 years after the onset of RA

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Conflict of interest: None

A 80-year-old female who was diagnosed as having RA based on a positive result for RF and anti-CCP antibody and typical polyarthritis for 26 years. She was admitted to our hospital because of fever and severe diarrhea and bloody stools. A colonoscopy and biopsy were performed, and she was diagnosed as UC. While RA was well controlled with tacrolimus and sulfasalazopyridine, RA disease activity was exacerbated synchronously colitis. Her colitis and arthritis was successfully treated by Golimumab therapy (100mg/4weeks). UC is an autoimmune disorder of unknown etiology. The frequent association of number of autoimmune diseases in the same patient has been described. However, the coexistence of UC and RA is rare. But on the course of RA, when severe diarrhea or bloody stools was detected, colon should be examined to rule out UC. And in this case, the presence of the following should be considered: rheumatoid vasculitis; drug-induced colitis; secondary amyloidosis; and infectious colitis.

P3-243

A case of overlap syndrome (SLE, RA, Sjögren syndrome) complicated multiple bursitises in right leg

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Conflict of interest: None

Case: 72 Years female. Clinical course: She was given medication of 5mg PSL, to treat SLE, RA and Sjogren syndrome. There was no use of DMARDs or immunosupressants. One day she was aware of both legs edema, especially right leg was severe. We considered worsen of Lupes nepritis and she admitted our hospital to exam. Multiple (10 or more) cystic structures covered by capsule with a contrast effect were observed on the dorsal side from the right hip joint to the knee by contrast CT. The puncture was a yellowish white cloudy liquid. Multiple abscesses were suspected and various culture tests were repeated, but no bacterial growth was observed. There were no signs of infection such as feverpain, or any other symptoms. A surgical biopsy of the cystoid structure of lower extremity was performed, and the pathological result was bursitis. Lupes nephritis IV+V was confirmed in the renal biopsy performed at the same time, when treatment was started with PSL0.8mg/kg, tacrolimus 2mg, MMF1g, bursitis all disappeared. Clinical significance: We experienced multiple bursitis requiring time to differentiate from abscess. There are few reports of such multiple bursitis in japan and abroad, only one case was confirmed. We will report it as a valuable case.

P3-244

A case of bilateral radial fatigue fractures after left wrist arthroplasty and right wrist arthrodesis for a patient of rheumatoid arthritis

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Conflict of interest: None

Wrist arthroplasty (AP) and wrist arthrodesis (AD) are common surgeries for wrist destruction of rheumatoid arthritis (RA). We report a patient who have had radial fractures (RF) on both sides after undergoing left (L) AD and right (R) AP. An 82-year-old woman. Orange farmer. She developed RA at 62 years old. At 79, L AP was performed and at 80 R AD was performed. At 2 months after AD, a RF around the plate occurred, and bone graft and internal fixation (IF) were performed. After 5 months after IF, a RF around the plate occurred again. The fracture (F) did not heel. The surgery for radial nonunion was performed after 5 months from the fracture. The F occurred on the insertion of the pronator teres (IPT). On the other hand, a L RF occurred during the R RF treatment, and treated conservatively. We cannot get the report on bilateral RF after AP. Nagira and Ochi reported the patient who underwent a RF after the ipsilateral AP. A RF occurred at ulnar osteotomy (UO) site and they considered the causes of F are increasing load on the radius due to the UO and effect of osteoporosis due to RA. In addition to the above causes, she often carried an oranges box. It was thought that mechanical stress at the IPT was cause fatigue F. We reported a case of bilateral fatigue RF afer L AP and R AD with RA.

P3-245

Concordance rate between musculoskeletal ultrasonography findings and palpation findings in patients with Rheumatoid arthritis by rheumatic care nurse

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Conflict of interest: None

[Objective] To improve the skills of joint examination, calculating the concordance rate of palpation findings of joints and ultrasound findings. [Methods] A total of 40 patients with rheumatoid arthritis in our hospital from November 2016 to September 2017 were included. We evaluated 28 joints. The concordance rate at the joints had GS≧2/PD≧1 by ultrasound were calculated. [Results] The concordance rate of the PIP, MP, elbow joints, shoulder joints were almost good, but of the wrist joints and knee joints were worse. In the wrist joints, palpation was overestimated compared with ultrasound. On the other hand, the knee joints were underestimated. Low levels of EGA (<16; p=0.008) and PGA (<20; p=0.005) remained as independent factors and aging and joint destruction has not progressed (<stage2) remained as tendency factor (p=0.084) associated with discrepancies in wrist joints. In knee joints, the progression of joint destruction (>stage3) remained as an independent factor and complication with knee osteoarthritis (>KL grade3) remained as tendency factor (p=0.049, p=0.084). [Conclusion] To know the characteristics of the discrepancies between these two evaluation tools helps for rheumatic care nurses to improve ultrasound skills and joints examination skills.

P3-246

Examination of validity of Nurse-Visual analogue scale for RA patients in our hospital

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Conflict of interest: None

[Introduction] In EULAR Recommendation 2010, the roles of nurses is being advocated in rheumatoid arthritis. In our hospital, rheumatic care nurse (RA-NS) care of outpatients including joint ultrasound in clinical practice. [Objective] To confirm the validity of NS-VAS for patients with

RA. [Method] A total of 40 patients with RA were included. We use data on age, gender, disease duration, disease activity score (DAS28-CRP) and their components (TJC, SJC, Pt-VAS, CRP and Doctor's VAS (Dr-VAS)) and analyzed. [Result] Six males, 34 females, average age 71 years, average DAS28 2.49, mean disease duration 31 months. Pt-VAS was significantly positive correlated with age, DAS 28, SJC, CRP (all $p<0.001$), tended to TJC ($p=0.07$). NS-VAS and Dr-VAS showed significant correlation ($p<0.001$) to DAS28, SJC and CRP, but no correlation was found in TJC. Pt-VAS, Ns-VAS and Dr-VAS correlated significantly with each other, and NS-VAS and Dr-VAS showed a very strong correlation. ($p<0.0001$, $R^2 = 0.824$) [Conclusion] Doctors and nurses use objective indicators such as SJC and CRP. In addition, a very strong correlation was found between Dr (rheumatologist)-VAS and NS-VAS. RA-NS can evaluate the disease activity of RA correctly and the roles of nurses for RA will increase in the future.

P3-247

Is there any difference among drugs in difficulty of oral administration in patients with rheumatoid arthritis? - from a large cohort of rheumatoid arthritis, KURAMA study -

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Conflict of interest: None

[Object] The purpose of this study was to investigate whether there is any difference among drugs in oral administration and which factors contribute to the difficulty in patients with rheumatoid arthritis (RA). [Methods] a total of 563 patients (mean age 63.4ys, mean disease duration 12.7ys) were included. The patients were surveyed on the difficulty of oral administration as 4 categories. Also demographic, laboratory, and physical examination data on disease activity were collected. Multivariate analyses were performed for the difficulty as an objective variable, especially for methotrexate (MTX), salazosulfapyridine (SASP), bucillamine (BUC), and prednisolone (PSL). [Results] The average and standard deviation of the difficulty were 0.08 ± 0.34 in MTX, 0.13 ± 0.41 in SASP, 0.05 ± 0.21 in BUC, and 0.18 ± 0.45 in PSL, respectively, indicating that patients who took SASP and PSL felt more difficulty. Multivariate analyses showed that HAQ-DI was a significant, universal risk factor in the 4 drugs. [Conclusions] This study revealed that there is obvious differences of difficulty in oral administration. Functionally-disabled patients tend to feel difficulty in oral administration and should be particularly helped in nursing practice.

P3-248

Images of biologics in rheumatoid arthritis patients

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Conflict of interest: None

[Object] In medical treatment of rheumatoid arthritis (RA), it is necessary for healthcare persons and patients to share problem consciousness in order to use biologics smoothly based on T2T. However, it is not easy within a limited time. Therefore, we aim to clarify the problems explaining with particular emphasis. [Methods] We asked RA patients who are administered biologics in our department 1) About the effect of expected biologics 2) About self injections 3) About change of lifestyle by using biologics 4 Regarding the adverse effects of biologics, 5. Consciousness for economic impact and current RA activity. Survey was conducted using the questionnaire method of 4 grades. [Results] We extracted 31 subjects, male / female ratio was 5: 26, Regarding the effect of biologics, 25/31 (80.6%) answered "superior than csDMARDs in effect", 26/31 (83.9%) " expected to suppress joint destruction ",23/31 (74.2%)" expected improvement in life prognosis ". On the other hand, 17/30 (56.7%) "Biologics are addictive", 20/31 (64.5%)"Side effects are horrible", 22/31 (71.0%) "We must last a lifetime", 22/31 (71.0%) "too high cost of treatment". [Conclusions] When introducing biologics into patients with RA, it is necessary to fully explain that biologics is non-addictive drugs.

P3-249

Which injection device is preferred in self-administration biologics?

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Conflict of interest: None

[Object] The pen-shaped injection device comes up in addition to a conventional syringe type in self-administration biologics. The drug industry recommends a pen type, but there are the patients and the caregiver appealing for inconvenience. The ratio of used device and a choice reason were investigated. [Patients and methods] Subcutaneous injection biologics was prescribed for 78 RA patients. They chose either syringe type or pen type. Nine men and 69 women, average age was 65.3 years old. [Results] Fifty Etanercept, 28 Abatacept, and 15 syringe types, 63 pen types. There were ten dementia patients. Sixty nine patients received biologics by self-administration, and 4 patients were injected by a family, and 5 patients were injected by the caregiver except the family. Nine patients have difficulty with pen-shaped device operation, and 3 patients have difficulty to grasp syringe. They disliked pen types because invisible needle could not regulate the administration speed. [Conclusion] Because patients did not see a needle with the pen type as compared with a syringe type, anxiety was relieved and thought to be preferred. It was not necessarily right, and device choice suitable for the individual patient was necessary.

P3-250

Understanding and implementation of risk management skills for nurses in treatment for rheumatoid arthritis

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Conflict of interest: None

[Object] Biologics has led to remission of rheumatoid arthritis (RA), while serious adverse events have increased. Nurses are, therefore, required risk management skills at therapy for RA. We investigated for nurses understanding and implementation of the risk management. We compared them between two groups of nurses experienced in RA therapy (group E) and those who have not (group NE). [Methods] The subjects were nurses working at hospitals for RA care. Their understanding and implementation of risk management were examined. The tested skills included targets for RA therapy, drugs and those risks, and utilization of package inserts. [Results] Fifty-two nurses (38 in group E,14 in NE) were involved. The nurse experience was 16.8 years (mean). More than half (group E:69.5%, NE:92.1%) did not understand standard treatment protocol for RA. No understanding and implementation of "potential infection","management at the perioperative period" and "observation along the package insert" was shown in a large population in both groups. [Conclusions] Nurses did not understand the treatments protocols for RA. Risk management skills were also poorly understood and implemented in a large proportion. We need to educate nurses more about these risk management skills to provide comprehensive care for RA.

P3-251

The knowledge of Pneumocystis pneumonia in our hospital and the roles of rheumatic care nurse in rheumatoid arthritis

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Conflict of interest: None

[Objective] We investigated the knowledge of Pneumocystis pneumonia (PCP) in our hospital and examine the roles of rheumatic care nurse (RA-Ns) in rheumatoid arthritis (RA). [Method] We use the questionnaire consists of 17 items about steroids and PCP. A total of 27 doctors and 28 nurses (within 5 RA-Ns) in our hospital. Group A: doctors of internal medicine, group B: doctors of the other departments, group C: RA-Ns and group D: the other nurses were analyzed in this study. [Result] A learning rates of doctors and nurses about steroids in group A, B and C (80%) were higher than that in group D (40%). About PCP knowledge, group A and C got the higher rate than group B and D. (about 80%, 30%). Items of steroid knowledge: group D<group A, B, C (all $p < 0.05$). Among all doctors and all nurses, the less the years of experience, the more lack of knowledge ($p=0.0001$, $p=0.03$). PCP knowledge: group A > group B ($p = 0.02$), group C> group D ($p=0.013$). There was no significant difference between group A and C. RA-Ns had knowledge of PCP equal to doctors of internal medicine. [Conclusion] There are differences of the knowledge of PCP among doctors and nurses. As a rheumatic care nurse, we need to learn more about collagen vascular disease, and also to educate medical stuff carefully in our hospital.

P3-252

Report for postoperative wound healing delay with methotrexate continuous administration for rheumatoid arthritis during perioperative period in our institute, and roles and obstacles for nurse

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Conflict of interest: None

[Object] Studied about postoperative infection, and wound healing delay report, and roles and obstacles for nurse during MTX continuous administration. [Methods] During orthopedic operation perioperative period for RA, compared case of MTX withdrawal and MTX continuous administration, with medical history, medical examination data, and treatment record. Defined as infection with definition for CDC guideline (SSI). [Results] With MTX withdrawal case including A group of 54 patients (Males:4 Females:50, average age 64.7, average disease duration 21.6 years, MTX average 7.7mg/week, average steroid 1.3 mg/day), admitted infection in wounded area for one total knee replacement case, and 4 forefoot surgery cases. Wound healing delay find in one total knee replacement case, and 2 forefoot surgery cases. With MTX continuous case, including B group of 43 patients (Males:7 Females:36, average age 65, average disease duration 21.5 years, MTX average 6.7mg/ week, average steroid 2.2 mg/day), admitted no infection case, and admitted wound healing delay in one forefoot surgery case. [Conclusion] Overserved many forefoot surgeries for infection or wound healing delay cases. Because found no infection case with MTX continuous administration, postoperative infection risk increased, is considered.

P3-253

Influence of "Fri Fri Gupper" exercise on pain and psychological state in elderly patients with rheumatoid arthritis

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Conflict of interest: None

[Objective] We investigated how effective the low-intensive exercise, "Fri Fri Gupper" exercise (FGE) for joint pain, mood, and self-efficacy in patients with rheumatoid arthritis (RA). [Methods] We enrolled 23 elderly (≧ 65 years old) women with RA at low disease activity who attended our clinic. They received instruction of FGE on the first visit, and had performed it once a day at home for 2 months. The change of pain VAS, DAS28, MHAQ, self-efficacy scale, and 2-dimensional mood scale (TDMS-TS) within 2 months after the intervention were assessed. [Results] The number of painful joints and pain VAS were significantly decreased after the intervention, and TDMS-TS was significantly improved. Eleven patients performed FGE more than 45 times within 2 months, and their pain VAS was significantly decreased than the others. Eight patients continued the exercise at home for a year, and they showed improvement of their physical condition and mood. [Conclusion] FGE may be effective for elderly patients with RA to relieve pain, and lead to motivation toward treatment.

P3-254

Nutrition guidance for patients with rheumatoid arthritis; importance of regular assessment of dietary habit

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Conflict of interest: None

Background: we reported the result of nutritional survey of our 187 RA out-patients at the last JCR meeting; 39% of them are either malnourished or at nutritional risk. Patients with lower muscle mass than those of age-matched control are also prevalent. Object: Individual dietary habit should be assessed in order to find strategy to improve their nutritional status. Methods: forty-six patient nutrition guidance records and medical records were retrospectively analyzed; Mini Nutritional Assessment, dietary records, body composition, prescription for osteoporosis, and blood chemistry. Results: 46 patients (33 females) aged 40 ~ 91 Six patients were underweight, thirty-four were normal, and five were obese. Six patients reported they took only two meals per day. Eight patients did not take dairy products, and nine did not eat meat or fish on daily-base. Five patients had some difficulties in self-feeding. Patients who lacked health consciousness, or who inadequately ate main meals by taking snack-foods, were also documented. Conclusions: Practitioners, nurses, and nutritional managers should co-operate to assess the nutritional status of RA patients regularly. Individual patient education and nutrition guidance by nutrition managers are necessary to provide tailored interventions.

P3-255

Satisfaction of outpatients with rheumatoid arthritis and related factors

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Conflict of interest: None

Object: The Leeds satisfaction questionnaire (LSQ) was developed by J Hill et al. in 1992 as a satisfaction rating scale of patients with rheumatoid arthritis (RA). But there is no report using LSQ in Japan. This study was designed to examine the satisfaction in Japanese RA patients using LSQ, which was translated into Japanese and to examine the factors related with satisfaction. **Methods:** The questionnaire was mailed to each home of 401 outpatients with RA at our hospital. That was composed of three parts, attributes, Japanese LSQ, disease activity (MDHAQ-RAPID3). **Results:** 190 patients returned a valid answer. The scores of satisfaction were more than 3 points out of 6 points in all the 6 groups LSQ contains ("general satisfaction", "giving of information", "empathy with the patient", "technical quality and competence", "attitude to the patient", "access and continuity"). The highest score was "quality and competence", the least was "empathy" and then "attitude". By analysis, it shown that PTGL (a patient global assessment for global health) was the factor that most affect the satisfaction of 5 groups. **Conclusion:** 1) The satisfaction of RA outpatients is high at our hospital, but we need to improve attitude and empathy to the patient. 2) The lower the PTGL, the

more satisfied.

P3-256

Investigation of the influence of disease on daily life in patients with rheumatoid arthritis by a questionnaire survey

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Conflict of interest: None

Purpose: As early remission is achieved by T to T on rheumatoid arthritis (RA), we consider that activities of daily living (ADL) of RA patients has improved. We investigated the details of the influence on the daily lives of RA patients who participated in a public program. Methods: For RA patients who participated in the citizen public program held in Nara in 2017, We conducted an investigation about four items of “laugh” “trouble” “efforts to health” “work”. Results: Available survey data were collected from 90 RA patients. In response to “laughing”, as answers, “every day” was 4, “once in 3 days” was 4, “ there is no” and “once in a week” was 0. In response to “troubling”, answered “yes” was 43, “increased spending” was 9, “decreased friendship” 4 as contents. Response “Yes” was 17, “None” was 6 for “health initiatives”. The contents included “health gymnastics”, “diet improvement”, and “the utmost in work”. Responding to “work”, “I retired because of suffering from RA” and/or “ there was no understanding of the surroundings” was found in 37. Conclusions: Although advanced treatment has led to the high remission rate, half of RA patients suffer from problems in daily life and 40% of patients have experienced retirement without obtaining understanding of RA and surroundings.

P3-257

A case of efficacy of Esflurbiprofen for active rheumatoid arthritis evaluated the clinical course using ultrasonography

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Conflict of interest: None

[Objective] We often experience rheumatoid arthritis (RA) patients who have sever joint pain before initial treatment and can not be treat with intensive treatment due to age and hepatorenal dysfunction. We experienced a case that Esflurbiprofen was effective medication for joint pain and evaluated the clinical course using ultrasonography. [Case] A 84-year-old male had polyarthritis and diagnosed with RA. He was treated with methotrexate (MTX), but it was stopped because of hepatopathy. After he was treated with salazosulfapyridine (SASP), but it was also stopped because of eruption. His joint pain and activities of dailylife (ADL) were getting worse. He had sever pain of right wrist joint and his ADL decreased. Rheumatic care nurse performed ultrasonography and detected active synovitis in the same joint. We administered Esflurbiprofen until initial treatment. Then, his pain and quality of life (QOL) improved remarkably, and active synovitis on the ultrasonography also. [Conclusion] We experienced efficacy of Esflurbiprofen for RA patient complicated with active synovitis and improvement of QOL. Esflurbiprofen may be useful therapy until initial treatment and effective to elderly patients who had complications and residual synovitis as well as steroid injections.

P3-258

Seronegative RA with dementia in very elderly patient

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Conflict of interest: None

(P.I) She was 95-year- old women with dementia admitted our hospital for treating cerebral infarction. The joint pain moved from right foot to right hand left joint subsequently. Systemic symptoms such as fever or appetite loss appeared. CRP and MMP-3 were showed high titer, but RF, anti-CCP antibody was negative, therefore, arthritis was treated with NSAIDs. However, arthritis did not improve and so, rheumatic care nurse as a qualified ultrasonographer palpated. But due to the influence of dementia, the complaint of joint pain varies from day to day Because joint echo showed multiple active synovitis characteristic of RA in the center of the wrist joint, arthritis was diagnosed as seronegative negative RA. RA treatment started. The CRP titer was negative and the patient’s ADL and dietary mass recovered, but the complaint of joint pain was not constant, it was difficult to grasp the activity in DAS, SDAI, CDAI. Therefore, the RA treatment is continuing by follow-up joint echo. (Discussion) Due to the aging of RA patients, seronegative RA patients like this case have increased and joint echoes are an indicator of diagnosis and treatment effectiveness, so the role of a qualified ultrasonographer will become increasingly important conceivable.

P3-259

Which criteria should we use to evaluate sarcopenia accompanied by rheumatoid arthritis? - from CHIKARA study -

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Conflict of interest: None

[Object] We reported 28% patients with rheumatoid arthritis (RA) accompanies sarcopenia. This is evaluated by Asian Working Group for Sarcopenia (AWGS) criteria, whereas European Working Group on Sarcopenia in Older People (EWGSOP) criteria is commonly used in the world. We compared these two criteria. [Methods] We investigated 65 patients older than 60 years old who were enrolled in CHIKARA study to investigate the correlation between disease activity and sarcopenia prospectively. Their walk speed is evaluated whether they can cross the street within the green light. Grip strength and appendicular skeletal muscle index (ASMI) were also collected. Prevalence of sarcopenia was compared by each criteria. [Results] The prevalence of sarcopenia was 28.3% (male 29.4%, female 27.9%) by AWGS, 70.0% (male 88.2%, female 62.8%) by EWGSOP. Their correspondence wasκ=0.290 (male 0.105, female 0.373). [Conclusions] The prevalence of sarcopenia by each criteria was quite different and show low correspondence. ASMI might be based on Europeans and Americans in EWGSOP. Considering the previous reports that the prevalence of sarcopenia in RA patients was 26-48% all over the world, we should evaluate sarcopenia by AWGSOP in our country.

P3-260

Clinical study of collagen disease associated pulmonary hypertension in our department

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Conflict of interest: None

Collagen disease associated pulmonary hypertension (CTD-PH) is a certain frequency, and greatly affect life prognosis. This study retrospectively evaluated clinical background of 25 patients diagnosed from January 2007 to the present. About half of the patients with CTD-PH were SSc. SSc showed a tendency to complicate PH in systemic type, interstitial pneumonitis, anti-Scl-70 antibody positive, anti-SS-A antibody posi-

tive case. WHO class II was the most frequent in severity and 5 cases of severe cases with class III/IV observed. Although treatment contents consistent with the guidelines were generally selected, in almost all patients of SSc patients, oral PGI 2 was administered. In collagen diseases other than SSc, improvement of PH was obtained in many cases due to therapeutic intervention with pulmonary vasodilators. And also, there were cases where improvement was made without administration of pulmonary vasodilator, which was considered to be an effect of immunosuppressive therapy. In SSc, immunosuppressive therapy for PH is less effective than other collagen diseases, and further study of treatment contents is necessary in the future. It is important to study the diagnosis method for disease and examination of treatment.

P3-261

Analysis of podoplanin expression in rheumatoid synovium using novel anti-podoplanin monoclonal antibody LpMab-3

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Conflict of interest: None

[Object] Podoplanin (PDPN), a platelet aggregation-inducing factor, is a selective marker of lymphatic endothelium. PDPN expression has reported in synovial tissue of rheumatoid arthritis (RA) patients. In this study, we established a novel monoclonal antibody, LpMab-3, and compared the features to commonly used and available mAb, NZ-1 in inflammatory synovial tissues obtained from RA patients by immunohistochemical (IHC) method. [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 (WB) and flow cytometry (FCM) analyses were performed. Several glycan-deficient cell lines (Lec1, Lec2, Lec8) were used in flow cytometry analyses. IHC method was performed against RA synovial tissues using LpMab-3 and NZ-1. [Results] Reaction of LpMab-3 was lost in point mutations of 76-81 animo acid by WB and FCM analyses. Furthermore LpMab-3 did not react with Lec2 (sialic acid deficient) cell lines. LpMab-3 stained much the same as NZ-1 in IHC analysis. [Conclusions] The epitope of LpMab-3 was identified as Thr76-Glu81 of human PDPN, which is a sialylated glycopeptide. Because LpMab-3 stain PDPN much the same as NZ-1, glycosylation of Thr76-Glu81 would be preserved in RA synovial tissues.

P3-262

Early diagnosis of rheumatoid arthritis by commumity collaboration possibility of intervention at an early stage

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Conflict of interest: None

[Object] An important factor for initiating early diagnosis and treatment of rheumatoid arthritis is that doctors who have visited patients due to pain suspect rheumatoid arthritis and introduce specialists as soon as possible. Consider the benefits of patients that collaboration with neighboring hospitals and clinics creates. [Methods] From November 2016 to October 2017, patients who started diagnosis and treatment from rheumatoid arthritis were extracted among those who were introduced for suspected rheumatoid arthritis. [Results] There were 162 people who were introduced for suspected rheumatoid arthritis. Among them 59 patients diagnosed with rheumatoid arthritis and started treatment. [Conclusions] In order to treat patients who are suffering from pain for a long period of time without being diagnosed as being rheumatoid arthritis, it is necessary to call medical specialists nearby to seek medical treatment as soon as possible. We aim to achieve early diagnosis and early treatment of rheumatoid arthritis, and to improve prognosis and improve quality of life by introducing remission at an early stage according to the policy of T2T. For that purpose, cooperation with neighboring medical facilities is necessary. Present what you are currently doing as a clinic and the results.

P3-263

The examination of clinical background and the content of the consultation in rheumatoid arthritis (RA) patients taken advice from medical social worker (MSW) ~ by SWEET cohort ~

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Conflict of interest: None

[Object] We examine the relationship between their clinical background and the content which we advised the RA outpatients as MSW. [Methods] (Study 1) 98 counseling cases were divided into 4 groups by disease activity (remission (REM), low disease activity (LDA), moderate disease activity (MDA) and high disease activity (HDA)). (Study 2) 105 counseling cases about the biological drugs (Bio) were divided into 4 groups; (a) Bio-continuing (b) Bio-switching (c) Bio-starting (d) Bio-considering. In both studies, we compared the content of the consultation, patient's pain assessment by visual analogue scale (VAS), patient's global assessment by VAS and doctor's global assessment by VAS between each group. [Results] (Study 1) Most patients in MDA and HDA groups asked for psychological support. Patient's global assessment of HDA group was significantly higher compared to doctor's one. (Study 2) Most patients in b, c and d groups asked for psychological support. Their patient's global assessment was significantly higher than doctor's one. [Conclusions] MSW can support our patients based on their changing social and psychological background. In addition, early intervention in consideration of their clinical background would do a lot to support self-determination about their treatment.

P3-264

Transitional care in patients with collagen disease in our hospital

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Conflict of interest: None

[Objective] As many children with chronic diseases have come to reach adulthood with the aid of advance in treatment, smooth transitional care from pediatrics department to department of internal medicine has become increasingly important. Here we investigated the current status of transitional care in our hospital. [Methods] We collected the data of demographic feature, treatment and clinical course from patients with rheumatic diseases who made the transition from pediatric department to our department from Mar., 2015 to Aug., 2017. [Results] The age of onset is younger and the disease duration is longer in the patients who made the transition as compared to the other. Smaller dose of glucocorticoid and/or larger amount of immunosuppressants tended to be prescribed to the patients after transition as compared to pre-transition. Their disease conditions were almost stable, although one patient discontinued to visit our hospital. [Conclusions] Since patients who need transitional care have been increasing, it is important to reinforce cooperation between pediatricians and physicians to make transitional care trouble-free.

P3-265

Medical partnership for patients with rheumatoid arthritis at a local core hospital in the central area of Nagasaki Prefecture

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Conflict of interest: None

[Background] Because there are few rheumatologists to the population in the central area of Nagasaki Prefecture, and many patients need long-distance hospital visit, a burden arose in both doctors and patients. Rheumatologists alone were not able to provide sufficient medical care, then, we encouraged family physicians to start medical partnership for patients with RA. [Methods] We performed prior questionnaire survey about DMARDs and biologics toward introduced medical institutions. The partnership was applied to cases of low disease activity or remission after introduction of RA treatment in our hospital. As a general rule, the patients treated with MTX or biologics were changed to double follow-up. [Results] From November 2014 to May 2017, 80 institutions participated in RA medical partnership and the number of double follow-up reached about 80 patients. RA disease activity was controlled even after the start of the partnership by maintaining structural and functional remission at the majority. In the questionnaire survey of patients at 2.5 years after the partnership started, approximately 75% of patients were satisfied and hoped to continue the RA medical partnership. [Conclusions] RA medical partnership in local area lacking rheumatologists is the most important and useful.

P3-266

Medication adherence and understanding level of side effects of methotrexate based on 245 patients surveys

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Conflict of interest: None

Purpose: Methotrexate (hereinafter referred to as "MTX") has many serious side effects. It is important for patients to follow the dosage and usage instructions and have a proper understanding of side effects. Because few researches have conducted, we did survey in this pharmacy which accepts prescriptions from Rheumatologists to study medication adherence and understanding level of MTX. **Method:** The subjects of the survey are patients taking MTX who came to the pharmacy in Aug. and Sep. 2017. They filled in questionnaires while they waited for their medications. **Result and Discussion:** Total 269 patients were agreed to fill-in the questionnaires, and 245 (91%) were valid. Patients under 30s tend to forget taking MTX, but the tendency falls as age rise. 90% of the patients answered that they understood necessity of MTX, but only 70% were satisfied with it. 44% experienced some side effects. If they have some symptoms suspected pneumonitis or hemopathy, 40% keep their medications without consultation of doctor or are not sure to stop MTX. As their condition changes, patients over 70s tend to have difficulty to make the decision if they stop MTX. It is important for patients to understand side effects and proper approachs in order to improve medication adherence and satisfaction.

P3-267

Efficacy of Educating Visiting Pharmacists Regarding Drug Administration for Patients with Rheumatoid Arthritis Who Poorly Adhere to Treatment Regimens

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Conflict of interest: None

[Object]: Patients with rheumatoid arthritis (RA) need to take lifelong oral or injectable medication to alleviate their symptoms and prevent disease progression. However, some patients may not adhere or poorly adhere to treatment and have poor understanding of medication. This study aimed at determining the effect of educating visiting pharmacists regarding administration of medication for patients with RA who poorly adhere to treatment regimens. [Methods]: A prospective analysis was performed by enrolling 19 patients with RA who were treated with different types of medication. DAS28-ESR, SDAI and CDAI as markers of RA disease activity were evaluated just before and after the pharmacist visit. [Results]: The Mean ± SD values of DAS28-ESR, SDAI, and CDAI just before and after the pharmacist visit showed improvements; they were 3.56 ± 1.46 and 3.12 ± 1.16 ($p = 0.084$), 7.99 ± 6.88 and 4.39 ± 3.47 ($p = 0.0176$), and 6.85 ± 5.74 and 3.90 ± 3.18 ($p = 0.0148$). [Conclusion]: Adherence to treatment in patients with RA may decline with increasing age. For such patients, education of visiting pharmacists oral and injectable medication may be useful in controlling RA activity and avoiding any adverse effects due to consumption of wrong medication.

P3-268

Appeal to free medical expenses for patients with highly active rheumatoid arthritis patients treated with biologic agents

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Conflict of interest: None

[OBJECTIVE] Goal for the treatment of rheumatoid arthritis (RA) is remission. Early RA has the time of therapeutic window, they have possibilities to aim for cure. Biological agents (bio) brought breakthroughs in the treatment of RA, but the economic burden is heavy. There are many highly active patients who have to treat by bio can not be introduced because of heavy burden within the period of therapeutic window. [METHODS] 50 cases consecutive high activity RA were followed for 5 years. We compaired the rate of self burdens (RSB) and using-bio percentage. We investigated the social resources they were using. [Results] In RSB>=0.3 group, 30% of patients had been treated with bio. In RSB<=1 group, 45% of patients had been treated with bio. In the social resources, livelihood protection and late elderly insurance were abundant, but specific diseases insurance and disabilities insurance were few. There were three users of the free low-cost system (Muteisin). [CONCLUSION] Bio develops in the treatment of RA and the outcome was dramatically improved. However, there are cases who can not bear the burden of self and can not be used. In cases of early RA, young onset, and RA patients who can not use MTX these patients when including bio for RA treatment should be relieve medical burden.

P3-269

A case of administering Abatacept after MTX-related lymphoproliferative disorder in patient with Rheumatoid Arthritis

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Conflict of interest: None

[Case] A 69-year-old woman. Stage 2 class 1. RA onset was 5 years ago. RA control was good with MTX 14 mg/week, tacrolimus (TAC) 0.5 mg/day. Dyspnea occurred, in the CT image 4 mm in diameter mass was found in the right lower lobe, and the right main bronchus was squeezed. Another tumor was found also in the adrenal glands. In the PET-CT image, multiple masses were found in the liver. Due to eating disorder, MTX and TAC were stopped on her judgment. Although pulmonary biopsy was performed several times, confirmed diagnosis was impossible with necrotic tissue alone. Two months later, CD20 positive cells suspected of B cell lymphoma were confirmed diffusely, and EBER-ISH was negative. In the CT image at the same period, all the tumor masses were shrinking. After 3 months arthralgia was appeared, Abatacept (ABT) 125 mg/week subcutaneous injection and TAC 0.5 mg/day were started. After 1 year, pneumonia developed and TAC was discontinued. After 1 year and 6 months from administering ABT, RA control was good and no lymphoma recurrence was observed. [Discussion] Currently there is no definite view on RA treatment after discontinuing MTX after MTX-LPD. ABT might be advantageous in that it has no CDC and ADCC activity

and is less likely to affect B cells.

P3-270

Case Report: Erdheim-Chester Disease after the treatment of breast cancer

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Conflict of interest: None

[Case] 45y.o. female [Complain] Dystopia, Diminished eyesight [Past history] Breast cander. Breast conservative surgery, chemotherapy, Hormpne therapy. [Present history] She visited a clinic for dystopia, and was founded choroidal tumor of the bilateral eyes. Suspected of the metastasis of breast cancer, she took whole body examination. No sign of metastasisi was founded but she had the wall thickening of Aorta, bilateral hydronephrosis, bilateral adrenal swelling. She was consulted to our hospital suspected of IgG4 related disease. [Labo Data] CRP0.73mg/dl, ESR20mm/hr, IgG1345mg/dl, IgG4 23.4mg/dl, sIL-2R1160mg/dl, HLA-B51positive. [Clinical Course] The symptoms progressed gradually, data showed gradual elevation of CRP and sIL-2R, and the thickness of Aortic wall was increased. At 46y.o. She complained of knee pain. X-ray and MRI of her knees showed osteosclerotic and osteolytic lesion in bilateral tibia with strong uptake in FDG-PET. Cardinal effusion was increased and dyspnea occurred at the same time, we performed pericardial drainage and then open biopsy of her tibia. Histolgical finding of the bone reported the infiltration by foamy histiocytes and fibrosis consistent with Erdheim-Chester disease. [Conclusion] We experienced a rare case of EDC.

P3-271

A Case of Weber-Christian Disease recurrence, reducing dose of calcineurin inhibitor

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Conflict of interest: None

[Case] 37year-old woman [Chief complaint] fever, subcutaneous nodules [Current history] She was diagnosed Weber-Christian disease at 8 years old. She took PSL, Cyclosporine (CyA) 150mg. 18 years ago, she was depressed and interrupted her medicine. Then she had fever, nodular again. We increased CyA 150mg, and improved her symptoms. 14 and 7 years ago she was recurrenced and increased PSL, CyA 150mg and was improved. After she married, she wanted to get pregnant. So she hoped to reduce her medicine. Then we decreased them for 2 years. In X year, she was taking PSL 5mg, CyA 50mg. However she recurrenced and was hospitalized. [Clinical progress] The rise of fever, LDH, ferritin, abdominal CT showed the inflammation of the mesentery. she was increased to PSL 20mg, however her serum deta was getting worse. Then we increased CyA to 150mg. As a result we confirmed improvements of her serum deta. [Discussion] Weber-Christian disease, in Japan, 164 reports from 1986 to 2003. There is no feature in the serological examination. Although the PSL treatment is effective, there are reports CyA is effective in the case of PSL resistance. In our case, there was a recurrence during CyA reduceing, we considered the increaseing CyA is effective in this disease.

P3-272

Case of pyogenic coxitis with suspected joint cleavages induced by acetabular bone hyperplastic changes with ectopic ossification

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Conflict of interest: None

Case of pyogenic coxitis with suspected joint cleavages induced by acetabular bone hyperplastic changes with ectopic ossification was experienced, so We report it. Patient: 65-year old male The patient presented with fever of around 40ºC, vomiting and diarrhea on February 11, 20XX. The following day a local doctor diagnosed him with viral enteritis. His symptoms persisted, and the next morning he experienced impaired consciousness caused by polyarthralgia. He arrived by ambulance at this hospital with septic shock-induced disseminated intravascular coagulation (DIC). Although tests did not elucidate the cause of infection, a catheter tip laboratory culture test done during March detected MRSA. The patient continued to relapse with fever and concomitant polyarthralgia if he stopped taking antimicrobial drugs; he was referred to this department on May 8 for careful examination of the symptoms' causes. An examination revealed severe pain in his right hip joint, while an x-ray showed ectopic ossification around both hip joints, and an MRI confirmed fluid accumulation in his right hip joint and brightness variation in the proximal femur. A right hip joint puncture and detected MRSA resulted in a diagnosis of pyogenic coxitis accompanied by osteomyelitis of the femur.

P3-273

Rheumatoid arthritis combined with optic neuromyelitis: a case report

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Conflict of interest: None

<Case> A 50-year-old female presented with atopic dermatitis and cataract. On May 17, she was admitted to the ophthalmology with a chief complaint of decrease in visual acuity of the right eye. Because MRI showed optic nerve atrophy and blood test showed a hyperinflammatory response, she was suspected of having an autoimmune disease. So she was admitted to our department. Anti-AQP4 antibody positive, MRI revealed spinal cord lesions of more than 3 vertebral bodies extending, leading to diagnosis of optic neuromyelitis (NMO). In addition, we confirmed swan-neck deformities of the fingers and ulnar side deviation; on examination, both RF and ACPA were negative, but synovitis of some joints was indicated; MRI showed that bone marrow edema in the wrist joint and annular axial vertebrae dislocation in the cervical region suggested the presence of rheumatoid arthritis. She was administered 5 cycles of plasma exchange therapy after one course of steroid pulse therapy and then continued on oral administration of prednisolone 20 mg/day for NMO. <Conclusion> A case report on the presence of systemic lupus erythematosus with NMO has previously been published, but no report of RA with NMO has been published. Thus, to the best of our knowledge, this is the first report on this condition.

P3-274

A case of rheumatoid arthritis that onset with atlantoaxial synovitis

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Conflict of interest: None

[Objective] I report a case of rheumatoid arthritis (RA) that onset with atlantoaxial synovitis. [Case] A 69-year old female. There is nothing particular in past medical history. With left upper leg pain, she visited our hospital. Her X - ray of cervical spine showed atlantoaxial joint subluxation and instability. In the blood test, rheumatoid factor was negative, ACPA was negative, no inflammatory finding was observed. MRI showed joint effusion in the atlantoaxial joint, and synovitis was suspected. However, there were no symptoms of peripheral arthritis, and no bone erosion were observed in X- ray of hands. We observed as unkwnon synovitis of atlantoaxial. Five years later, she visited our hospital with right thumb pain. X - ray revealed bone erosion in the hands. In the blood test, ACPA was negative, but rheumatoid factor was increasing. She was diagnosed as RA. [Dicussion] AAS associated with RA most often develops in more than a few years after onset of RA. In this case, we assumed that before

peripheral arthritis, AAS developed due to atlantoaxial synovitis by RA. [Conclusions] We reported a case of AAS preceding RA. When diagnosing AAS without a history of underlying diseases or trauma, it is necessary to follow a patient with careful attention to RA onset.

Luncheon Seminar

LS1-1

Pathophysiology of Spondyloarthritis: the role of IL-17A in inflammation, enthesitis, and new bone formation

Dirk Elewaut
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Conflict of interest: Yes

Enthesitis is a hallmark of spondyloarthritis. Despite this, relatively little is known about the immunobiology of enthesitis. The enthesis is composed of stromal cells, tendon structures and a rare population of innate like T cells composed primarily of gamma delta T cells. Curiously, these rare cells respond vividly to IL-23 by secreting IL-17A, IL-22 and other inflammatory mediators leading to enthesitis. It should be noted that there may be other means how enthesitis occurs including by tissue resident cells. The overall immunobiology of enthesitis will be discussed with special emphasis on IL-17A as a key driver of inflammation and tissue remodeling.

LS1-2

Current practice of spondyloarthritis

Hideto Kameda
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Conflict of interest: Yes

Spondyloarthritis (SpA) is a disease category characterized by axial joint inflammation and the association with HLA-B27, which includes ankylosing spondylitis (AS) and psoriatic arthritis (PsA). The concept of non-radiographic axial SpA, which may be partly the early phase of AS, and the concept of treat to target (T2T) have been prevailing. Enthesitis is the primary pathophysiological disorder in SpA, in which various immune cells and cytokines such as interleukin (IL)-22, 23, 17 and tumor necrosis factor (TNF) produced from those cells play important roles in the pathogenesis of SpA. Molecular targeted therapies against those cytokines demonstrated the exciting efficacy and effectiveness, and thus the importance of early diagnosis and therapeutic intervention was well acknowledged. For early diagnosis of SpA, ultrasound examination is convenient and useful for peripheral arthritis, while magnetic resonance imaging (MRI) is usually required for the detection of axial joint diseases. SpA commonly involves cutaneous, ocular and gastrointestinal lesions, and therefore, medical cooporation among, at least, the divisions/departments of Rheumatology, Orthopedic surgery, Dermatology, Ophthalmology and Gastroenterology is mandatory.

LS2

Novel strategy for the treatment of rheumatoid arthritis

Sakae Tanaka
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Conflict of interest: Yes

Rheumatoid arthritis (RA) is a systemic disorder characterized by inflammatory synovitis, which results in massive joint destruction. RA patients are frequently associated with osteoporosis. The osteoporosis in RA patients exhibits a combined pathology of local periarticular osteoporosis and general osteoporosis. Periarticular osteoporosis is caused by the excessive bone resorption caused by inflammatory cytokines. General osteoporosis is caused by the cytokine-induced inflammation, but it is also related to the steroid usage, immobility and vitamin D deficiency. Antirheumatic drugs including biological agents are not enough to recover the reduced bone mineral density (BMD) or reduce fragility fractures in RA patients. Recent studies have indicated the critical involvement of osteoclasts in bone destruction in RA. The osteoclast differentiation factor receptor activator of NF-κB ligand (RANKL), which belongs to the tumor necrosis factor-α superfamily, plays a critical role in osteoclast differentiation and bone destruction in RA. Denosumab, an antibody against human RANKL, efficiently suppressed the progression of bone erosion in

RA patients in a randomized controlled study, and is considered as a putative therapeutic option for preventing bone destruction in RA. However, denosumab did not affect the inflammation of RA, and therefore, combination of anti-rheumatic drugs and anti-osteoporosis drugs are required to treat osteoporosis in RA patients.

LS3

Development of etanercept biosimilar

Hiroaki Matsuno
Matsuno Clinic for Rheumatic Diseases

Conflict of interest: Yes

We conducted a phase 3 study of etanercept biosimilar (ETN-BS) in Japan and the Republic of Korea (ROK). When ETN-BS was compared with original etanercept (ETN-OR) in a phase 1 study, the total area under the curve (AUCt: 90% confidence interval [CI], 0.87 to 1.06) and maximum drug concentration (Cmax: 0.92 to 1.13) were within the acceptable range of equivalence (0.80 to 1.25). To unify study conditions between the two countries, the maximum dose of methotrexate (MTX) was set at 16 mg/week; however, in the ROK, as only 2.5 mg MTX tablets were available, the maximum dose was set at 15 mg/week. The primary endpoint was change in Disease Activity Score 28-Erythrocyte Sedimentation Rate (DAS-ESR) at week 24 after start of treatment. In the ROK, these drugs are evaluated based on the core data set of the American College of Rheumatology, and DAS28-ESR is not generally used. Therefore, we distributed educational DVDs in Korean to participating facilities and unified the evaluation method. We determined the acceptable range of comparability with ETN-OR as -0.6 to 0.6, because the European League against Rheumatism criteria state that a change > 0.6 in DAS28-ESR is clinically relevant. The target sample size was calculated backward from this acceptable range, using a simulation. Thus, the success rate of the study would be 90% or higher when the two-sided 95% CI of the between-group difference and the point estimate of the difference between the Japanese and Korean groups was within the acceptable range of equivalence. A comparative study of 296 patents (148 in each group) would be needed to confirm comparability using DAS28-ESR. Based on a predicted drop rate of 20%, a double-blind study protocol with 372 patients was submitted to the PMDA and eventually approved. The numbers of patients in the primary efficacy analysis set at week 24 were 164 in the ETN-BS group and 165 in the ETN-OR group. The changes in DAS28-ESR were -3.009 (95% CI, -3.198 to -2.820) for ETN-BS and -2.859 (-3.05 to -2.667) for ETN-OR, and the between-group difference was -0.150 (-0.377 to 0.078). As this was within the acceptable range of equivalence, the comparability of the 2 biologics was demonstrated. In addition, the incidence of all adverse reactions during the study period was 51.3% in the ETN-BS group and 62.0% in the ETN-OR group. Furthermore, the frequency of anti-drug antibody generation in the ETN-BS group did not exceed that in the ETN-OR group. Thus, we believe that ETN-BS can be used for RA therapy.

LS4-1

Efficacy and safety of iguratimod in daily clinical practice of rheumatoid arthritis

Nobunori Takahashi
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Conflict of interest: Yes

There has been great progress in the treatment strategy of rheumatoid arthritis (RA). Methotrexate (MTX) and molecular target drugs (biologics and JAK inhibitors) play the pivotal role in the modern RA treatment. Primary treatment target in RA should be the clinical remission and it can be achieved by using these drugs in major proportion of patients. However, some patients who cannot use these drugs because of some comorbidities or economic problems are quite difficult to achieve the remission. In that cases, we may have to lower the treatment goal to low disease activity. Conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) including iguratimod (IGT) are playing very important role in those who are difficult to be applied the modern treatment strategy. Tsurumai Biologics Communication Registry (TBCR) are established to register the RA patients treated with biologics. Patients treated with recently developed csDMARDs (IGT and JAK inhibitors) are also registered in the TBCR-plus system and clinical outcomes are evaluated. We already reported some results obtained from the IGT cohort in the TBCR-plus. The predictive factors for achieving LDA at 24 weeks (Modern Rheumatology). IGT is effective even in the patients with low dose MTX (JCR 2014). IGT effectively improved the power doppler signal of joint ultrasonography (JCR 2016). We still have some patient population who are contra-indication for modern RA treatment strategy (MTX or molecular target drugs). In those patients, it is often difficult to achieve the clinical remission as a primary treatment target. Even in those difficult cases, we the specialists of RA treatment have to make a maximal effort to achieve at least low disease activity by using the alternative treatment options. In this paper, we would like to demonstrate the potential efficacy of iguratimod in the patients treated without modern strategy.

LS4-2

What is good clinical practice with high patient satisfaction using ultrasound examination?

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Conflict of interest: None

I will consider an ideal clinical practice with high patient satisfaction. Good communication with the doctor in charge and having a relationship of trust, doing joint palpation every time, to be decided after adequately consulting and convincing treatment medicine and policy, make yourself understand the condition and treatment, the disease is stable, there is no pain and it is not inconvenient in daily life, there is little worry about drug side effects, treatment expenses not too high, to be able to see diseases and complications other than arthritis. It is thought that polite efforts and practices to these various matters will contribute to medical treatment with high patient satisfaction. Ultrasound examination is also a useful imaging diagnostic tool that plays a part. A questionnaire was given to 100 patients after joint ultrasound examination. 1. Is it easier to understand than verbal explanation? 2. Has your understanding of joints or medical conditions deeper than before? 3. Did you reduce the anxiety about symptoms and diseases? 4. Do you think it is useful or necessary examination? 5. Did it help in communicating with your doctor? 6. Do you choose a hospital that you can do rather than a hospital that you can not do? 7. Do you want to do it again in the future? The majority answered as, I think so · I think so very much. In the elderly, with point of care ultrasonography (POCUS), there was a tendency to be more satisfied. Ultrasound examination improves patient understanding, not only by the benefit from doctor's side, such as lesion detection sensitivity and high accuracy, but also by utilizing picture superiority effect (PSE), you can see that it helps for medical treatment with high satisfaction. I would like to present and consider a medical treatment plan that utilize ultrasound examination and increases patient satisfaction.

LS5-1

The role of surgical treatment in sustaining remission of RA

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Conflict of interest: Yes

Major goal of the treatment in RA is obtaining both clinical and structural remission, preventing consequent physical disorders, and improving vital prognosis. In fact, owing to the progress of medical treatment, lifetime of RA patients is expanding, and the demanding levels toward functional and cosmetic outcome is increasing. However, in clinical practice, progression of joint destruction is still frequently observed, due to insufficient medication because of aging, various complications, or economic burden. In addition, even in patients who obtained clinical remission assessed by composite measures, delay of obtaining clinical remission or remaining synovitis of small joints which is not always reflected in laboratory tests, leads to joint destruction. It has been reported that synovectomy is decreasing and duration of disease till undergoing

total knee or hip arthroplasty is expanding. However, due to extended lifetime and improvement of activity levels of RA, these arthroplasties due to osteoarthritis change may increase as well as non RA populations in the future. On the other hand, there is increase in hand and foot arthroplasty, may be due to high frequency of remaining synovitis and soft tissue fragility caused by glucocorticoid in these small joints, high demands of cosmetic and functional outcomes, and improvement of operative procedures. This lecture aims to share the up-to-date information about limitation of present medication and tendency of joint destruction, and improvement of recent operative procedures, which may lead to the optimization of RA treatment.

LS5-2

Current issues of Treatment for Induction and Maintenance of Remission and Low disease activity in RA

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Conflict of interest: None

The initial goal on the treatment of rheumatoid arthritis (RA) is to induce remission. In order to achieve the induction of remission, treatment strategies using various agents including csDMARDs, tsDMARDs, boDMARDs, and bsDMARDs have become established. Especially, it could be widely recognized that bDMARDs treatment had changed the life of many rheumatologists as well as that of 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 revised in 2016, the recommendation 2 indicated that "Treatment should be aimed at reaching a target of sustained remission or low disease activity in each patient". Additionally, the treatment strategy after achievement of sustained remission is included as tapering of csDMARDs or bDMARDs. To achieve this goal, methotrexate (MTX) is used as initial treatment in RA. Based on the treat-to-target strategy, bDMARDs treatment is considered in cases response insufficient to MTX therapy. 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 treatment with bDMARDs becomes an important issue. The treatment strategy for RA patients of child bearing age or having some comorbidities is another 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 outcomes of RA patients throughout considering the optimal treatment strategies.

LS6-1

Update on Treatment of Lupus Nephritis

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Conflict of interest: None

For the management of adult and pediatric lupus nephritis (LN), Joint European League Against Rheumatism and European Renal Association-European Dialysis and Transplant Association (EULAR/ERA-EDTA) have recommended that immunosuppressive treatment should be guided by renal biopsy, and aiming for complete renal response (proteinuria <0.5 g/24 h with normal or near-normal renal function). Hydroxychloroquine is recommended for all patients with LN. Because of a more favorable efficacy/toxicity ratio, as initial treatment for patients with class III-IV (A) or (A/C) (±V) LN according to the International Society of Nephrology/Renal Pathology Society 2003 classification, mycophenolic acid (MPA) or low-dose intravenous cyclophosphamide (CY) in combination with glucocorticoids is recommended. In patients with adverse clinical or histological features, CY can be prescribed at higher doses, while azathioprine is an alternative for milder cases. For pure class V LN with nephrotic-range proteinuria, MPA in combination with oral glucocorticoids is recommended as initial treatment. In patients improving after initial treatment, subsequent immunosuppression with MPA or azathioprine is recommended for at least 3 years; in such cases, initial treatment with MPA should be followed by MPA. American College of Rheumatology also published similar recommendations. Later, Liu et al. reported their randomized trial results of "multitarget therapy" for induction treatment of LN. After 24 weeks of therapy, more patients in the multitarget group (tacrolimus and mycophenolate mofetil) than in the intravenous CY group showed complete remission (45.9% vs. 25.6%; $p < 0.001$ by Fisher's exact test). Both groups received 3 days of pulse methylprednisolone followed by a tapering course of oral prednisone therapy. In this seminar, update on treatment of LN is to be discussed.

LS6-2

Strategy of corticosteroid sparing in systemic lupus erythematosus by mycophenolate and hydroxychloroquine

Hajime Kono
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Conflict of interest: Yes

SLE is a complex, heterogeneous autoimmune disease, which involves inflammatory processes in multiple-organ systems resulting in a broad range of clinical phenotypes from mild to severe. It is a remitting and relapsing disease with substantial patient-to-patient variation in clinical and serological manifestations. For many decades, corticosteroids have been central to the treatment of SLE due to their anti-inflammatory properties in the short term and immunosuppressive actions in the long term, although corticosteroid treatment is not without complications. Patients on corticosteroids are in danger of accumulating damage even in the minimal dosage such as osteoporosis or atherosclerosis. To avoid the long-term damage due to corticosteroids, combination use of immunosuppressive medication was investigated. Studies showed that mycophenolate is as effective as IV cyclophosphamide for the induction of remission and maintenance therapy in patients with lupus nephritis. Its combination with tacrolimus showed superior efficacy than IV cyclophosphamide in remission induction. Owing to its anti-inflammatory and immunomodulatory properties, hydroxychloroquine has a significant effect on the long-term outcome by modifying the course of illness through reduction of low-grade flares and hence slows progression to severe disease requiring more intense treatment. Accrual of long-term damage was reduced in patients on hydroxychloroquine compared with those not given. In summary, treatment of SLE should be planned on an individual basis with consideration for using the best-suited therapy to target the affected organ systems. The heterogeneity of the disease, lack of a specific biological marker and absence of a definite outcome measurement for improvement makes this process difficult. To prevent corticosteroid-related damage, concomitant usage of hydroxychloroquine and mycophanolate is warranted.

LS7

The importance of patient reported outcomes and the clinical implications of Baricitinib in the treatment of RA

Naoki Ishiguro
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Conflict of interest: Yes

Rheumatoid arthritis treatment has made remarkable progress by standardization of treatment strategy as well as advancement of medicine represented by generalization of biological preparation. Physicians are required to set treatment goals for each patient and achieve them. Overall, it is obvious that the treatment outcome has improved dramatically. The repeated disease activity evaluation and review of treatment based on it are working effectively. However, limitations of biological drugs are also being debated. Not all patients can benefit from that, there are a few cases in which it is difficult to continue treatment sufficiently due to ineffective discontinuation or side effects. Although the number of biological drugs appear to have increased, in reality there are many drugs with the same target. Drugs with totally different mechanisms of action are needed to further improve the treatment outcomes. Furthermore, subjective symptoms such as joint pain, stiffness, and fatigue affect the daily life of the patient to the patient still. Subjective evaluation of patients is carried out in items not included in conventional disease activity evaluation. It seems

that there is such a discrepancy between evaluation by a doctor and evaluation by a patient because such items exist. As the ultimate beneficiary of treatment is a patient, improvement of the subjective evaluation of the patient must be taken into consideration for treatment selection. We must think about treatment options that lead to an improvement in patient satisfaction. From treating the disease, it will be necessary to convert it to treating patients suffering from the disease. The effectiveness of "Baricitinib" is rheumatoid arthritis which is insufficiently effective in existing treatments such as MTX, and of course including the prevention of structural damage of joints. In clinical trials, patient report outcome (PRO) was also evaluated and the results have been obtained that PRO improvement effect of Baricitinib is remarkable. Recent research suggests that items considered as patient subjective evaluation such as stiffness and fatigue in the morning suggest that the lesion remains as a result of image evaluation such as MRI. It is possible that the condition of some patients may not be sufficiently evaluated because the doctor and the patient evaluate differently. In this presentation, I would like to consider the advancement of rheumatoid arthritis treatment so far and its clinical significance expected from the clinical trial results of Baricitinib.

LS8

Transition of a topic of total knee arthroplasty: Which topic is evidence-based?

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Conflict of interest: None

Many orthopaedic procedures, including total knee arthroplasty (TKA), have been performed without sufficiently evidence-based background. In this seminar, recent clinical studies were reviewed to clarify which topic is evidence-based or not evidence-based in TKA. 1. The evidence of the efficacy of TKA There was a paucity of high-quality evidence to support the TKA itself. Skou et al. performed RCT comparing TKA and rehabilitation, and concluded that the TKA was superior to the rehabilitation in terms of patient-reported knee score. This study had a profound impact on the orthopaedic surgeons. 2. The evidence-based topics The blood management and postoperative pain control strategies have been dramatically changed in the last decade. The modern blood management strategy using effective regimen of tranexamic acid was reported to reduce perioperative blood loss without increasing the complications. The utility of multimodal pain management including periarticular multidrug injection has been widely accepted. Many patients experienced no pain until 24 hours postoperatively using multimodal pain management. 3. The not evidence-based topics Although minimum invasive surgery (MIS) technique became very popular formerly, recent articles have denied the utility of MIS technique, especially the mini-incision technique. The RCT performed by Wegrzyn et al (CORR 2013) won the John Insall Award, in which the mini-subvastus approach did not confer a substantial advantage in early function after TKA compared with conventional medial parapatellar approach. Further studies are required to clarity the real effective surgical technique to improve the clinical outcome for patients undergoing TKA.

LS9

Therapeutic strategy of polymyositis/ dermatomyositis with interstitial lung disease

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Conflict of interest: None

Polymyositis/ Dermatomyositis (PM/DM) is often accompanied by interstitial lung disease (ILD) which is one of the important prognostic factors. Recently, increasing numbers of myositis-specific autoantibodies (MSAs) have been reported and their clinical meanings have been elucidated. Among MSAs, anti-aminoacyl-tRNA synthetase (ARS) antibodies and anti-melanoma differentiation-associated gene 5 (MDA5) antibody have most strong association with ILD. In Japan, anti-ARS can be detected in 40-50% of PM/DM-ILD patients and anti-MDA5 in 25-30%. Most anti-ARS-positive ILD shows chronic disease course and tends to respond well to initial glucocorticoid (GC) therapy but often recur. On the other hand, anti-MDA5-positive ILD shows acute/ subacute disease course and is often resistant to immunosuppressive therapy, showing rapidly progressive respiratory distress. Thus, MSAs can be useful in prediction of clinical course and determination of treatment strategy. The 5-year survival of anti-ARS-positive patients is good, 90-95%, but 10-year-survival gradually fall down to 70-80%. This is mainly due to repetition of recurrence resulting in deterioration of pulmonary function. Moreover, activity of daily living (ADL) can also deteriorate because of steroid myopathy or necessity of home oxygen therapy. Thus, in anti-ARS-positive patients, factors on prognosis and recurrence should be elucidated and administration of immunosuppressants in early disease phase are recommended with such factors. In anti-MDA5-positive patients, combined immunosuppressive therapy including high-dose GC, oral calcineurin inhibitors and intravenous cyclophosphamide pulse in early stage of the disease is recommended because they show poor 6-month-survival (30-45%) with conventional step-up therapy. In this seminar, I will suggest therapeutic strategy of PM/DM-ILD introducing results of our clinical trials.

LS10-1

Early remission induction of rheumatoid arthritis considering immunology

Kensuke Oryoji
Center for Rheumatic Diseases, Matsuyama Red Cross Hospital

Conflict of interest: Yes

The earlier the achievement of remission of rheumatoid arthritis, the better. Treatment of rheumatoid arthritis is started with methotrexate (MTX) unless contraindicated. However, the proportion of early rheumatoid arthritis patients who can maintain SDAI remission after one year by MTX monotherapy is about 30%. About 70% of patients can not maintain remission with methotrexate alone. TNFα may be involved in rheumatoid arthritis patients which they were administered sufficient MTX but the the efficacy is insufficient. This is because MTX decreases IL-6 but not TNFα. Moreover, in order to achieve SDAI low disease activity at 70% of patients 6 months after the start of treatment, it is necessary that SDAI after 3 months of treatment fall by more than 80% from the start of treatment. Considering the above, MTX should be started and increased to a sufficient amount promptly, and administration of TNFα inhibitor should be considered immediately as soon as the efficacy is insufficient. And to achieve the goal of 80% SDAI reduction after 3 months as described above, administration of TNFα inhibitor should be started by at least 1-2 months after MTX start. When administering a TNFα inhibitor, sufficient neutralization of TNFα in each patient is important from the viewpoint of efficacy and immunogenicity. It is reported that TNFα is abundant in patients with high titers of ACPA and RF. Considering the immunological influence of the introduction of early remission of patients with rheumatoid arthritis, consider the importance of leading rheumatoid arthritis to remission at an early stage.

LS10-2

Control of rheumatoid arthritis (RA) from the perspective of the synovium

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Conflict of interest: Yes

Recent research has suggested that epigenetic as well as genetic abnormalities are closely linked to the onset and severity of RA. DNA methylation is a typical epigenetic mechanism, and there have been reports that RA patients show abnormal DNA methylation. The present authors have shown, in a comprehensive analysis of genomic DNA methylation, that fibroblast-like synoviocytes (FLS) derived from RA patients show a DNA methylation pattern that is characteristic of RA, and most genes that show abnormal methylation are closely connected to RA pathology. For RA, treatment that involves targeting inflammatory cytokines using biological agents is familiar as remission induction. However,

there is what may be termed “a window of opportunity” for RA treatment, and delays in initiation of treatment mean that therapeutic efficacy is limited. This suggests that maintenance of an inflammatory environment has the potential to convert cells at loci showing synovitis to more aggressive and treatment-resistant phenotypes, but the detailed mechanism for this is unclear. The authors are currently investigating the possibility that continuous exposure of the synovium in RA patients to inflammatory cytokines, typified by TNF and IL-1, modifies the expression of DNA methylase and demethylase; modifies the phenotype of FLS as an inflammatory memory; and leads to formation of pannus, which is a synovial tissue directed toward breakdown of bone and cartilage. From the above perspective, the best approach that can be provisionally put forward for RA clinical practice, until a preemptive therapy has been established, is to ascertain which drugs are and are not effective as quickly as possible, and to avoid continuous exposure to inflammatory cytokines. The authors hope that this presentation will provide an opportunity to think about optimization of RA treatment, at the same time as introducing the preliminary results of clinical research that is currently in progress at our department.

LS11

Impact of biosimilars on medical cost of rheumatoid arthritis from an economic perspective

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Conflict of interest: None

Along with introducing biologics in patients with rheumatoid arthritis (RA), the treatment strategy has changed significantly. The treatment goal is shifting from inflammation control to prevention of joint damage and improve long-term quality of life, and remission is now defined as a realistic goal. A cohort study, IORRA (Institute of Rheumatology, Rheumatoid Arthritis), ongoing since 2000, has observed improved outcomes in patients with RA over time. On the other hand, an increase in the medical cost of RA with the advances in therapy has been causing concern and it is becoming a significant burden both on the patients and on society. In RA, not only the direct, but also the indirect costs are a great concern. However, pharmacoeconomic analyses of RA have not yet been performed in Japan. We evaluated the direct cost and working impairment in Japanese RA patients in the IORRA cohort. It was observed that patients’ economic burden through both direct and indirect costs increased with progression of functional impairment and a decrease in the quality of life. Therefore, it was suggested that controlling disease activity from an early stage could reduce the total medical cost, including not only the direct, but also the indirect cost. Furthermore, pharmacoeconomic analyses evaluating both clinical effectiveness and medication cost should be performed, especially for expensive drugs like biologics used to treat patients with RA. As we performed a cost-effectiveness analysis on biologics for RA treatment based on the IORRA cohort, we additionally discuss these findings. In addition, infliximab biosimilar is available. In contrast, biosimilar drugs have entered the global biologics market significantly faster, especially in the European countries. Guidelines for use of biosimilars have been introduced based on these situations, and major cost savings for RA treatment are expected. Several biosimilar research results from Japan and worldwide will be presented.

LS12

Total Management of Rheumatoid Arthritis in Akita Orthopedic Group on Rheumatoid Arthritis

Yoichi Shimada
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Conflict of interest: None

Since Akita is very large and an aging prefecture of the national first place, long-distance going to hospital is difficult. In 2010, we established the Akita Orthopedic Group on Rheumatoid Arthritis (AORA) for standardization of the RA treatment and cancellation of the regional disparity. Eighteen hospitals and 10 clinics have been participated and covered all area of the prefecture. We have performed a study session, a joint echo workshop, clinical conference regularly. Furthermore, we have conducted all case registration (AORA registry). The ratio of elderly people is high with 62.1% in AORA registry. The superiority for orthopedic surgeons on RA practice is to be familiar with the rehabilitation, treatment of osteoporosis, and the surgery. The pain of the RA patients is summation of the synovitis, bone, cartilage, and the joint destruction which occurred as a result of synovitis. We aim at the joint preservation surgery in the foot and ankle. We have used an external skeletal fixation for early walk to prevent disuse atrophy. Although cervical lesion has been based on in the backbone, there are some failures to detect the subluxation of the atlantaxial joint in outpatient clinic. There are destructive changes in not only cervical but also thoracic and lumbar spine, and it is necessary to deal precisely. I would like to emphasis the fact that the rehabilitation in the RA medical care of our country is delayed very much. The ability improvement of the RA patients with the rehabilitation, the evidence of the arms function improvement are clear. It is possible that the appropriate surgical care, rehabilitation intervention can prevent body function disorder progression by Paradigm shift of the medical treatment. There are many advantages that orthopedic surgeons gives RA treatment with tight connection with physicians.

LS13-1

A Clinical Update in Osteoporosis ~Rheumatologist's Point of View~

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Conflict of interest: Yes

Osteoporosis and related conditions are common cause of disability in the Japan. An increased prevalence of osteoporosis is seen in rheumatic diseases resulting in a potential increase in risk of fracture. The clinical significance of osteoporosis is in the occurrence of fractures and it`s recurrence. The major risk factor of recurrence is a previous fracture, however, a recent fracture is a better fracture risk factor than fracture history. This imminent risk is explained by both bone-related factors (underlying osteoporosis, medications to lower bone density, underlying diseases) and fall-related factors (including risk of falls and sarcopenia related to the locomotive syndrome). Such a short-term increased risk has been shown also in patients initiating corticosteroids and in frail osteoporotic subjects with central nervous system (CNS) diseases or drugs targeting CNS, and thus a high risk of falls. Patients with an imminent risk of refracture should be followed closely in priority in order to receive an immediate treatment and a therapy of fall prevention. In this session, we aim to emphasize the early assessment and treatment of imminent fracture risks. In addition, I would introduce a recent advances in the management of osteoporosis, especially focusing of Glucocorticoid induced osteoporosis (GIO), which includes currently available strong anti-resorptive agents (bisphosphonates and an anti-receptor activator of nuclear factor-kappa B ligand (RANKL) antibody, denosumab) and, as anabolic agents, PTH.

LS13-2

Act Against Osteoporosis in Patients with Rheumatoid Arthritis

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Conflict of interest: None

Both generalized and juxta-articular osteoporosis is a well-known complication of rheumatoid arthritis (RA), and patients with RA are at increased risk of osteoporotic fractures especially under long-term use of oral glucocorticoids or in the elderly. These fractures were associated with functional disability in patients with RA, so it is widely accepted that fracture should be prevented. However, tight control of fracture prevention to improve the long-term functional prognosis are not necessarily implemented or disseminated in clinical practice of early RA. It is important that we are aware of the reasons why some physicians apt to be tolerant of fractures in patients with RA, since it shows us the strategies required for guarding the patients with RA against fracture-induced functional loss. I think that possible three steps are associated to this pit-

fall. When we are fighting with the synovitis or inflammatory disease activity in patients with RA, we tend to believe in the exemption from obligation to reduce the possible fracture risk in the future. Educational strategies to cultivate professionalism could avoid this pitfall. We had to care more particularly for the individual patients than for the special features of the disease. When we have no experience of care for the patient with impaired walking ability due to insufficiency fracture (IF) of pelvis, it is difficult to notice the disadvantages of IF that are often more severe than those of continued small joints swelling or tenderness. This neglect of IF could reduce the sense of urgency to prevent the fracture. Educational strategies to improve diagnosis of IF in clinical practice could avoid this pitfall. When we have no skill to prevent the fracture using multidisciplinary approach including appropriate pharmacological and non-pharmacological treatment, it is difficult to prevent fracture successfully. It is required that we maintain the physical activity, healthy nutritional status, kidney function and reduced disease activity in patients with RA, as a prior condition of effective treatment by anti-fracture agents. Educational strategies of multidisciplinary approach in osteoporosis management of patients with RA could avoid this failure. In my clinical practice, I always endeavor to take these three into consideration.

LS14-1

Overview of sarilumab clinical trials

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Conflict of interest: Yes

Effective treatment of Rheumatoid arthritis (RA) has been progressed dramatically in the recent years and ACR/EULAR have initiated the treatment recommendations, T2T, for better outcome of the RA treatment. Owing to these activities, current RA treatment could have extended a RA patient's life prognosis by suppressing not only inflammation of whole body but also irreversible joint destruction. IL-6 is a pleiotropic pro-inflammatory cytokines that is involved in worsening pathophysiological condition of RA. Excess IL-6 in synovial fluid and serum leads joint destruction by activating synovitis, so that the drugs inhibiting IL-6 -medicated signaling is very important for RA treatment strategy. Sarilumab is a fully human IgG1 monoclonal antibody that binds specifically to both soluble and membrane-bound IL-6 receptor. Last year, subcutaneous sarilmab (200mg/150mg) was approved in Canada, EU, and US for the treatment of adult patients with moderate to severe active RA. In this seminar, we summarize the results of sarilumab global/Japanese clinical trials (MOBILITY study in patients with inadequate response to Methotrexate (MTX), TARGET study in patients with an inadequate response to or intolerance of TNF alpha inhibitors, MONARCH study in patients with an inadequate response or intolerant of MTX) respectively and discuss availability of 2 dosage (200mg/150mg) of sarilumab.

LS14-2

Safety of sarilumab and its preferred dose of 200 mg

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Conflict of interest: Yes

In KAKEHASI study, which was aimed to assess efficacy and safety of sarilumab plus methotrexate (MTX) in Japanese patients with active rheumatoid arthritis (RA) and inadequate response to MTX (MTX-IR), patients received subcutaneous sarilumab 150 mg q2w + MTX (S150), 200 mg q2w + MTX (S200), or placebo + MTX (P) for 24 weeks, then patients in P switched to S150 or S200. The most common treatment-emergent AEs (TEAEs) were infection such as nasopharyngitis, liver dysfunction and neutropenia, which were considered to be associated with interleukin (IL)-6 inhibition, although neutropenia was not associated with infection. Sarilumab was shown to be well-tolerated in HARUKA study, which was aimed to assess long-term safety and efficacy of sarilumab added to non-MTX conventional synthetic DMARDs (Combo) or as monotherapy (Mono) in Japanese patients with active RA. Sarilumab 150 mg and 200 mg injection showed comparable safety in both studies, and also comparable in the primary endpoint of KAKEHASI study, ACR20 response rate at week 24. However, at week 12, ACR50/70 in S200 was numerically higher (31.3%/18.8%) than that in S150 (27.2%/6.2%). Remission rates for DAS28-CRP/CDAI/SDAI were also numerically higher in S200 than in S150 (33.8%/6.3%/8.8% versus 25.9%/1.2%/2.5%). A numerically greater proportion of patients who were treated with S200 achieved complete CRP inhibition compared to patients treated with S150 at Week 2 and throughout the period. With considering the results from the global MOBILITY study, the above results support sarilumab 200 mg as the recommended dose for moderate to severe Japanese patients with RA.

LS15-1

The current state for the management of ANCA-associated vasculitis

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Conflict of interest: None

The primary systemic vasculitides (PSV) are characterized by inflammation of blood vessels. PSV often could cause multiple tissue and organs damage which are strongly associated to death. Chapel Hill nomenclature is widely used to define different forms of vasculitis according to the size of the predominantly affected vessels. Vasculitis associated with the presence of anti-neutrophil cytoplasm antibody (ANCA), termed AAV, advances have been made in understanding the pathogenesis and evidence based treatment for AAV. However in AAV, morbidity and mortality is still very high, in the initial phase due to disease activity and infections, in the late phase due to cardiovascular disease and malignancies. AAV is divided into three major forms: granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA). In diagnosis, ANCA are associated in the pathogenesis of AAV and major biomarker for diagnosis of AAV. However all patients have not positivity of AAV. Additionally, the frequency of positivity of ANCA (c-ANCA or p-ANCA) in Japanese AAV patients is different from those of another country such as Europe or USA. We will consider carefully about ANCA positivity at the diagnosis of AAV. In treatment of AAV, use of high dose corticosteroids and cyclophosphamide (CYC) plays a major role in morbidity and mortality. Recent studies have shown that CYC could be replaced by rituximab (RTX). We will review recent EULAR and Japanese guidelines on therapy for AAV. Both guidelines indicate that cyclophosphamide or rituximab (plus glucocorticoid) is the mainstay of remission induction therapy. For very severe disease such as alveolar hemorrage complications or RPGN, plasmapheresis is recommended. Recently the effectiveness of rituximab treatment for maintenance is also being established. These evidences for effectiveness is clear for MPA and GPA. A number of studies are marching to improve our use of these existing agents and to examine agents focused in AAV. In this seminar, we reconfirm and discuss about these issues of management in AAV.

LS15-2

Tocilizumab for large-vessel vasculitis

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Conflict of interest: None

IL-6 plays a significant role in the pathogenesis of Takayasu arteritis (TAK) and giant cell arteritis (GCA), both of which are large vessel vasculitis (LVV). Steroids have been a mainstay treatment for LVV for a long time. However, there are some LVV patients refractory to steroids. And prolonged steroid therapy definitely cause Cushing-like signs and symptoms such as moon face, vertebral fractures related to steroid induced osteoporosis and cardiovascular events related to hyperlipidemia, diabetes and hypertension are also problems in elderly patients with GCA. Various immunosuppressive agents were tried as a steroid-sparing agent in the treatment of LVV but there is little evidence for the usefulness of these agents. In 2008, Nishimoto N, et al. reported the efficacy of tocilizumab (TCZ), humanized anti-IL-6 receptor monoclonal antibody, for a TAK patient for the first time. From 2011, when Seitz M, et al. re-

ported the efficacy of TCZ for GCA and TAK (Swiss Med Wkly), many similar reports have been published so far, leading to the hypothesis that IL-6 blockade may be effective for LVV. The GiACTA study demonstrated that subcutaneous TCZ (scTCZ), weekly or every other week, with glucocorticoid tapering off within 26 weeks, was effective with higher remission rate at week 52 than placebo. And also cumulative prednisolone dose was significantly lower in patients treated with scTCZ (Stone JH, et al.: NEJM 2017; 377: 317). Recently, TAKT study has revealed that scTCZ could safely reduce relapse rate in refractory TAK patients, leading to the approval of scTCZ for TAK and GCA in Japan on August 25 2017. In this session I'd like to discuss how and when to use TCZ for LVV patients in daily practice.

LS16

How the management of RA may change by the introduction of tofacitinib ?

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Conflict of interest: Yes

Along with advances in basic medical research, drugs specifically targeting rheumatoid arthritis (RA) or molecules deeply involved in cancer pathology have been developed. Many biologic DMARDs (bDMARDs) have also been developed and are being used against various diseases to great effect. Attention is currently being focused on JAK inhibitors as a new MOA agent. Tofacitinib was the first targeted synthetic DMARDs (tsDMARDs) that inhibits the JAK1/3 molecule intracellularly. Tofacitinib was approved in Japan in 2013 and an all case PMS study is now on-going. When the safety profile is confirmed, tofacitinib will be used more frequently. In fact, JAK inhibitors are categorized as a 2nd line treatment option in EU and US Guidelines. I would like to consider how the management of RA may change by the use of tofacitinib, especially in comparison to bDMARDs. First, clinical studies have found that the efficacy of tofacitinib is statistically similar to bDMARDs. It is also effective in anti-TNF refractory patients. In addition, a recent clinical study shows the possibility for "Mono therapy" in MTX-IR patients. The safety profile should be carefully investigated since tofacitinib belongs to a new drug category, but by the preliminary report of the ongoing PMS study is encouraging and the safety profile will be confirmed shortly. However, we have to be aware of the cytotoxicity of tofacitinib, since tofacitinib acts intracellularly, where bDMARDs act extracellularly. Tofacitinib is an oral medicine, thus, there is no need to subject patients, and medical staff, to the burdensome and time consuming efforts of infusions or injections, which are required with bDMARDs. On the other hand, patient adherence must be monitored. Regarding the cost of tofacitinib, it is comparable to bDMARDs, thus, pharmacoeconomical analysis will be necessary to confirm its real value. In summary, tofacitinib has a comparable efficacy to bDMARDs, but the burden of infusion or injection will eliminated. This means the drug is likely to be widely used, not only by rheumatology specialists, but also by non-specialists. Therefore, we need to disseminate precise knowledge and information to ensure proper use of this drug at a wide variety of medical facilities.

LS17-1

Imaging evaluation of effectiveness of anti-TNFs on rheumatoid arthritis

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Conflict of interest: Yes

Conventional radiography (X-ray) has been the mainstay of imaging in rheumatoid arthritis (RA) for decades. However, X-ray only depicts the late results of preceding disease activity, as it visualizes bone erosions (when they have reached a certain size) and joint space narrowing. Joint inflammation is not visualized. In contrast, modern imaging methods as magnetic resonance imaging (MRI) and ultrasonography (US) allows direct visualization and assessment of the disease activity, such as synovitis, osteitis (only MRI) and tenosynovitis. Futhermore, MRI is more sensitive for assessment of early damage to bone and cartilage than X-ray. Tumor necrosis factor inhibitors (TNF-I) have revolutionized the options of treatment of difficult RA. Numerous studies using X-ray have documented that TNF-I significantly reduce structural damge progression (progression in bone erosion and joints pace narrowing), compared to conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs). This has been confirmed in randomized controlled trials using MRI as measure of structural damage. Due to the higher senitivity to change of MRI as compared to X-ray, MRI studies need fewer patients to demonstrate a statistically significant difference in structural progression between treatment groups. MRI and US studies have also documented that that TNF-I effectively inhibits and quickly reduces inflammation both in the synovium (synovitis), bone (bone marrow edema, osteitis, only MRI) and tendon sheaths (tenosynovitis). Osteitis at baseline, and early treatment-induce changes in osteitis, have been shown to be a strong predictor of subsquent radiographic progression. Moreoever, MRI findings of inflammation have been documented to be important to key patient reported outcomes such as functional ability (heath assessment questionaire (HAQ) score), patient pain and patient global assessment. In conclusion, both modern imaging and the use of TNF-I are key aspects of modern stae-of the art management of RA.

LS17-2

Clinical efficacy of certolizumab pegol in rheumatoid arthritis patients without sufficient dose of methotrexate treatment

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Conflict of interest: Yes

The treatment with sufficient dose of methotrexate (MTX) plays the pivotal role in the modern rheumatoid arthritis (RA) treatment strategy in all over the world. When treated with sufficient MTX, all kinds of biologics and JAK inhibitors will demonstrate the maximal efficacy according to a lot of evidence based on randomized control trials. However, we have no distinct treatment strategy when treated without or with only low dose MTX. In those cases, we have to choose additional drugs based on each drug's unique property. The long-term efficacy including the joint destruction have to be considered as well as the short-term clinical response. Certolizumab pegol (CZP) demonstrated the similar efficacy on joint destruction (ΔmTSS < 0.5 /year) irrespective of MTX dose in Japanese RA patients; 11.6 mg/week in C-OPERA, 7.4 mg/week in J-RAPID, and 0.0 mg/week in HIKARI study. The reason why CZP sufficiently suppressed the joint destruction in all studies with different dose of MTX was uncertain. The sufficient neutralization of TNF was reported to result in the sufficient suppression of joint destruction irrespective of clinical response to treatment. The trough serum concentration of CZP has been known to be quite high compared to other TNF inhibitors. The CZP has smaller molecular weight and has property to easily penetrate into the inflamed synovium tissue. We assumed that sufficiently high CZP concentration especially in the inflamed joint could result in the suppression of joint destruction irrespective of MTX dose. Many previous reports demonstrated that concomitant MTX treatment can maximize the potential clinical efficacy of TNF inhibitors. The property of CZP that it can suppress the joint destruction without sufficient dose of MTX is quite unique as a member of TNF inhibitors. CZP would be one of suitable treatment options in the patients who are contraindication for high dose of MTX treatment.

LS18

Management of opportunistic infection in patients with systemic rheumatic diseases

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Conflict of interest: Yes

Patients with systemic rheumatic diseases are prone to develop infections because of immunological abnormalities, use of immunosuppressive drugs, and comorbidities. Organ damage, flare after discontinuation of immunosuppressive treatment, and limited treatment option for rheu-

matic diseases incur poor vital and functional prognosis of patients with rheumatic diseases. Recent progress in the development of new immunosuppressants and molecular targeting drugs for systemic rheumatic diseases has enhanced the importance of management of infections, especially opportunistic infections (OI). In clinical settings in Japan, rheumatologists should pay heed to OI including tuberculosis, pneumocystis jirovecii pneumonia (PCP), herpes zoster, and reactivation of hepatitis B virus (HBV). Current annual incidence of tuberculosis in Japan has decreased down to 13.9/100,000 person, but is still higher than those of other developed countries. The Japanese package inserts of biologics and immunosuppressants describe necessity of proper screening and monitoring of tuberculosis. With unknown reasons, incidence of PCP in Japan is higher than overseas. Early diagnosis and treatment of PCP is mandatory because delayed diagnosis leads to poor prognosis. Low-dose sulfamethoxazole-trimethoprim is widely used for prophylaxis of PCP, and we have to make all kinds of effort to continue prophylaxis despite the high incidence of adverse events Clinical trials of Janus kinase inhibitors showed significantly higher incidence of herpes zoster in Asian countries compared to the rest of the world. Subunit vaccine is under review for approval and expected to be widely used in clinical settings. Reactivation of hepatitis B virus (HBV) has still been reported. From a pharmacoeconomical point of view, proper monitoring intervals and conditions for starting nucleoside/nucleotide analogues are currently investigated. In this seminar, management of these important OI will be discussed.

LS19-1

Optimising treatment of RA - pathogenesis directed therapies to assist physicians and patients?

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Conflict of interest: None

The advances in the last two decades in the treatment of rheumatoid arthritis (RA) have been remarkable and have been driven by two key advances. First, the advent of novel therapeutics that target specific cytokines, cell surface immune receptors or intracellular immune signaling pathways, has brought a step change in the magnitude and duration of clinical responses that can be achieved in people with RA. The initial introduction of TNF inhibition lead the way to a range of immune targeting approaches that include IL-6Ri, co-stimulatory inhibition, B cell depletion and JAK inhibition. The second key advance was a re-evaluation of the strategic approaches that can optimize treatment. In particular the value of early intervention, and the positive outcomes that ensue upon a treat to target approach have been demonstrably beneficial for patients. IN this lecture I will discuss the key lessons learned from this biologic revolution, review the key clinical datasets that support the notion of novel strategic approaches, and thereafter will move to discuss state of the art approaches to the identification of therapeutic targets and the allocation of therapeutics to the correct patient at the ideal time, embodied in the concept of Precision Medicine in rheumatology.

LS19-2

Toward “real” remission and beyond remission

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Conflict of interest: Yes

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

LS20

Bone damage in RA-when dose it start?

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LS21

Efficacy of selexipag for the treatment of pulmonary arterial hypertension with systemic sclerosis

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Conflict of interest: Yes

The pathological study revelaed that it was different between pulmonary hypertension (PH) associated with systemic sclerosis (SSc) and PH associated with collagen disease other than SSc. It is estimated that pulmonary arteritis may be related to the pathogenesis of PH other than SSc. Therefore, immunosuppressive therapy could be performed for PH other than SSc. On the other hand, it is rare to report that immunosuppressive therapy is effective for SSc-related PH, and treatment with a vasodilator has been given priority. In the past two decades, the treatment of idiopathic pulmonary arterial hypertension (iPAH) has made remarkable progress as vasodilators with high selectivity for pulmonary arteries. However, SSc-PH has poor therapeutic effect. There is a difference in the frequency of intravenous prostacyclin preparations used for treatment with iPAH. Therefore, beraprost has been frequently used as an oral prostacyclin preparation. As an alternative to prostacyclin, an agonist to the IP receptor, a prostacyclin receptor, has been developed. That is selexipag. This formulation has high selectivity for IP receptor and strong vasodilator action. In the clinical study of selexipag (GRIPHON Trial), PAH-related events were significantly reduced in patients with SSc-PAH by the treatment of selexipag. In the guidelines of AMBITION Trial and ESC / ERS announced in 2015, initial oral combination therapy was announced effective for PAH patients with WHO FC II and III. Thereafter, initial oral combination therapy using endothelin receptor antagonist and cGMP stimulator was started to be carried out internationally for SSc-related PAH. Although there is no report on the effectiveness in the long term, it is speculated that in the future it will become increasingly popular to select Sexipag as the third combination therapy.

LS22

Multitarget therapy of lupus nephritis with tacrolimus

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Conflict of interest: Yes

Tacrolimus is a key immunosuppressant in multitarget treatment of lupus nephritis. Multitarget therapy has advantages in the oral route of the administration which does not require hospitalization, possibility of rapid tapering of glucocorticoid, and easy adjustment of the dose of each medications. As the overall prognosis of systemic lupus erythematosus and lupus nephritis remarkably improved, the regimen without high risks of irreversible adverse effects is one of the most crutial factors to be chosed by patients.

LS23

From the standpoint of the systemic inflammatory condition, a pharmacological treatment strategy for musculoskeletal pain

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Conflict of interest: Yes

Rheumatoid arthritis (RA) is an inflammatory autoimmune disease, and its main symptom is arthralgia, mainly caused by inflammation of the joint and its synovial membranes. This mechanism of pain is caused by stimulation of nociceptors on the peripheral nerve endings distributed in peripheral tissues like as joints, by inflammatory molecules secreted from inflammatory cells. This is called as nociceptive/inflammatory pain. Worse yet, RA arthralgia is usually accompanied by psychological distress and insomnia, both of which are not only secondary to pain but make a vicious cycle to deteriorate pain severer. Rheumatoid arthritis patients complain of numerous pain immediately after movements, and RA prevents them to spend free time away from pain. Obesity is known as one of risk factors for some musculoskeletal pain conditions such as low back pain, neck pain and knee pain. Also, obesity is known as the risk factor for migraine and neuropathic pain like as post-herpetic neuralgia, which are unrelated with excessive mechanical load on the musculoskeletal system. Now we have currently investigated the relationship between pain and obesity and its-related systemic inflammatory condition, called as the metabolic syndrome. In fact, there are reports that patients with obesity and the metabolic syndrome are at increased risk of RA and that the effectiveness of the biological therapy is diminished, and therefore obesity should be recognized as a therapeutic target for improving pain. In this presentation, from the standpoint of the systemic inflammatory condition, we discuss a pharmacological treatment strategy for pain in rheumatic diseases.

LS24

Clinical utility of iguratimod in the treatments for patients with rheumatoid arthritis

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Conflict of interest: Yes

For patients with rheumatoid arthritis (RA), rheumatologists have a lot of treatment options including conventional synthetic disease-modifying antirheumatic drugs (csDMARD), targeted synthetic DMARD (tsDMARD) and biological DMARD (bDMARD). Although bDMARD may be the 2nd line drugs for RA patients with MTX-insufficient response, infectious diseases sometimes occur during bDMARD use for elderly RA patients with pulmonary comorbidity. Also, in RA patients with MTX-lymphoproliferative disorders (LPD), some immunosuppressive agents including MTX are contraindicated and treatment to target strategy is really difficult. Such unmet medical needs for RA treatment is still problem. Iguratimod (IGU) is one of the csDMARD without strong immunosuppressive effects. IGU, however, has the potential for suppressing proinflammatory cytokines (e.g., TNF-α, IL-17, and IL-6). Actually, IGU is sometimes effective even for patients with other csDMARD-insufficient response. IGU might be distinct antirheumatic agents from the other csDMARD. Of note, the usefulness of combination therapy between MTX and IGU has been published (Ishiguro N, *et al, Mod Rheumatol*, 2013) and concomitant use of IGU with MTX is recommended in the 2016 clinical practical guideline of MTX for patients with RA. An additional use of IGU to bDMARD seems to be popular in clinical practice, whereas their combination effect may not be evident. Taken together with several publications, IGU is the unique csDMARD and the useful treatment option for RA patients. Whereas warfarin use with IGU is contraindicated and suppressive effects on bone erosion appeared not to be evident, IGU is one of the major csDMARD in Japan. In this seminar, clinical evidences of IGU and the 2016 clinical practical guideline of MTX for patients with RA will be discussed.

LS25

Early diagnosis and management of Eosinophilic granulomatosis with polyangiitis

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Conflict of interest: None

Eosinophilic granulomatosis with polyangiitis (EGPA; also known as Churg-Strauss syndrome (CSS)) is a rare disease that is characterized by allergic granulomatosis, necrotizing vasculitis and peripheral blood eosinophilia. Chronic eosinophilic pneumonia (CEP) and eosinophilic gastroenteritis, precedes systemic vasculitis in half of all patients with EGPA. However, most patients with asthma complicated by CEP do not develop EGPA. Therefore, EGPA is often difficult to diagnose in the early phase. Recently, we have seen a marked improvement in the prognosis and mortality rates for EGPA as a result of implementation of the American College of Rheumatology 1990 criteria for the classification of CSS and the development of more effective treatments. Indeed, the 5-, 10-, and 20-year survival rates reported in 2011 by Guillevin *et al.* were approximately 90%, 75%, and 45%, respectively, and those reported in 2013 by Moosig *et al.* were 97%, 89%, and 72%, respectively. However, the long-term (20-year) prognosis for patients with EGPA remains poor. The mainstay treatment for EGPA is systemic corticosteroid therapy (CS). Additional treatment with immunosuppressive agents, such as cyclophosphamide (CYC) or azathioprine, may also be effective in some patients. New treatment options anti-CD20 monoclonal antibodies, anti-IgE therapy, anti-IL-5 antibody therapy, or intravenous immunoglobulin (IVIG). We previously showed that IVIG therapy was effective against severe mononeuritis multiplex with EGPA that did not respond to CS-CYC therapy. Whether the timing of administration and the patient's treatment history affect the clinical efficacy of IVIG is unknown in patients with mononeuritis multiplex that is not improved by conventional treatments. Here, I discuss the early diagnosis and treatment options for maximizing the long-term prognosis of patients with EGPA. I also show using the questionnaire of motor and sensory neuropathy for the management of mononeuritis multiplex (www.anca-aav.com/).

LS26-1

Characteristics of pediatric patients with Sjögren's syndrome and early diagnosis, importance of follow-up

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Conflict of interest: None

Sjögren's syndrome (SS) has been considered rare in pediatric age groups, because these patients lack sicca symptoms. However, severe extraglandular organ involvement and sicca symptoms may occur during follow up in some patients. Therefore, diagnosis of SS shoud be done at an early stage and patients require close observation. Moreover, as the majority of patients are female and have anti-SS-A/Ro antibodies, careful monitoring is necessary during pregnancy. Because the diagnosis of SS in pediatric age groups is often difficult, the Japanese Pediatric Sjögren's Syndrome Study Group developed new criteria. In this presentation, I will discuss the characteristics of pediatric SS and the guidance for diagnosis of SS in pediatric age groups (2015). SS is a chronic disease, and transition to adult care is important. I will comment on our projects about transition of patients with SS.

LS26-2

New findings in Sjögren's syndrome and significance of early diagnosis and continuous treatment for improvement in patients' QOL

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Conflict of interest: None

Sjögren's syndrome (SS) with major symptoms of chronic sialadenitis, keratoconjunctivitis sicca, and polyarthritis is an autoimmune disease

that causes the appearance of various autoantibodies or hypergammaglobulinemia. The disease, commonly developed in middle-aged women, shows lesions in systemic organs in addition to a dry mouth and dry eyes, and even psychiatric and neurological symptoms. Thus, patients' quality of life (QOL) markedly decreases. Unfortunately, no radical treatment has been found for SS. The treatment of this disease is to relieve dryness and to prevent the progress by suppressing the activity of the disease. However, without an early diagnosis and appropriate intervention, various symptoms will develop and decrease QOL. Thus, an early diagnosis is particularly important. Since dryness also directly causes the decrease in QOL, a continuous treatment is necessary. According to the survey conducted on SS patients, sialogogues are prescribed only for 15% of all the patients, and a dry mouth affected the daily life of 80% of patients without using sialogogues. We suppose many patients with the evident symptoms of SS do not receive treatment for some reasons and have troubles in their daily life. In this seminar, we will introduce new findings and treatment methods for SS and discuss what we can do for SS patients.

LS27

Target molecules in autoimmune diseases: current treatments and future prospects

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Conflict of interest: Yes

The autoimmune disease is a condition in which immune tolerance is failed due to excessive immunoreaction to the autoantigen, resulting in organ-specific or systemic clinical symptoms. Recently, the identification of various autoantibodies has led us to discover numerous autoimmune diseases where specific cytokines, chemokines, and their producer cells such as T-cell and B-cell are involved as underlying pathogenesis. In particular, TNFα has been focused as an effective target molecule from early on. In fact, the treatment of rheumatoid arthritis (RA) has been greatly improved thanks to the paradigm shift brought by the development of anti-TNFα antibodies, enabling us to prevent the progression of joint destruction and achieve sustained remission. In addition, clinical trials revealed that anti-TNFα antibodies are also effective in other autoimmune diseases such as ankylosing spondylitis (AS), psoriasis (PsO), psoriatic arthritis (PsA), juvenile idiopathic arthritis (JIA), crohn's disease (CD) and ulcerative colitis (UC), and thus the use of anti-TNFα antibodies is nowadays one of the major options in the treatment of autoimmune diseases. Likewise, IL-6 blockade is highly effective in RA treatment. This approach, however, turned out not to be as effective for PsO, PsA, CD and AS, but was proven to be effective for JIA and large vessel vasculitis (takayasu arteritis, giant cell arteritis). Therefore, although our understanding of signaling cascades and their components has allowed us to improve the treatment of autoimmune diseases, there remains to be a substantial unmet need to develop new therapeutic strategies. Recently, new biologic agents have become available: CD80/86 and CD20 for RA, IL-23 (p40) for PsO, PsA and CD, IL-17 for PsO, PsA and AS, the adhesion molecules α4/β1 and α4/β7 integrins for CD and UC, and BLys (B Lymphocyte stimulator) for systemic lupus erythematodes (SLE). In addition, novel molecules have emerged as therapeutic targets: IL-23 (p40) for UC and SLE, IL-23 (p19) for PsO, PsA and CD, and IFNα for SLE, all of which led to ongoing clinical trials, and thus further improvement in the treatment of these diseases is expected. In this seminar, I discuss the current status, challenges and prospects pertaining to molecular targeted agents for autoimmune diseases.

LS28

Treatment of systemic lupus erythematosus and lupus nephritis

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Conflict of interest: Yes

Systemic lupus erythematosus (SLE) is a prototype of systemic autoimmune disease. Multiple organs and tissues are affected in patients with SLE in a different way, and such heterogeneity of clinical aspect is making difficult to standardise the management of lupus patients in clinical practice. In the history, corticosteroids (CS) dramatically improved the mortality of lupus patients; on the other hand, major or minor adverse events of CS would significantly affect to their morbidity. Recently, the potent immunosuppressants are efficiently used for the remission induction in patients with SLE. Amongst the lupus organ involvements, lupus nephritis (LN) is one of the most common and important manifestation, and the better use of immunosuppressnats are described in two major guidelines for lupus nephritis. Hydroxychroloquine was described as the basic drug for all LN patients, Mycophenolate mofetil (MMF) has been recommended for the initial and maintenance treatment. Cyclophosphamide (CY) and tacrolimus (TAC) are commonly used immunosuppressants. TAC has been approved for LN in a maintenance phase of the treatment in Japan. In clinical practice, however, TAC is often considered as a partner for MMF or CY in the induction phase for cases with insufficient response for MMF or CY. We should establish a strategy how to use those potent immunosuppressants to improve the outcome of lupus treatments.

LS29

Best use of TNF inhibitors in the treatment for patients with rheumatoid arthritis - Dose optimization of Infliximab using the newly approved tool, Immunochromatograhpic test for detection of Infliximab serum levels

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Conflict of interest: Yes

Recently, many antirheumatic drugs are available and rheumatologists are treating rheumatoid arthritis (RA) patients to the target (e.g., clinical remission). Additionally, dose optimization for each patient is recommended. In another word, biological disease-modifying antirheumatic drugs (bDMARD) should be used for the right patient, in the right time, and with right agent including dose. Although clinical practice guideline in the treatment for patients with RA published by the Japan College of Rheumatology is definitely helpful, the unsolved problem is to select the best useful bDMARD for each patient. Whereas five TNF inhibitor originators and one biosimilar DMARD are now available in Japan, their efficacy might be equivalent. Rather, their usefulness may depend on patients' factors (e.g., comorbidity) and the prior DMARD use. Also, in some TNF inhibitors, dose modification is limited toward and beyond remission. Infliximab is the unique anti-TNF-α antibody agent with modified dose and infusion duration. There are many evidences regarding treatment holiday beyond remission (e.g., RRR study) and dose optimization toward remission (e.g., RISING study). In 2017, REMI check Q, which is the determination kit for effective trough levels of serum Infliximab concentration (1mg/mL), was approved for RA patients treated with Infliximab. While serum concentration of proinflammatory cytokines such as TNF-α cannot be measured, the result of REMI check Q may be helpful for our clinical decision regarding Infliximab dose optimization. In this seminar, dose optimization of Infliximab using the newly approved tool, REMI check Q, will be shown and discuss for the better RA management.

LS30

Autoinflammatory syndrome rheumatologist should know

Hiroaki Ida
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Conflict of interest: Yes

Autoinflammatory syndrome is a syndrome that causes systemic inflammation, similar to infections and collagen diseases, but pathogens are not detected and autoimmune reactions are limited. In the narrow sense, hereditary periodic fever syndrome such as familial Mediterranean fever (FMF), TNF receptor-associated periodic syndrome (TRAPS), cryopyrin -associated periodic syndrome (CAPS), etc. are representative. Autoinflammatory syndrome, unlike autoimmune diseases in which adaptive

immunity is the subject, plays a large role in innate immunity and diseases in which innate immunity is the main subject are also broadly classified. For example, the systemic type of juvenile idiopathic arthritis in the pediatric department shows high clinical symptoms and clinical course different from the joint type with strong general symptoms accompanied by high fever, but it is classified as autoinflammatory syndrome. Likewise, collagen diseases include adult onset Still's disease, Behcet's disease and so on. In the clinical setting, autoinflammatory syndrome occupies an important position in the differential diagnosis of unknown fever, and became known as the fourth unknown fever after three major unknown fevers (infectious disease, malignancy, and collagen disease). There are joint symptoms in many of the autoinflammatory syndromes. Epidemiological investigations of each autoinflammatory syndrome show joint symptoms such as arthritis in 30.2% of FMF, 59.1% of TRAPS, and most of CAPS. Especially, the joint findings of Blau syndrome and Nakajo/Nishimura syndrome are distinctive. As the pathology of autoinflammatory syndrome progresses, new autoimmune inflammatory syndrome and its disease genes have been identified each year. Many of the autoinflammatory syndrome arise due to abnormality of huge protein complex inflammasome, but in recent years the function of each inflammasome (NLRP3, NLRP1, NLRC4, AIM 2, Pyrin) has been elucidated. There are diseases in which autoinflammatory syndrome research is important in considering the pathology of rheumatic and collagen disease. A 20 haplo insufficiency showing symptoms similar to Behcet's disease, ADA 2 deficiency exhibiting symptoms of polyarteritis nodosa, Aicardi-Goutières syndrome (AGS) showing symptoms similar to systemic lupus erythematosus. Although the number of patients with autoinflammatory syndrome is small, the role of inflammation-related molecules clarified from clinical studies of autoinflammatory syndrome is important as a point of contact with rheumatic and collagen disease and it is becoming a breakthrough.

LS31

The study of immune systems and its clinical applications, including development of biologics focusing on IL-6

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Conflict of interest: Yes

The immune system is categorized into two systems, innate immunity and adaptive immunity. These systems sophisticatedly interact and overlap, in which cell-cell contacts and cytokines play critical roles. Cumulative achievement in immunological research fields have made significant contributions to the development of biologics for immunological disorders, which target the inflammatory cytokines such as TNF-a and IL-6 and co-stimulatory molecules such as CD80/CD86-CTLA-4. Here I briefly overview the study of immune systems and its clinical applications including IL-6/IL-6R and related signals. In addition, I will discuss the involvement of IL-6-meidated signals in our semaphorin research and immunometabolism.

LS32-1

A Clinical Update in Psoriatic Arthritis

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Conflict of interest: Yes

The prevalence of psoriatic arthritis (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. Further improvements in awareness of this disease entity is necessary to allow patients to receive early and appropriate care. Another potential problem is misdiagnosis as rheumatoid arthritis (RA) or another joint condition. A recent systematic literature review reported that the 2010 ACR/EULAR RA classification criteria have a moderate specificity of 61%. However, clinical application of these criteria are is only valid after careful consideration of alternative diagnoses. Awareness of clinical characteristics of PsA, including both articular and extra-articular manifestations, is essential for this process, especially because clinical characteristics of PsA are highly variable across patients. In this session, we aim to characterize the distinguishing clinical features of PsA in Japanese patients, which will allow us to improve both under-diagnosis and misdiagnosis of an the increasingly treatable disease, and emphasize the need for early diagnosis and appropriate differential diagnosis. Finally, the treatment guideline and recommendation for PsA is changing constantly with the advent of new therapies in the EULAR, ACR, and GRAPPA internationally. I would introduce a current treatment strategy "T2T" and updated guidelines for PsA.

LS32-2

UPDATE of axial spondyloarthritis

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Conflict of interest: Yes

Ankylosing spondylitis (AS), a prototype of Spondyloarthritis (SpA), is a disorder causing chronic inflammation of axial joints, such as sacroiliac joint (SIJ) and spine, following new syndesmophyte (Synd) formation and irreversible bony ankylosis. Considering predominance of axial or peripheral involvement, SpA could be currently classified as axial SpA (axSpA) including non-radiographic axial SpA (nr-axSpA) as early or mild axSpA and peripheral SpA (pSpA) due to ASAS criteria. In axSpA, mainly AS, it is recently thought that genetic factors including HLA-B27, mechanical stress and gut inflammation activated IL-23-IL-17-TNF pathway, and caused enthesitis following Synd formation. Moreover, as extrarticular manifestations, uveitis, inflammatory bowel disease, psoriasis and aortic regurgitation could also be associated. We also need to pay attention to cardiovascular event. After assessment of inflammatory back pain, we need to promptly evaluate X-ray and MRI of SIJ and spine. Especially in diagnostic MRI, it's also important to assess not only BME on STIR but also erosion and fat metaplasia (FM) on T1WI. Notably, it's indicated that BME and FM of SIJ and spine could predict the radiographic progression. Currently, as the treatment for axSpA, NSAID and physical therapy are initiated and then TNF inhibitors (TNFi) are considered according to ASAS/EULAR/ACR strategy. The long-use outcome of TNFi over 4 years showed that long-term TNFi could significantly prevent Synd formation and progression. Furthermore, it has recently reported that TNFi had good efficacy for early axSpA including nr-axSpA for 3 years. New potential agents other than TNF inhibitor are also recently noticed. Especially, the use of IL-17 inhibitor for 4 years has recently reported to have good efficacy. Moreover, clinical trials of IL-12/23 and JAK inhibitor for axSpA (AS) are in progress. Thus, the diagnostic and therapeutic strategy for axSpA is globally established and goes on, and it's time to establish the diagnostic and therapeutic strategy in Japan.

LS33

Surgery and drug therapy in rheumatoid arthritis

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Conflict of interest: Yes

Recent advance in the treatment strategy markedly improved the disease activity of rheumatoid arthritis (RA) patients. In particular, it has been reported that biological DMARDs and targeted synthetic DMARDs not only improve the disease activity but also ameliorate joint destruction of RA patients. We investigated the changes in clinical outcome, treatment, and incidence of orthopedic surgery in RA patients using the Japanese nationwide cohort database, NinJa (National Database of Rheumatic Diseases by iR-net in Japan), from 2004 to 2014. The incidence of orthopedic surgeries in patients with RA consistently decreased from 72.2 pro-

cedures per 1000 patients in 2004 to 51.5 procedures per 1000 patients in 2014. In particular the number of total knee arthroplasty and total hip arthroplasty was markedly decreased. Disease activity and functional disability improved significantly over this decade. The proportions of patients receiving methotrexate and biologic disease-modifying antirheumatic drugs were significantly increased. In conclusion, the overall incidence of orthopedic surgeries in patients with RA significantly decreased, accompanied by improved clinical outcomes because of the expanded use of effective drugs. However, the declining trend differed between procedures or locations. The results from the present study suggest that there might be a change in supply and demand for orthopedic surgeries.

LS34-1

Differential diagnosis of seronegative rheumatoid arthritis (RA) -Hypophosphatasia (HPP)-

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Conflict of interest: None

RA is a common disease afflicting 0.6-0.7 percent of the Japanese population. Recent advances in diagnostic imaging and in pharmacotherapy has enabled to set complete remission without pain, joint destruction, and minimal effects on activities of daily living (ADL) as a practical therapeutic target; therefore, it is important to diagnose RA as early as possible and design appropriate therapeutic approaches. According to the American College of Rheumatology/European League against Rheumatology Classification Criteria, RA is diagnosed based on the number of joints with swelling and/or tenderness, serological reaction, inflammatory reactions, and disease duration. However, it is known that sensitivities of serological reactions such as rheumatoid factor and anti-cyclic citrullinated peptide antibody are relatively low. Therefore the differential diagnoses particularly among diseases such as early RA, psoriatic arthritis, spondylitis, fibromyalgia and other conditions exhibiting musculoskeletal symptoms including arthralgia are important. Detailed interviews and careful assessment of medical histories, physical examinations and X-ray images would help identify key unrecognized signs and symptoms for the diagnoses. Diseases exhibiting polyarthralgia which has recently become treatable include a disease called HPP. Onsets of the disease vary from in utero to adult. Due to variable and unspecific symptoms especially old children and adults, HPP may be easily overlooked. HPP is a hereditary metabolic disease caused by decreased alkaline phosphatase (ALP) activity due to the mutation of the *ALPL* gene that encodes ALP involved in bone mineralization. HPP is mostly known to develop perinatally, in infants, and in children. However, it is also known to develop in adults accompanying various symptoms, including musculoskeletal pain, muscular weakness, chondrocalcinosis, and stress fractures. The symptoms and severity vary among patients, which impairs their ADL and quality of life. The differential diagnosis of HPP can be made by confirming low blood levels of ALP as well as elevated urine phosphoethanolamine as a supplementary abnormal laboratory value. This lecture will outline the disease characteristics pf polyarthritis which rheumatologists encounter and should know, focusing particularly on differential diagnosis of seronegative rheumatism. Furthermore, as a recent topic, the pathogenesis and points of diagnosis HPP, which rheumatologists should know, will be explained. I hope this lecture help rheumatologists diagnose the “Don’t miss disease”.

LS34-2

A Case of Hypophosphatasia (HPP) and Enzyme Replacement Therapy (ERT)

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Conflict of interest: None

HPP is an inherited disease caused by a loss-of-function mutation of the *ALPL* gene coding tissue-nonspecific alkaline phosphatase (TNSALP). Recently, an enzyme replacement therapy (ERT) with asfotase alfa (AA) was approved, and dramatically improved the prognosis of perinatal and infantile HPP patients. Additionally, significant improvements in growth, muscular strength, motor function, activities of daily living (ADL), and quality of life (QoL) were observed after 5 years with AA in pediatric patients aged 6-12 years. The main adverse events (AEs) were injection site reactions but none of them were serious. In this presentation, the efficacy and safety of AA based on the result of clinical trials as well as my experience of AA in an adult HPP case with myopathy related to HPP will be introduced. The patient was a 37-year-old man who has a heterozygous mutation, c.1559delT, in *ALPL* that caused the ALP activity loss and was identified by familial study of his first child who died of perinatal HPP (homozygous mutation of c.1559delT) at age 2. He had experienced bone fractures twice. He started to suffer from muscular weakness and myalgia in lower limbs at age 26. The symptoms gradually worsened; therefore, muscle biopsy was performed at age 30. No morphological abnormality was observed histopathologically and no marked abnormality in electromyography was detected. The ALP level was slightly low (50-80IU/L). Based on these observations, he was provisionally diagnosed as having myopathy caused by HPP. At age 34, he participated in a physician-initiated clinical trial of AA and the ERT was started. After 2 months, pain assessed by the visual analogue scale [VAS] was vastly improved and muscular strength was regained. Various symptoms were worsened by dose reduction or withdrawal of AA, and a correlation between the dose and pain reduction was found. No treatment-related AE has been observed. After 3 years treatment, he has become able to work due to improvement of his symptoms. Based on remarkable efficacy of AA, his myopathy was confirmed as a HPP related symptom. Adult HPP presents easy-to-fracture, bone deformity, bone pain, myalgia, muscle weakness, and tooth abnormality besides low ALP. Because manifestations, age of onset, and severities in HPP are diverse, it is difficult to make a differential diagnosis in cases with muscular symptoms as described. Now because AA brings dramatic change to HPP treatment, accurate diagnosis of HPP becomes more important and then accumulating of reliable clinical data and increasing awareness of HPP are further required.

LS35

PsA treatment for improving patients’ Quality Of Life

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Conflict of interest: None

Psoriasis is a typical disease of inflammatory keratosis, and prevalence in Japan at 0.34%. Psoriatic arthritis (PsA) is characterized by arthritis / spondylitis / dactylitis / enthesitis occurs in about 10 to 15% of psoriasis and there are many comorbidities with metabolic syndrome (such as obesity 26%, hyperlipidemia 23.9%, diabetes 15.1%, hyperuricemia 20.9%, hypertension 23.2%, hepatic enzyme disorder 29.2%). Especially young people are regarded as having a high incidence of myocardial infarction. It is regarded as a problem. In addition, about 30% of PsA is associated with spondylitis, so if proper treatment intervention is not done at an early stage, ankylosing bone will occur and the patient’s quality of life will be severely impaired, so the rheumatologist is unknown PsA needs to be taken into account as one of the differential diagnoses of patients who have chronic low back pain or arthritis coming home. What is the optimal treatment method to obtain better quality of life for patients with PsA? The first is to improve metabolic-related comorbidity more effectively by positively conducting basic guidance such as living guidance, exercise therapy, nutritional guidance and so on. This is considered to be one of the key to maximizing the effect of drug therapy and contributing to the increase of continuation rate. Another treatment method is drug treatment. Biological products have become available for psoriasis and psoriatic arthritis in Japan in 2010. As a result, psoriasis & PsA treatment has changed dramatically, contributing to improvement of patient’s QOL. When considering the optimal therapeutic drugs, it is necessary to think about what kind of disease condition occurs in bone / joint in PsA. What kind of factor triggers the development of arthritis? Why does inconsistency such as bone erosion and bone formation occur at the same lesion site? It has recently been reported that IL-17A is deeply involved in these pathologies as one of the central roles. In this lecture, I would like to talk about the involvement in the department of PsA patients with many metabolic syndrome and the relationship between the bone joint / enthesitis and IL-17 in PsA where new findings

have been confirmed in recent years and the results of the treatment.

LS36

Distinctive Clinical Aspects of Pulmonary Arterial Hypertension Associated with Connective Tissue Diseases

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Conflict of interest: None

Recent studies have clarified that pulmonary arterial hypertension associated with connective tissue diseases (CTD-PAH) has some distinctive clinical aspects from other PAH, such as high prevalence, venous and cardiac involvement, less favorable outcome, helpfulness of detection algorithm, response to immunosuppression, pre-PAH conditions in borderline pulmonary arterial pressure, and coexistence of interstitial lung disease. In the management of CTD-PAH, there still remain important issues to be solved, such as discrimination of the case coexisting WHO group 1' (pulmonary veno-occlusive disease), group 2 (left heart disease), and/or group 3 (interstitial lung disease) pulmonary hypertension, the optimal regimen of immunosuppressive therapy, and the management of borderline pulmonary arterial pressure case. In this seminar, by focusing on these distinctive aspects, we discuss how to provide an efficacious and safe management of CTD-PAH and garner attention to areas where further evidence is desired. We also discuss the role of riociguat, which uniquely stimulates soluble guanylate cyclase in a nitric oxide independent manner, in the treatment of CTD-PAH, particularly of PAH associated with systemic sclerosis, a most challenging form of PAH.

LS37

Elementary knowledge of how to make early diagnosis and how to evaluate disease status in patients with systemic sclerosis

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Conflict of interest: Yes

Currently, systemic sclerosis (SSc) remains an intractable disease with poor functional and survival outcomes, which lacks evidence-based treatment strategies. This is due partly to difficulty in developing anti-fibrotic agents, but, more importantly, to lack of understandings of natural disease course and highly variable clinical presentation of the disease by healthcare providers. For example, concept of "disease activity", "remission", and "flare" is lacking for representing disease status of SSc. Pathologic vascular changes progresses slowly and latently during the course of the disease, whereas fibrotic processes spontaneously subside in some point of the disease unless progression to severe functional impairment. Acute exacerbation is rare during the course except renal crisis. At this moment, disease severity indices, which reflect both ongoing fibrotic process and accumulation of irreversible organ damage, are the only general measure of SSc disease status. Since current treatment goal is intervention of natural disease course and resultant suppression of damage accumulation, disease-modifying treatment is the main strategy rather than remission induction/maintenance treatment. Therefore, it is useless and meaningless without full understandings of unique features of SSc, and discussion of treatment responses in observational cases without adequate controls is always inadequate and often leads wrong prejudice. Tremendous efforts of basic researches successfully lead to implementation of a number of clinical trials of potential anti-fibrotic agents in SSc patients. However, if clinical trial results turned out positive, these potential agents are indicated only for a small subset of patients with certain disease duration; it is far from enthusiasm for developing "SSc treatment drugs". This seminar features basic knowledge of diagnosis and evaluation of disease status in patients with systemic sclerosis before the dawn of SSc-treatment era.

LS38-1

Technique of communication with patients that supports decision making by patients and improves motivation toward treatment

Hiroaki Harai
Japan Association of Motivational Interviewing

Conflict of interest: None

Motivational Interviewing (hereinafter referred to as MI) is effective when proposing a new treatment method to patients in the field where new drugs are developed one after another within a relatively short period of time. Even though an effective drug is launched, it is meaningless unless patients actually try it. Healthcare professionals (HCPs) tend to simply show only the facts to their patients, or explain by saying "this works extremely well" or "the evidence is so and so" based on the view point of experts. When a patient makes a decision to change the familiar treatment method to something else, it is desirable to provide information from the patient's standpoint. Now, MI is a useful technique that strategically and intentionally brings out the feeling of the patients themselves to change. The more HCPs are at the cutting edge, the more they are experts, the more they want to use new and the best treatment methods and they think it is natural for patients to follow the best treatment. If a patient does not follow the treatment, they think the patient will do so if they explain in further detail. However, the method that a HCPs teaches what they want to teach is not always useful for anyone. Offering more information to a patient who resisted when the information was given the first time would be counterproductive. If information is provided and is not appropriate for the patient's desire to "know," it strengthens the patient's feeling, i.e., "I don't want to know". Ultimately, if a HCPs comes to feel that "this patient is stubborn and bigoted", there is a huge gap that cannot be overcome between a HCPs and patient. What can we do to avoid creating such a gap? How can patients themselves be guided to change their behavior without using forcible guidance? I would like to talk about an overview of MI and actual clinical examples to show you that with MI you can lead the conversation with patients in constructive direction without going around and around.

LS38-2

Practice of guiding RA patients utilizing the technique of "Motivational Interviewing"

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Conflict of interest: None

Even though a doctor suggests a treatment that seems to be the most appropriate for the patient, the patient often does not accept it. In such a case, it is effective to use the "Motivational Interviewing" technique as a method to promote changes in patient behavior. In a situation where the patient has a negative feeling such as "I do not want to change the treatment", or "I do not want to take medicine", instead of trying to convince the patient by saying something like "If you do not change your treatment, it will get worse and worse" or "If you do not take medicine your pain will come back", "Motivational Interviewing" is used to determine the reasons why the patient has become negative about treatment, what are the obstacles, what the patient wants to do in future and other problems points of each patient. It is important to obtain permission on providing information related to treatment after using the "Motivational Interviewing" technique to understand the problems of the patient themselves and after the patient themselves become ready to accept the treatment. If a situation can be created where the patient has ears to hear correct knowledge and information about treatment and the patient positively faces the treatment on their own will, it becomes possible to approach to improve satisfaction with drug treatment. I am using the Motivational Interviewing skill in outpatient-basis nursing consultation to provide advice to patients. At first, a patient is negative about the treatment proposed by the doctor. However, after the meeting, the patient says "Inside of my head is cleared and my body feels lighter" and then leaves the meeting room. In the next medical examination, the patient themself speak out, saying "I am going to try the new medicine" and there are many cases where doctors are surprised about the change in their patients. If many medical professionals acquire the "Motivational Interviewing" skill and exercise it in medical consultation settings or when patients talk to them, I believe that it becomes possible to achieve the treatment goals of individual patients and provide high quality care to rheumatism patients.

LS39-1

Characteristics of Connective Tissue Disease Associated Pulmonary Arterial Hypertension in the Elderly

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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 (CTD-PAH) is still poor. Lung disease, left ventricular disease, perivascular fibrosis, and pulmonary venous involvement has been reported in patients with CTD-PAH patients, and supposed to associated with the poor improvement in clinically with the PAH targeted therapy. Aging also associated stiffening of pulmonary vasculature and heart, and the frequency of diagnosis with PH in the elderly has been increasing, especially in the CTD-PAH patients. Although elderly PAH patients were supposed to show the poor prognosis and poor quality of life even introduction of PAH-specific drug therapy, there was little data as to the clinilcal characteristics of elderly PAH patients. In this seminar we review the characteristics of connective tissue associated pulmonary arterial hypertension in the elderly, and also discuss the pathophysiology and therapeutic strategy in the elderly CTD-PAH patients.

LS39-2

Characteristics of Pulmonary Arterial Hypertension Associated with Connective Tissue Disease (CTD-PAH) - Recent approach for the improvement of the prognosis

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Conflict of interest: None

More than half of patients with pulmonary arterial hypertension (PAH) are explained by complication with connective-tissue diseases (CTDs) in Japan. Emergence of 3 classes of vasodilators, such as endothelin receptor antagonists, phosphodiesterase 5 inhibitors and prostanoids, brought the bless to the patients with PAH, such as improvement of their prognosis. However, even choices of treatment arms are increasing, the prognosis of CTD-PAH patients is still worse compared with that of patients with idiopathic PAH. One of reasons is that CTDs are systemic diseases and each patient may have various organ involvements other than pulmonary arteries. Thus, each CTD patient with pulmonary hypertension (PH) can be classified not only into group 1 (PAH), but group 1' (pulmonary veno-occlusive disease (PVOD)), group 2 (PH due to left heart disease), and/or group 3 (PH due to lung diseases and/or hypoxia) of the clinical classification. Recent progress associated with CTD-PAH is focused on two approaches, 1) early diagnosis and initiation of the treatment and 2) application of immunosuppressive treatment (IS). As for the former approach, an annual screening of PAH, which is recommended in 2015 ESC/ERS guidelines especially for SSc, is a major topic. Furthermore, the importance of follow-up of patients with borderline mean pulmonary arterial pressure, the emergence of novel modalities for detection of PAH such as the stress echocardiography, and the development of algorithm to screen candidates for right heart catheter test using multiple modalities, such asDETECT algorithm, are also the highlights. As for the latter approach, the efficacy of IS treatment is expected and reported especially in SLE, MCTD and Sjogren's syndrome. However, only few reports showed which patients were good candidates for the IS treatment or expected to have a better, long-term prognosis with IS. In this session, we will summarize the recent progress and discuss the topics with our own data.

LS40

Reimaging the physician-patient communication ~How to get the most from a time-pressured office visit~

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Conflict of interest: Yes

Limiting the intended audience of physicians to 30, this luncheon seminar shall be conducted in a workshop including a lecture, discussions, and role-play. CONVERSATIONS in MOTION (CIM) is a communication technique program designed for physicians to improve physician-patient communications in the time-pressured reality of office visit. Developed collaboratively by linguistic and communication experts and rheumatologists in and out of Japan, the effectiveness of each techniques in the program have been empirically verified. CIM is comprised of four modules: Module I: Shared decision making (SDM); Module II: Empathy and Trust; Module III: Practice efficiency; and Module IV: Medication adherence. This luncheon seminar shall focus on Module 1. SDM represents an evolution from informed choice, and it is a concept that physician/patient bi-directionally share information and make a decision. Those among the participating physicians who already practice this idea are urged to stop and review its process. CIM conceives of the process of shared decision making as consisting of six steps. First the physician invites the patient to participate in the decision making regarding the treatment. Then the physician presents treatment options and provide information on benefits and risks, and assists in evaluating options based on their goals and concerns. Furthermore the physician facilitates the decision making process and continues to assist patients to follow through on their decision. Three critical points in this process are setting expectations, weighing pros/cons, and eliciting patient preferences. The details will be explicated in the lecture part of the workshop, to be followed by group discussions on selected points, so they may be put to use in day-to-day practice. We look forward to a lively discussion at this workshop.

Evening Seminar

ES1-1

Reconsideration of IL-6 signal blocking therapy - From global and Japanese evidence -

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Conflict of interest: None

Rheumatoid arthritis (RA) is chronic inflammatory disease that carries a substantial burden for both the individual and society. The inflammatory milieu in the synovial compartment of RA is regulated by a complex cytokine and chemokine network. Tumor necrosis factor (TNF) and interleukin-6 (IL-6) are essential to the process, and these cytokines lead to the induction or aggravation of the inflammatory response, and the progression of joint destruction and functional disability. IL-6 inhibition is achieved by treatment with tocilizumab (TCZ), which is a humanized monoclonal antibody directed at the IL-6 receptor (R). Another IL-6R inhibitor has recently been approved in Europe and antibodies to the IL-6 ligand are developing. Biologic (b) DMARDs should preferably be combined with a conventional synthetic (cs) DMARD, but if a monotherapy of a biological DMARD must be given because of intolerance of all csDMARDs, then IL-6 inhibitors are the preferred bDMARD, since their efficacy is superior to TNF inhibitor monotherapy. A therapeutic revolution in the treatment of RA such as the advent of bDMARDs in the past decade has transformed articular and systemic outcomes. However, many open issues remain in spite of advances made over the past two decades. For example, we do not understand if profound responses are elicited by different agents in the same, totally different, or overlapping RA patient populations. Additionally, many patients do not reach the target of remission. Thus, setting a treatment target of remission or at least low disease activity, following patients regularly using composite disease activity measures like CDAI, and adapting therapy rapidly if the targeted state is not achieved within few months leads to better outcomes than routine care. In this seminar, recent insights into these aspects of RA, from diagnosis to treatment strategies, will be addressed, focusing on IL-6 inhibition.

ES1-2

From the discovery of IL-6 and the development of anti-IL-6R anti body

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Conflict of interest: None

A series of our studies in IL-6 have revealed that it has a pleiotropic activity in various tissues and cells and its deregulated expression is responsible for several chronic inflammations and hemopoietic malignancies. Humanized antibody against 80kd IL-6R (Tocilizumab) has shown therapeutic effect in RA, JIA, Castleman's diseases and LVV. Recently, TH17 is shown to be responsible for the pathogenesis of autoimmune diseases and IL-6 together with TGF-b are essential for the induction of TH17. We identified a new transcription factor required for Th17 cell induction. This molecule, aryl hydrocarbon receptor (Ahr) interacts with Stat1 and Stat5 and abrogate their negative activity in the induction of Th17 cell differentiation. Experimental arthritis is completely abrogated in T cell-specific Ahr-deficient mice. Therapeutic effect of Tocilizumab confirmed that over and constitutive-production of IL-6 is responsible for the pathogenesis of autoimmune diseases. Then, the question to be asked is how is IL-6 production regulated. We identified a novel molecule called Arid5a which binds with the 3'-UTR of IL-6 mRNA and protects its degradation by competing with Regnase-1. Interestingly, this molecule is present in nuclei and inflammatory stimulation induced translocation of Arid5a from nuclei into cytoplasm and it competes with Regnase-1 for the protection of mRNA of IL-6. Arid5a binds with the 3'-UTR of not only IL-6mRNA but also STAT3 mRNA in TH17 cells as well as T-bet mRNA in TH1 cells. Thus, Arid5a accelerates Th17cell differentiation in inflammation as well as exacerbation of IFN-γ-mediated septic shock. All these results indicate that Arid5a is one of the key molecules for inflammation as well as the development of septic shock. The results also suggest the therapeutic potential of anti-agonistic agents for Arid5a in the prevention of various incurable inflammatory diseases and septic shock.

ES2-1

The mechanism of ACPA production and modification and the effect of Abatacept in rheumatoid arthritis

Motomu Hashimoto
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Conflict of interest: Yes

Anti-citrullinated protein/peptide antibodies (ACPA) are a useful marker for the diagnosis of RA and for the prediction of joint outcome. Protein citrullination can be induced by peptidyl arginine deiminase at the site of inflammation. However, the fact that ACPA can be detected years before the joint symptom suggests that the protein citrullination might occur at the sites of inflammation other than in the joint, for example, in periodontitis and in lung diseases. The titer of ACPA in RA are higher than those in periodontitis or in lung diseases. Follicular helper T cells help B cell production of high titer of ACPA in RA. In addition, ACPA in RA are different from those in periodontitis or in lung disease in terms of the modification of Fc portion of IgG. Th17 cells driven by the cytokine IL-23 are reported to be responsible for the modification. Abatacept, a co-stimulatory molecule inhibitor, might inhibit ACPA production and modification by suppressing follicular helper T cells and Th17 cells. In this seminar, the recent topics about the mechanism of ACPA production and modification and the effect of Abatacept will be discussed.

ES2-2

Pathological involvement of T and B cells in RA

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Conflict of interest: None

Antibody production by B cells requires two machineries, that is, cytokines produced by T cells and cell-cell interactions between T and B cells. In 1980', a series of cytokines produced by T cells such as IL-4, IL-5 and IL-6 have been identified. Biologics against these cytokine-mediated signals are now used for clinics. On the other hand, co-stimulatory molecules which are critical for B cell activation through the contacts with T cells have been determined as well. The representative molecules are CD80/CD86-CD28, of which interactions are demonstrated to be critical for T cell activation and differentiation through the contacts with antigen-presenting cells. Of note, once T cells are activated, the expression of an inhibitory molecule CTLA-4 is induced on the cell surface of T cells, resulting in regulating T cell activation. Here I briefly overview the study of immune systems and its clinical applications includingCD80/86-CTLA-4 and discuss the implications of inhibitory co-stimulation in the pathogenesis of rheumatoid arthritis.

ES3-1

Trends of biosimilar use for treatment of rheumatoid arthritis in the world

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Conflict of interest: Yes

The national medical expenses of Japan continue increasing, primarily owing to drastic increase in direct drug costs. There is no doubt that the development of new therapeutic agents is necessary for overcoming intractable conditions, but, as the compensation, it is an urgent issue to increase the use of generic drugs to reduce medical expenses. In terms of the biologic disease-modifying anti-rheumatic drugs (DMARDs), which have greatly contributed to improvement of rheumatoid arthritis (RA) management, biosimilars (BS) are already marketed and the number of BS choices is expected to increase in future. BS is defined as a biologic medical product that is almost an identical copy of an "originator" prod-

uct. However, unlike generic drugs of small molecules, biologics exhibit high molecular complexity, and is quite sensitive to changes in manufacturing processes, leading to potential differences in efficacy and immunogenicity between bio-originators and BS. In EULAR recommendations 2016 updates, if the treatment target is not achieved with the first conventional synthetic DMARD strategy, addition of a biologic DMARD, including European Medicines Agency- or Food and Drug Administration-approved BS, is recommended. The recently published consensus-based recommendations for the use of BS to treat rheumatologic diseases reported overarching principles and consensus recommendations, encompassing considerations regarding clinical trials, immunogenicity, extrapolation of indications, switching between bio-originators and BS and among BS, and cost. In this seminar, roles of BS in our daily clinical practice will be discussed based on updated information.

ES3-2

Biological disease-modifying antirheumatic drugs -Present and Future-

Katsuhiko Takabayashi
Kanae Hospital

Conflict of interest: Yes

The authors have been analyzing claims data of 12 national university hospitals (CISA). We analyzed 8,304 cases with rheumatoid arthritis injected with biological disease modifying antirheumatic drugs, 6,425 cases are naïve, while 1,882 cases are those switched. Tocilizumab and abatacept are most administered in 2017, and retention rates are highest in tocilizumab for both naïve and switched cases. Infliximab BS, the first biosimilar agent in this country are administered only 1.9% in total patients and 6.8 % in infliximab related drugs. Though the effect of infliximab BS is comparable as original infliximab, usage of biosimilar is still limited in this country. However in the future, we cannot neglect biosimilar agents from economical point of view.

ES4-1

The current situation and treatment issues for WoCBA (Women of Child-Bearing Age) Patients - The mechanism to maintain pregnancy in terms of immunity and its failure -

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Conflict of interest: None

In recent years, with the development of biological products, women with RA who had given up on childbearing are starting to achieve remission and think positively about pregnancy and childbirth. As 35% of patients with RA are aged 20-39 years, so approximately 175,000 women have a chance of getting pregnant and giving birth. Since the low birthrate in Japan is a serious problem, it is important that patients with RA achieve remission and are guided through pregnancy and delivery to increase the birth rate. Although data sharing between internists, orthopedists, and obstetricians before pregnancy is needed, only approximately 50% of pregnancies in women with RA are planned according to our study supported by Health and Labor Sciences Research Grants, the Health, Labor and Welfare Ministry in Japan. As many pregnant women with RA are treated for infertility, such as ovulation induction (5.7%), in vitro fertilization (13.6%), and microinsemination (7.9%), collaboration with fertility clinics is also necessary. When we compared the number of births by women with RA with the expected number from vital statistics using data from a multicenter database (NinJa); the number of births by women with RA was only 42.2% of the expected value (i.e., they are hesitant to get pregnant). We encourage the doctors of patients with RA to inform them that they can get pregnant after remission. As regulatory T cells increase during pregnancy, RA symptoms resolve in many cases. Anti-TNF-α antibodies are used to treat implantation failure (a type of infertility) and recurrent miscarriages or stillbirths in Europe and the USA, and the risks of infertility, miscarriage, and stillbirth are reduced after anti-TNF-α antibody therapy. The risk of teratogenicity caused by the anti-TNF-α antibody has also been denied. Anti-TNF-α antibodies, prednisolone (up to 15 mg/day), and azathioprine are safe to use during pregnancy. Cyclosporine and tacrolimus are also allowed during pregnancy under certain circumstances. Drugs contraindicated for use in pregnancy include methotrexate, leflunomide, mizoribine, bisphosphonate, ARB, and ACE inhibitors. NSAIDs are contraindicated in late pregnancy. When patients wish to get pregnant, contraindicated drugs should be swapped with safe ones. Women taking methotrexate or leflunomide should not breastfeed. Anti-TNF-α antibody preparations can be used during breastfeeding as little is excreted in breast milk and absorption from the gastrointestinal tract is poor. We aim to ensure that as many patients with RA as possible can give birth.

ES4-2

Discourse on Women of Child-bearding age (WoCBA) around the world, and recent treatment results of RA WoCBA in Japan

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Conflict of interest: None

The treatment of Rheumatoid Arthritis (RA) has largely progressed over the past decade and undergone a paradigm shift. With the new classification standard formulated by ACR/EULAR in 2010, the sensitivity for early RA diagnosis improved. Advocating the 'treat to target' (T2T) method, the process to achieve the treatment goal was clarified, and a treatment strategy with a clear 'goal' became established. Needless to say, for this paradigm shift, the progress in medication based on biological formula also played a major role. In the 'Recommendations' formulated by EULAR in 2016, it was specified how to proceed after successful treatment, unrelated to the treatment aims (remission, or low disease activity). Since then, the therapeutic strategy to retain patients' improved condition has been heatedly discussed. At the same time, despite the progress in RA treatment, there are still patients who suffer from life with RA. One example of such patients is women of childbearing age (WoCBA). The majority of them are female RA patients who developed RA aged between 30 and 50. For most women, this aforementioned period tends to be centred upon happy life events such as love, marriage, pregnancy/childbirth, and childrearing, among others. In our hospital, we believe that RA WoCBA patients should not be deprived of their right to enjoy these events to the same degree as healthy women, for which we increasingly focus on treatment of RA WoCBA patients. In this presentation, we hope to share the results of our patient interviews and their treatments. We will introduce our doctors' and nurses' strategies and tools to understand patients' child-bearing wishes, to provide guidance on the treatment process, and to eliminate their fears and doubts among patients. This presentation provides ample examples of successful cases, sharing our patients' experiences and evaluations of their treatment and childbirth.

ES5-1

Quality of BS Preparations: Comparability with Forerunner Biopharmaceutical Products

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Med.Co.LTA PS Clinic

Conflict of interest: None

Biological preparations, such as antibody preparations, are indispensable pharmaceutical products not only in advanced healthcare, but also in routine clinical practice. Drug development faces diverse obstacles such as target identification, synthesis and industrialization of candidate protein, and evaluation of safety and efficacy through clinical trials. Hence, drugs in this category are expensive compared to preparations of low-molecular-weight substances, leading to non-negligible economic burden on society and individual patients. Therefore, there is a demand for biosimilars, which are comparable to forerunner products in terms of efficacy and safety. Bioequivalence test is not required if chemically synthesized low-molecular-weight substances are developed as active ingredients for intravenous injections. The pharmacokinetics of oral preparations in blood can vary based on the nature of active ingredients and formulation technology. Therefore, a bioequivalent test to compare these preparations with the forerunner product is conducted in healthy volunteers; phase 2 and 3 studies are usually unnecessary. Equivalent pharma-

cokinetics implies equivalent efficacy and safety. In biological preparations, particularly antibody preparations and those used for rheumatoid arthritis, the amino acid sequence of the forerunner product has been made public; however, detailed information, such as material and size of flasks used for manufacture and frequency of agitation, has not been published. Biological preparations contain impurities, although only in small quantities. The preparations must demonstrate equivalence in time course of blood levels (PK) [A1] compared with the forerunner product in healthy adults. Next, a phase 3 study must be performed in patients to verify equivalence in efficacy and safety. Biosimilars are marketed through these steps. In today's presentation, I will explain how to conduct clinical studies on biosimilars.

ES5-2

Clinical Efficacy of Biosimilars: Data from clinical studies

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

Conflict of interest: Yes

Biosimilars are one of the options in modern medical treatment of rheumatoid arthritis in Japan. In European countrits, where national health insurance system is used as in Japan, biosimilars has been widely prescribed in the recent years. Large clinical data on efficacy and safety are available from these countries, but differences due to enviromental and racial variaruciation can be expected. It is crutial to evaluate clinical data from Asian countries to apply the important therapeutic modality.

ES5-3

Biosimilars for rheumatoid arthritis treatment from an economic and patients' perspective

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Conflict of interest: None

An increase in the medical cost of rheumatoid arthritis (RA) with the advances in therapy has been causing concern and it is becoming a significant burden both on the patients and on society. In RA, which is a chronic disease with a long disease duration, not only the direct, but also the indirect costs are a great concern. However, to our knowledge, pharmacoeconomic analyses of RA have not yet been performed in Japan. We evaluated the direct cost and working impairment in Japanese RA patients in the IORRA (Institute of Rheumatology, Rheumatoid Arthritis) cohort. It was observed that patients' economic burden through both direct and indirect costs increased with progression of functional impairment and a decrease in the quality of life. Therefore, it was suggested that controlling disease activity from an early stage could reduce the total medical cost, including not only the direct, but also the indirect cost. Furthermore, pharmacoeconomic analyses evaluating both clinical effectiveness and medication cost should be performed, especially for expensive drugs like biologics used to treat patients with RA. As we performed a cost-effectiveness analysis on biologics for RA treatment based on the IORRA cohort, we additionally discuss these findings. Moreover, biosimilars are currently being developed; infliximab biosimilar is already available in the Japanese market, while etanercept biosimilar will soon be available. In contrast, biosimilars are entering the biologics market significantly faster overseas, especially in the European Union. Guidelines for use of biosimilars have been introduced based on these situations, and substantial impact on the cost of RA treatment is expected. Several researches on biosimilars from domestic as well as global will be presented.

ES5-4

The problem and landscape of biosimilar DMARD in Japanese patients with rheumatoid arthritis

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Conflict of interest: None

Presently, around 30% of all patients with RA use high-priced biological DMARDs, increasing the overall medical expenditure related to RA treatment in Japan. According to the estimate by "NinJa2016," the annual medical expenditure for DMARD therapy per RA patient increased linearly from 51,838 Yen in 2003 to 434,513 Yen in 2013, following the widespread use of biological DMARDs. Therefore, instead of attempting to resolve medico-economic issues related to biological DMARDs through achieving bio-free status, we should create an atmosphere where biological DMARDs with reduced prices can be used easily and administered in a stable and continuous manner at sufficient dose levels. To materialize this plan, the price of biological original DMARD should be reduced or the use of biosimilar DMARD whose price is 70% of biological original DMARD should be promoted. The major obstacles from the patients' side are mistrust in biosimilar DMARD in general, misunderstanding that biosimilar DMARD are inferior to original in quality, and misunderstanding that switching from the original is impossible. However, similar misunderstandings are prevalent among physicians in charge in Japan. The obstacles from the side of healthcare provider include the one increase-one decrease principle in hospitals (generic drug adoption leads to discontinuation of purchase of forerunner products), inadequate setting of indications for infliximab, and profit from the difference between NHI price and wholesale price of originals. In case of infliximab, if the dose level or dosing interval is changed among individual patients, the drug is excluded from the coverage of high-priced healthcare support system, resulting in increased financial burden on the patients. However, it is incorrect to say that the future of biosimilar DMARDs in Japan is not bright. Besides biosimilar infliximab in the form of preparations for drip infusion in medical facilities, global development on biosimilar DMARDs to etanercept and adalimumab is underway. Such biosimilars have already been approved in some countries, and take the form of preparations for subcutaneous injection, allowing self-injection by patients. Moreover, these biosimilars can be supplied through pharmacies outside hospitals, facilitating their adoption. In today's evening seminar, I will present the 10 year long-term results of treatment with infliximab and etanercept at Nagoya Medical Center, with new evidence, outline the expectations and perspectives related to biosimilar DMARD to etanercept awaiting approval in Japan in near future.

ES6-1

Synovial change in osteoarthritis

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

Currently, osteoarthritis (OA) is considered a cartilage disease, while rheumatoid arthritis (RA) is regarded as a disease of synovium. This conventional view of OA has been challenged by the results of recent epidemiological studies, which demonstrate that the synovial change is closely correlated with the symptoms and progression of OA. Although these studies suggest that synovial change may be pivotal in the pathology of OA, the mechanism (s) underlying the synovial change in OA has not yet been determined. We conducted a series of studies to elucidate the mechanism (s) underlying the synovial change in OA. Among these studies, a possible clue was obtained through the analysis of proteins released from degenerated cartilage. Considering that the presence of degenerated cartilage is a prerequisite for the synovial change in OA, we analyzed the proteins released from OA cartilage by antibody arrays and Luminex, and identified several proteins that could be involved in the development of synovial change. Several angiogenic factors were among these proteins. In parallel with the above analysis, we conducted a gene expression analysis of the synovial tissues. Based on the correlations in the gene expression, TNF-α was considered a primary inducer of proteinases in RA synovium, while the proteinases in OA synovium seemed to be induced in association with angiogenesis. The activation of the synovial fibroblasts may be another mechanism involved in the proteinase expression

in OA synovium. In OA synovium, fibroblasts may be activated through the degeneration of surrounding matrix, and may come to synthesize MMPs-1 and 3 abundantly. These MMPs are released into the synovial fluid, and may play a role in cartilage degeneration within OA joints. In this presentation, our proposed mechanisms for the synovial change in OA will be presented together with a possible therapeutic strategy for OA aiming at the resolution of synovial pathology.

ES6-2

Utility of biomarkers in rheumatoid arthritis treatment

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Conflict of interest: Yes

Rheumatoid arthritis (RA) is a disease that causes joint destruction rapidly from the early stage and causes irreversible physical dysfunction. In clinical RA, "Treat to target" is suggested as a guideline from the diagnosis to the achievement of the therapeutic goal, study of the therapeutic strategy for maintenance of QOL through the prevention of joint destruction and maintenance of daily living behavior has been advanced There. Therapeutic policy of RA has greatly improved with the introduction of MTX and biological DMARD (bDMARD) clinically. It became possible to aim for clinical, structural and functional remission. Meanwhile, in daily practice, there are many problems to be addressed in the future, such as adding a patient reported outcome in addition to disease activity evaluation, and treatment strategy to prevent secondary inadequate response. In using MTX and bDMARD efficiently, it is useful to utilize inflammatory markers and joint-derived biomarkers in addition to disease activity evaluation as an evaluation index of drug efficacy. Especially biomarkers directly related to joint destruction of rheumatoid arthritis can be used for prognosis prediction. Tsurumai Biologics Communication Registry (TBCR) is a registry launched by Nagoya University in 2008 with the aim of investigating longitudinal cases of bDMARD use cases in RA. We have also reported the evaluation index of effectiveness at the time of using MTX and bDMARD in research using TBCR. A series of studies also examines the possibility of biomarkers. Based on the results of these clinical studies, I would like to discuss the usefulness of biomarkers at this seminar, focusing on the evaluation of bDMARD's efficacy under clinical practice.

ES7

RA Treatment and Respiratory Infection Risk: The Importance of Prevention and the Significance of Vaccination

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Conflict of interest: Yes

It is widely known that rheumatoid arthritis (RA) patients are at a high risk for infection. In addition to having autoimmune abnormalities, RA patients frequently have concomitant disease due to infectious diseases/opportunistic infections, and they are exposed to a serious risk of infection due to the use of immunosuppressive treatments such as steroids, immunosuppressants, and biological agents. Particularly due to the high treatment efficacy seen since the introduction of biological agents, it is thought that the risk of infection has increased due to the ability of these agents to target and suppress inflammatory cytokines. As for TNF inhibitors, while there are increases in tubercular/non-tubercular mycobacterial infections and pneumocystis pneumonia among others, there are also reports of the propagation/proliferation by healthy individuals of resistant strains such as community-associated MRSA, carbapenem-resistant enterobacteriaceae, and ESBL-producing bacterium. In Japan, regarding comprehensive efforts to counter drug-resistance headed up by the Ministry of Health, Labour and Welfare, the 'National Action Plan on Antimicrobial Resistance (AMR) 2016-2020' was announced in April 2016. The most frequent infection in RA patients is pneumonia, and it is reported that primary causative pneumococcal bacteria have the highest frequency of isolation. The importance of prevention is also stressed, with pneumococcal bacteria being indicated as part of the National Action Plan on AMR with a numerical goal of reducing the penicillin insensitivity rate from 48% to 15% or below by 2020. One strategy for preventing of pneumococcal pneumonia is to vaccinate against pneumococcus. Currently, the American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) recommend that adult patients with suppressed immune systems such as RA patients receive both influenza and pneumococcus vaccinations. Additionally, in Japan, the Guidelines for the Use of Methotrexate in the Treatment of Rheumatoid Arthritis by the Japan College of Rheumatology recommend pneumococcus vaccination. Currently, there are two pneumococcus vaccinations that are available for use in Japan in adults 65-years of age or older, the 23-valent pneumococcal polysaccharide vaccine (PPSV23) and the 13-valent pneumococcal conjugate vaccine (PCV13/Prevnar 13). Since June 2014, the indication for PCV13 has been widened to include adult patients 65-years of age or older. In October of the same year, routine immunization with PPSV23 was initiated, and in January 2015, with regards to the use of these two immunizations, a joint committee meeting by The Japanese Respiratory Society and The Japanese Association for Infectious Diseases announced their 'thoughts regarding the use of pneumococcus vaccines in adult patients 65-years of age or older'. At this lecture, I will talk about the importance of preventing pneumonia, introduce the risk of infectious diseases associated with the use of such agents as biologics in RA treatment including cases that I have experienced, while bringing together the various topics and issues we are facing with the transformation of immunology in infectious disease including resistant strains and emerging/re-emerging infectious disease.

ES8-1

Pathophysiology of spondyloarthritis -central role of enthesitis-

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Conflict of interest: None

The primary inflammatory lesion in spondyloarthritis (SpA) is thought to be the enthesis, and appreciating anatomy and physiology of the enthesis is important in understanding the pathophysiology of enthesitis. Entheses are subject to strong mechanical stress. The "enthesis organ concept" helps us understanding the pathophysiology of enthesitis. At the attachment site, the cortical bone is thinner than the trabecular bone, partially porous with blood vessels emerging from the neighbouring bone marrow enabling the supply of the entheses with nutrients. This findings are quoted frequently on microanatomical backgrounds that may accompany bone marrow edema on MRI to enthesitis. HLA-B27 transgenic rats develop SpA-like features in the presence of gut bacteria, suggesting that gut flora as well as HLA-B27 molecule plays a role in the onset of SpA. The Achilles enthesitis in TNF-α transgenic mice is alleviated by reducing the load of the hind limb by tail suspension. It can be hypothesized that threshold for triggering entheseal inflammation is substantially lower in patients with SpA. A similar phenomenon of the skin is well known as the Koebner phenomenon in psoriatic patients. In addition to genetic background such as HLA-B27 and IL-23R gene polymorphism, disturbed epithelial barrier function due to concomitant clinical or subclinical psoriasis and colitis may also result in increased exposure to microbial stress and prolonged immune responses. As a mediators, inflammatory cytokines such as IL-17, IL-23, TNF etc. in addition to PGE2 have been suggested to be involved in the pathophysiology of enthesitis. Several clinical trials have suggested that the inhibition of those cytokines is clinically efficacious in controlling enthesitis.

ES8-2

How is PsA different from RA?

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Conflict of interest: Yes

Psoriatic arthritis, a spondyloarthritis associated with psoriasis, mainly affects peripheral joints and occasionally axial joints. Dactylitis and enthesitis can be observed, and nail diseases are related to DIP arthritis in PsA. In rheumatoid arthritis (RA), inflammation occurs primarily in synovium whereas enthesitis is the initial lesion and the inflammation

spreads secondary to the synovium in PsA. Enthesis is a site easy to have mechanical stress that can provoke inflammation. Enthesis easily cause synovitis and tenosynovitis in the synovio-entheseal complex. While increased vascularity and accumulation of innate immune cells, such as neutrophils and macrophages, are more prominent in pathology of PsA synovium, thickness of synovial membrane accompanied with plasma cells and dendritic cells is noticeable in RA synovium. Although IL-17, TNFα and IFNγ, are key cytokines in the pathogenesis of PsA and RA, IL-17/IL-23 axis seems more striking in PsA. It is reported that enthesiophytes can be observed in patients with psoriasis even if they don't have joint disease. Both of erosive change and new bone formation can occur simultaneously in PsA, and IL-22 possibly induce the osteogenesis. Methotrexate, the first-line drug in the treatment of RA, is also effective in PsA. TNF inhibitors decrease the disease activity in RA and also in PsA. On the other hand IL-23/IL-17 inhibitors are effective only in PsA. TNF inhibitors and IL-17 inhibitors can prevent progression of joint destruction, however, it is unclear they can reduce new bone formation in PsA.

ES8-3

Treatment strategy for Inflammatory Bowel Disease: Benefit and Issue in the era of anti-TNF antibody

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Conflict of interest: Yes

In Japan, the number of IBD patients is dramatically increasing and actual number of UC and CD patients in 2014 was more than 180,000 and 40,000 respectively. The characteristic feature of UC is classified in pancolitis type, left-sided colitis type, distal type, and proctitis type, and the characteristic feature of CD is also classified in small bowel type, colonic type, and ileo-colonic type. At present both disease is incurable disease, therefore the treatment strategy is to achieve remission and maintain a complete remission. The clinical stratification of UC and CD are classified in mild, moderate, and severe to fulminant. Therefore, it is important to control mild active IBD by 5-ASA or salazosulfapyridine. Steroid is required if it doesn't work well. In general, the efficacy rate of steroid treatment to IBD is approximately 80%, but some case is refractory to steroid treatment. Medical management of UC refractory to steroid is limited to calcineurin inhibitor or anti-TNF antibody such as IFX, ADA, GOL. Recently, surgical treatment ratio for UC is decreasing dramatically because the efficacy ratio by anti-TNF antibody treatment is extremely positive results. Since 2002 when we started to use IFX, we also got the high induction rate and maintenance rate for CD. Anti-TNF antibody is also useful for corticosteroid refractory or dependent CD. Accordingly, IBD patients with sustained remission can keep stable condition and can recover quality of life. We have still discussed about the best timing to start anti-TNF antibody (step-up? or top-down?). We also have some cases who have psoriasis-like exanthema or arthritis as paradoxical phenomenon under the anti-TNF treatment. It is hard to decide whether we should intensify the anti-TNF antibody treatment or not when we see the arthritis, because this symptom is very common to IBD. In this session, I will present how to evaluate, treat, and manage IBD and also show the management of arthritis as complications.

ES9-1

What do Baricitinib and JAK inhibition offer in terms of therapeutic algorithm?

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Conflict of interest: Yes

Despite advances in the management of rheumatoid arthritis, limitations in treatment remain. These include limitations associated with parenteral delivery of biologic drugs, cost of treatment, and the fact that not all patients have response to conventional synthetic DMARDS or biologic DMARDS. Furthermore, a number of studies have revealed that even when patients do respond and achieve LDA or remission, many of them are still suffering from residual symptoms such as pain, fatigue and morning joint stiffness. In 2017, Baricitinib, an oral, reversible inhibitor of the Janus Kinases JAK1 and JAK2 became available to use in multiple regions including Europe and Japan. In recent years, its unique profile and phase 3 trial data has set high expectations for its contribution to RA treatment. This presentation will propose where in the treatment algorithm the drug could be considered through exploration of Baricitinib's mode of action, trial evidence and the practical considerations of how it may benefit the patients we treat.

ES9-2

Safety and proper use of baricitinib for patients with rheumatoid arthritis

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Conflict of interest: Yes

Baricitinib, a novel Janus kinase (JAK) 1/2 inhibitor, has been approved for rheumatoid arthritis in 2017 in Japan and Europe. A series of phase III clinical trials and their long-term extension studies enrolling RA patients with inadequate response to methotrexate (MTX), conventional synthetic disease modifying antirheumatic drugs (csDMARDs), and tumor necrosis factor inhibitors, and MTX-naïve RA patients established efficacy and safety of baricitinib. The EULAR recommendations 2016 place JAK inhibitors as one of the DMARDs which should be considered if the treatment target is not achieved by the treatment of Phase I in the presence of poor prognostic factors or Phase II. The overarching principles recommend that treatment of RA must be based on a shared decision between the patient and the rheumatologist considering risk-benefit balance which includes disease activity and other patient factors, such as progression of structural damage, comorbidities and safety issues. Pooled safety analysis of baricitinib showed incidence (/100 patient-years) of adverse events as follows; SAE resulting in death 0.3, non-melanoma skin cancer 0.7, major adverse cardiovascular events 0.5, serious infection 3.2, and herpes zoster 3.4. Incidences of hospitalized infection from RA registries were reported as 1.14-1.62/100 patient-years, and rheumatologists should pay strong attention to serious infection during treatment with baricitinib. Both baricitinib and tofacitinib showed similarly high incidence of herpes zoster especially in Japanese patients. Although tuberculosis was not reported from clinical trial in Japan, cases with extra-pulmonary and miliary tuberculosis were reported. Other pertinent but low-incidence adverse events include interstitial pneumonia and deep vein thrombosis/pulmonary embolism. We can draw the best out of baricitinib if we select patients with RA based on appropriate screening procedure and consideration of these risks.

ES10-1

Psoriatic arthritis from rheumatologist's view point

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Conflict of interest: Yes

The central sites in the pathogenesis of psoriatic arthritis are skin and enthesis, however its symptoms and phenotypes are very various including skin rash, peripheral arthropathy, axial arthropathy, dactylytis, uveitis, and inflammatory bowel syndrome. The prevalence of psoriatic arthritis were considered to be low in Japanese population, but recent studies have reported that up to 30% of patients with psoriasis could have psroatic arthritis. Many doctors and patients used to not connect psoriasis and joint or lumbar symptoms, resulting in misdiagnosis with osteoarthritis or nonspecific back pain. Psoriatic arthritis has no specific diagnostic biomarker like anti-CCP antibodies in rheumatoid arthritis, early diagnosis is sometimes difficult. However, with the remarkable progress in treatment of psoriatic arthritis such as TNF inhibitors, IL-12/23 inhibitors, and IL-17 inhibitors, early intervention has become essential. In addition, many basic studies and clinical trials are facilitating the understanding the pathogenesis of psoriatic arthritis. In this lecture, we would like to discuss the pathogenesis and management of psoriatic arthritis from the rheumatolo-

gist perspective.

ES10-2

Therapeutic strategy in patients with psoriasis and psoriatic arthritis

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Conflict of interest: Yes

Psoriasis is a chronic auto-inflammatory disease in which IL-23/IL-17 plays a pivotal role. The crosstalk of immune cells and keratinocytes induces STAT3-dependent abnormal proliferation and activation of keratinocytes. Psoriasis is known to be a systemic inflammatory disorder with a higher incidence of comorbidities, such as arthritis, enthesitis, metabolic syndrome, cardiovascular diseases, and uveitis. Therefore a clinical collaboration of specialized doctors in different fields, such as dermatologist and rheumatologist, is recommended. The prevalence of psoriatic arthritis (PsA) is about 15 % in patients with psoriasis and skin symptom develops prior to arthritis in 70-80% of PsA patients in Japan. Since PsA is a progressive disorder, appropriate diagnosis in the early stage is important. The theory of Treat to Target recommended in RA treatment is also applied to PsA. In addition to NSAIDs and DMARDs, six different biologics against to TNFα (infliximab, adalimumab), IL-12/23p40 (ustekinumab), IL-17A (secukinumab, ixekizumab), and IL-17 receptor A (brodalumab) became therapeutical options for psoriasis in Japan. Moreover, PDE4 inhibitor is also approved for psoriasis treatment in 2017. These effective drugs cause paradigm shift in psoriasis therapy. On the other hand, the majority of the clinical recommendations for PsA are conditional due to a lack of high-quality evidence. Proper selection of drugs based on the appropriate evaluation of severity in each clinical domains including peripheral arthritis, axial disease, enthesitis, and skin is critical for PsA treatment.

ES11-1

New therapeutic strategies for rheumatoid arthritis

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Conflict of interest: Yes

Molecular targeted therapy for rheumatoid arthritis treatment had started from TNF inhibitors, and now, four kinds of molecules including IL-6, CTLA4, and JAK are targeted. It has become clear that each targeted therapy shows a very high effect, and it is indispensable to the concept of treat to target. However, since there is little change in the clinical efficacy among the targeted therapies, the choice of drug is left to the discretion of the doctor. The evidence how to select targeted therapy in rheumatoid arthritis is inadequate, and the way has not been described in EULAR recommendation. In our rheumatoid arthritis therapy cohort (the FIRST registry), we have used over 3,000 patients with molecular targeted therapy. We reported that several factors in the patient background may be able to predict the efficacy of each biological product. On the other hand, the concept of tailor-made medicine for various diseases has been expected in Japan since around 2000. However, tailor-made medicine is not easy, and it was unknown whether balances corresponding to the cost can be taken, especially in areas other than oncology. Under such circumstances, US President Barack Obama announced the development to precision medicine in the State of the Union Address 2015. This concept is a tailor-made medicine in a broad sense. However, this concept is based on the subpopulation identification rather than considering a suitable treatment for each patient. It is a realistic and cost-effective concept. In terms of the treatment of rheumatoid arthritis, it was reported that different molecular targeted therapy had different effects on the immunophenotypes. These evidences suggest the possibility of precision medicine by immunophenotype. This seminar will outline the attempt and possibility of precision medicine for rheumatoid arthritis.

ES11-2

T cell-targeted therapy to rheumatoid arthritis

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Center for Rheumatic Diseases, Matsuyama Red Cross Hospital

Conflict of interest: Yes

Rheumatoid arthritis patients are immunologically heterogeneous populations. Among them, there is a significant difference between ACPA positive rheumatoid arthritis patients and ACPA negatives. ACPA is an antibody against citrullinated peptides and is an antibody produced in a T cell dependent manner. In agreement with such findings, it has been reported that abatacept, a drug that blocks interaction between antigen presenting cells and T cells, is successful in ACPA positive and high titer cases. Meanwhile, HLA-DRB1 shared epitope (SE) which is a disease susceptibility gene of rheumatoid arthritis strongly binds to citrullinated peptides and thereby strongly activates T cells. It is also known that high titers of ACPA are associated with the presence of SE. Considering the above, we examined the presence or absence of SE possessions and the therapeutic reactivity of abatacept and reported that abatacept is particularly successful in patients with rheumatoid arthritis possessing SE. Since the titer of ACPA is influenced by non-SE allele HLA-DRB 1 1501/1502 and 0901, the effectiveness of abatacept can be predicted more accurately for SE positivity than the titer of ACPA. Recently, the researches of the interaction between ACPA and RF, and of carbohydrate chains of ACPA are progressing. We will discuss the T cell-targeted therapy to rheumatoid arthritis, together with new findings of ACPA, which is a T cell dependent antibody and used in clinical practice.

ES12-1

The past, the present and the future of operative treatment of the hands in rheumatoid arthritis

Yasunori Kobata
The Center for Rheumatic Diseases and Musculoskeletal Disorders, Minami Nara General Medical Center

Conflict of interest: None

This study group seminar, which has been held once a year since 1999, become the 20th this time. Fifteen years have passed since the introduction of biological agents for rheumatoid arthritis in Japan, during which the disease control of patients with rheumatoid arthritis has achieved remarkable advancement. Tight control with methotrexate and biologics leads to remission and low disease activity in the majority of patients, and it seems that there has been a big change in patient needs and the indications even in surgical treatment. Therefore, this time, we made two part consisting of a floor participation type case examination using Answer Pad and a special lecture with the theme of the history of hand surgery in RA patients. In case examination, we present some cases of thumb, fingers and wrist joints, and we would like to discuss with participants how we face patients at the stage of remission, what needs to be addressed, and how to treat with them. Also, as a special lecture at the 20th meeting, Dr. Yoshitaka Minamikawa will give a lecture on the history of rheumatoid surgical treatment in Japan. We would like to make this workshop useful for clinical practice of all participants and to make it possible to contribute to realization of higher treatment target of RA patients.

ES12-2

Surgery of the rheumatoid hand; historical perspective

Yoshitaka Minamikawa
Minamikawa Orthopaedic Surgery, Namba Hand Center

Conflict of interest: None

This is not a literature review but rather my personal experience through mentor Prof. Ogawa and his relation to Europe. History of the rheumatoid surgery has spread from Scandinavia to England and German speaking area. N. Gschwend from Zurich was noted as one of the pioneer in rheumatoid surgeon in Europe and established orthopedic surgery at Schulthess clinic. Although, he performed all aspect of orthopedic surgery, his famous GSB total elbow endoprosthesis was succeeded to Beat

Simmen (Shoulder, elbow & hand specialist) then to Daniel Herren (hand specialist). In Japan, Masuta Mori introduced synovectomy as early as 1950' and published Mori's approach for knee synovectomy. In 1961, Mori presented "synovectomy of the wrist" at 5th Japanese Society Surgery of the hand. Soon after this introduction Ogawa started synovectomy of the finger joint and several surgery for RA hand. Both THA and TKA were introduced in early 1970' and spread for rheumatoid patient as well as OA. After less than 20 years of enthusiasm period for rheumatoid hand surgery, rheumatoid surgeons found outcomes of the surgeries were not as good as expected. And, therefore, almost no hand surgery except extensor rupture had been recommended until 2000. Author and 6 rheumatoid surgeons interested in hand problems, founded "Rheumatoid Hand Surgical Society" in 1999 and started educational meeting focused in basic surgical procedure for rheumatoid hand. Founding members believed that time of introduction of the RA hand surgery to Japan was too early because both hand surgery nor hand therapy were not established yet at that time. Now surgery for rheumatoid hand is accepted and number of cases are increasing. In order to prove our hypothesis, histories of rheumatoid hand surgery at different countries were presented at "International symposium of RA hand surgery in Tokyo, 2013". Outline of their presentation will be presented.

ES13-1

Essential roles of biological DMARDs in the treatment of elderly-onset rheumatoid arthritis

Takahiko Sugihara
Department of Medicine and Rheumatology, Tokyo Metropolitan Geriatric Hospital, Tokyo, Japan

Conflict of interest: Yes

The age of onset of rheumatoid arthritis (RA) shifted to elderly side in line with the increasing life expectancy. Recently, management of elderly-onset RA is common in clinical practice for rheumatologists. The aims of treatment for RA are abrogation of disease activity, no progression of joint damage, normal physical function and improvement of long-term outcomes as presented in principles of treat-to target strategy. However short-term outcomes are sometimes prioritized in the treatment of elderly patients, and glucocorticosteroids (GCs) are often preferred in clinical practice although harmful effects of GCs have been reported in many observational studies. Our previous prospective study showed that achieving low disease activity (LDA) and structural and functional remission were realistic goals for patients with elderly-onset RA. In this study, the treatment was scheduled in advance to achieve LDA, and 32% of the patients were receiving biological DMARDs at week 52. This study suggests that biological DMARDs may have a major role in the treat-to-target strategy of elderly-onset RA, because a high dose of MTX was intolerable in our cohort, and GCs use was associated with serious infection. On the other hands, clinically relevant radiographic progression (CRRP) was observed at 40 % of the patients, and anti CCP antibody positive, high disease activity, presence of bone erosion are all associated with CRRP. Interestingly, no response by EULAR response criteria and non-achievement of LDA at week 24 were both strongly associated with CRRP. Rapid improvement of disease activity and achievement of LDA followed by improvement of physical function are clearly major targets of the treatment strategy of elderly-onset RA. Essential roles of biological DMARDs are emphasized in the study. Aging is associated with serious infection in patients receiving biological DMARDs, and we reported various adverse events (AEs) throughout observational periods. Management of AEs and treatment of RA after the occurrence of AEs are important issues. In this seminar, I will focus on the role of biological DMARDs on the strategy to sustain treatment targets and to manage AEs.

ES13-2

Treatment strategy for elderly rheumatoid arthritis patients by Golimumab

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

Conflict of interest: Yes

In this aging society, current treatment strategy for RA needs to consider not only inhibiting joint destruction but also preserving their physical ability and keep their ADL/QOL. The preservation of physical ability is highly associated with the state of sarcopenia, an age-related decrease of muscle mass and strength. The prevalence of sarcopenia is much higher in RA patients than in healthy elderly people. In addition, frailty, a physical, social, and psychological vulnerability of the elderly, and cachexia, abnormal metabolic state accompanied by body weight loss, are also highly prevalent in RA patients. Given that inflammatory cytokines such as TNF and IL-6 are central to those pathophysiology, inhibiting TNF by biological DMARDs might help decrease sarcopenia in RA patients. In fact, the increase of muscle strength in RA patients with continuous treatment by TNF inhibitors were observed in the KURAMA cohort. On the other hand, although the short time use of glucocorticoid is useful for inhibition inflammation, the long term use of high dose of glucocorticoid may decrease muscle mass or strength by inducing steroid myopathy. Therefore, achieving remission by TNF inhibitors while decreasing the use of glucocorticoid will help preserve physical ability and improve ADL/QOL of RA patients. In this seminar, the optimal treatment strategy for elderly RA patients using a TNF inhibitor, golimumab will be discussed.

ES14

Confronting Systemic Lupus Erythematosus: State-of-the-art lecture on new Therapeutic Strategies for Improving Disease Activity

Yoshiya Tanaka
The First Department of Internal Medicine, School of Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan

Conflict of interest: None

Systemic Lupus Erythematosus (SLE) is a systemic inflammatory disease mainly caused by immune abnormality such as autoantibody production (e.g. antinuclear antibody) and B cell dysfunction, and it is designated as an intractable disease. Although about 60,000 SLE patients are registered in the intractable diseases in Japan, it is estimated that there are more than 100,000 patients including non-registered patients. In the 1960's, the 5-year survival rate was as low as 50%, and there were many women with SLE who ended their life at young age. However, due to the improvement of disease activity management utilizing steroids, the prognosis has been greatly improved. (5-year survival rate: 94.79%, 10-year rate: 91.41%) (Mak 2012). Since long-term use of steroid may increase the risk of complications such as osteonecrosis, osteoporosis and infectious diseases, it is ideal to reduce the dose of steroid to the minimum level as possible. Recent progress in SLE research revealed that the cytokine BAFF, which acts on the differentiation of B cells, is involved in autoantibody production in SLE. Based on those research, BAFF has been focused as a molecular target for new SLE therapy. Belimumab is a fully human IgG1 monoclonal antibody targeted to BAFF, and inhibition of the biological activity of BAFF with belimumab is expected to reduce autoreactive antibodies and improve the disease activity (Furie 2011). In the phase III trial (BLISS-NEA study) of belimumab conducted in SLE patients living in North East Asia from 2011 to 2015, by adding belimumab to the standard of care using steroids and/or immunosuppressant demonstrated disease activity improvement (Zhang 2018). Although belimumab is expected as the first effective biologic in SLE treatment, it is necessary to confirm efficacy and safety in actual clinical practice through all cases post marketing survey because of limited experiences in Japanese patients at the moment. In this lecture, current and future prospects in SLE treatment and also belimumab product profile including mode of action, results of clinical trials and its role in SLE treatment will be presented.

Annual Course Lecture Luncheon Seminar

ACL-LS

Methotrexate (MTX) for the treatment of rheumatoid arthritis (RA) - Recent concern about adverse events and future direction -

Yasuo Suzuki
Division of Rheumatology, Tokai University School of Medicine

Conflict of interest: Yes

A recent paradigm shift of the treatment of RA is to aim for remission by the T2T strategy, using DMARDs as early as possible in the disease process. Among the DMARDs, MTX is a highly effective drug both as monotherapy and in combination with other DMARDs or biologics and has served as an anchor drug in the treatment of RA. At Tokai University Rheumatology Division, more than 80% of RA patients receive MTX. In Japan, an increase in dose of MTX up to 16mg/week was approved in 2011. The analysis of a post marketing surveillance (PMS) of MTX showed that remission rate increased approximately 3 times by increasing MTX from 8mg to more than 10mg/week. Based on the recent evidence including the results of the PMS and C-OPERA study, the 2016 revised guidelines for the treatment of RA with MTX recommend to use up to 10-12 mg /week of MTX aggressively if the response to MTX is inadequate. On the other hands, 666 cases of adverse events (AEs) leading to death have been reported between 1999 and 2016. Among them, 157 cases were reported after the approval of higher doses up to 16mg/week. Myelosuppression (26.8%) pneumonitis (15.7%), infections (24.8%), and lymphoproliferative disorders (LPD) (20.9%) are major fatal AEs and are composed about 90% of total AEs leading to death. Especially infection and LPD tend to increase during recent 5 years. The majority of patients with infections or LPD were older age and were taking more than 8mg/week for more than 2 years. This suggest that these AEs are might be associated with both immunosenescence and long-term immunosuppression by anti-rheumatic drugs. In this lecture, I discuss recent concern about adverse events during MTX therapy for RA and future direction how to use MTX after the achievement of remission including the reduction of MTX dose.

Session for Medical Students and Junior Residents

MSJR-P1-1

A case of intestinal pseudo-obstruction in systemic lupus erythematosus with long disease duration improved by steroid therapy

Koji Nishida, Yuko Kimura, Takaaki Ishida, Shuzo Yoshida, Tohru Takeuchi, Shigeki Makino, Shigeki Arawaka
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[Background] Systemic lupus erythematosus (SLE) frequently has gastrointestinal lesions, but rarely complicates intestinal pseudo-obstruction (IPO), which delays diagnose and treatment. [Case] Patient is a 42-year-old-female. 21 years ago, the previous doctor diagnosed her as SLE for photosensitivity, anti-ds-DNA antibody positive, and lupus nephritis (WHO classes II). She had taken orally prednisolone (PSL) 60 mg/day. She had lupus cystitis and hydronephrosis, and repeatedly complicated intestinal obstruction. 1 year ago, anti-ds-DNA antibody and complement value were stable with PSL 2 mg/day, but intestinal obstruction appeared. She took some treatment under fasting, but no reactions. In February, she visited our hospital for surgery but CRP was elevated, so surgery was impossible. Abdominal computed tomography revealed significant fecal accumulation in the large intestine, and haustra disappeared. We diagnosed intestinal obstruction as IPO due to disease activity of SLE for decreased C3 level as 49 mg/dL and history of hydronephrosis. After PSL was increased to 40 mg/day, intestinal peristalsis improved immediately. [Discussion] We experienced a case in which treatment with steroids was effective in patients with long-term afflicted SLE complicated with IPO.

MSJR-P1-2

A case of myositis with double-positive anti-Ku antibody and anti-mitochondria antibody

Hiroshi Kobe[1], Satoshi Omura[2], Atsushi Omoto[2], Takuya Yanagida[2], Masatoshi Kadoya[2], Wataru Fukuda[2]
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[Case] A 32-year-old woman was admitted to Cardiology department of this hospital, because her blood test had revealed raised serum CK (2675IU/L) in the local clinic. In this hospital, her blood test showed serum troponin T was positive, otherwise EKG and heart ultrasound echo was clear. Her skin appeared rash with itching in the lower extremities, and she was consulted to Rheumatology department of this hospital. Her rash was not specific for myositis, but her lower extremities proximal muscle were weak. Then we checked myositis associated autoantibodies, and it revealed anti-Ku anti-body were positive, and anti-nuclear antibody and anti-mitochondria antibody were positive, too. In additional examination, we done muscle biopsy of her thin muscle and electromyography (EMG). In the pathological examination CD4 positive lymphocytes invaded the perivascular of muscle membrane, and EMG showed iliopsoas was myogenic change. From the above, we made the diagnosis of myositis of anti-Ku antibody, anti-mitochondrial antibody positive. After that we suspected primary biliary cirrhosis (PBC), we performed liver biopsy, and no abnormal findings was noted. We started prednisolone 35mg per day. She was doing well, and add the azathioprine 75mg/day, it has been reduced to prednisolone 12.5mg. [Consideration] Recently, there are many reports of anti-mitochondria antibody positive myositis. Although its concept has not been established, certain trends such as chronic elapsed, myocardial damage has been reported. This case applies this trend. In this study, we report our experience of anti-mitochondria antibody positive myositis that anti Ku antibody positive along with some literature review.

MSJR-P1-3

An Autopsy case with systemic sclerosis complicated with Pulmonary Tumor Thrombotic Microangiopathy (PTTM)

Satsuki Matsunaga[1], Kazuhisa Nakano[2], Ippei Miyagawa[2], Yusuke Yamauchi[2], Yasutaro Tamaki[2], Shingo Nakayamada[2], Shigeru Iwata[2], Kentaro Hanami[2], Shunsuke Fukuyo[2], Satoshi Kubo[2], Yuna Inaba[3], Aya Nawata[4], Yoshiya Tanaka[2]

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MSJR-P1-4

A case of MEFV variants in a patient with Granulomatosis with polyangiitis

Ryuki Kadomatsu[1], Momoko Okamoto[1], Keita Fujikawa[1], Yushiro Endo[2], Masataka Umeda[2], Tomohiro Koga[2], Akinari Mizokami[1], Atsushi Kawakami[2]
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MSJR-P1-5

A case report of Visual Disturbance and Ocular Motility Disorder in Refractory Orbital Granulomatosis With Polyangitis

Ryo Kuwata[1], Yuko Shirota[2], Yusho Ishii[2], Yosuke Hoshi[2], Yoko Fujita[2], Tsuyoshi Shirai[2], Hiroshi Fujii[2], Tomonori Ishii[2], Hideo Harigae[2]
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MSJR-P1-6

Attainment of steroid free remission in ANCA-associated vasculitis

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MSJR-P1-7

A case of Polymyalgia Rheumatica without tenosynovitis and bursitis by ultrasonographic examination diagnosed by clinical course and PET-CT

Rina Saito[1], Akihiko Nakabayashi[1], Masashi Okamoto[1], Hiroshi Shimagami[1], Michiko Ohashi[1], Tomomi Fujisaka[1], Takehiro Hirayama[1], Yuta Yamaguchi[1], Akira Mega[1], Hiroki Ikai[1], Madoka Morimoto[1], Kazushi Konma[1], Yoshinori Katada[2]
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MSJR-P1-8

A case of neuro-Behçet disease complicated with suspected paraneoplastic cerebellar degeneration

Taeka Yamaki[1], Ryosuke Hiwa[2], Ran Nakashima[2], Shuji Akizuki[2], Nobuo Kuramoto[2], Kosaku Murakami[2], Motomu Hashimoto[3], Hajime Yoshifuji[2], Masao Tanaka[3], Koichiro Ohmura[2], Tsuneyo Mimori[2]
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MSJR-P2-1

A case of systemic lupus erythematosus complicated with aseptic meningitis and suspected hemophagocytic syndrome by trimethoprim/sulfamethoxazole

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Case: A 29-year-old woman was diagnosed with systemic lupus erythematosus base on clinical symptoms and laboratory findings 4 years ago. She received no medication because there were no severe complications. She developed fever and elevated anti-dsDNA antibody 3 years ago, she was started prednisolone (PSL) 40 mg/day, her symptoms were improved. On September 5th, trimethoprim/sulfamethoxazole (TMP/SMX) was started for preventing pneumocystis pneumonia. On September 27th, she noticed high fever and palpebral conjunctival congestion after a few hours of TMP/SMX administration, her symptoms were relieved with PSL increased to 10 mg/day for 3 days. On October 4th, she developed fever, headache, palpebral conjunctival congestion, and lip edema after 1 hour of TMP/SMX administration, and she was treated with PSL 30 mg/day. However, her symptoms were worthened, her laboratory data revealed elevated AST/ALT, elevated ferritin and cytopenia. We considered that she was developed hemophagocytic syndrome. She also diagnosed as aseptic meningitis base on cerebrospinal fluid examination. She administered pulse prednisolone, her symptoms and laboratory data improved. Discussion: We should know these complications by TMP/SMX so that we notice patients' pathophysiology and treat them earlier.

MSJR-P2-2

Sjögren's syndrome needed to distinguish from PFAPA syndrome: a case report

Yuya Terajima, Yu Katayama, Takashi Katayama, Takahiro Terami, Masatsugu Ozawa, Masaaki Usui, Hiroshi Wakabayashi
Rheumatism Center, Okayama City Hospital

Case presentation: A 20-year-old female was admitted to the hospital because of periodic fever in July 2017. She repeated 39°C fever lasted from 4 days to 7 days once a month, since 2015. She had painful cervical lymphadenopathy and stomatitis in the period of fever. Her symptoms were satisfied with four points of Thomas criteria except for age, and satisfied with five points of Pader criteria except for reactivity to steroids. Diagnostically, these facts suggested Periodic Fever, Aphthous stomatitis, Pharyngitis, cervical Adenitis (PFAPA) syndrome. However, she had dryness of eyes and mouth previously. In the function of salivary gland, Saxon test was positive. In the function of lachrymal gland, Schirmar test was positive, and fluorescein stain test indicated spotted corneal injury. Immunological findings showed that anti-SS-A antibody was positive. Thus, her final diagnosis was Sjögren's syndrome. Discussion: PFAPA syndrome that the pathogenesis is unknown, is one of the autoinflammatory diseases. It has periodic fever with aphthous ulcer, cervical adenopathy and pharyngitis with tosillar exudates. Generally, it usually begins under 5-year-old children, but adult-onset PFAPA syndrome was often reported lately. However, there are no specific symptoms and examinations, so it needs diagnosis of exclusion. Fortunately, our case was diagnosed with Sjögren's syndrome finally. Our experience suggests that it needs to be careful, because both symptoms of Sjögren's syndrome and PFAPA syndrome are similar.

MSJR-P2-3

Concurrent Development of two types of Vasculitis

Satoko Fujimoto[1], Yoshinori Matsumoto[2], Yosuke Asano[2], Keigo Hayashi[2], Yuriko Yamamura[2], Sumie Hiramatsu[2], Michiko Morishita[2], Keiji Ohashi[2], Yoshia Miyawaki[2], Haruki Watanabe[2], Tomoko Kawabata[2], Ken-ei Sada[2], Jun Wada[2]
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Background: Immunoglobulin A (IgA) vasculitis (IgAV) is characterized by a small vessel vasculitis with deposition of the IgA-mediated immune complex and presents cutaneous purpura, arthralgias and/or arthritis, acute enteritis and glomerulonephritis. Eosinophilic granulomatosis with polyangiitis (EGPA) is an anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) characterized by granulomatous formation with eosinophilic infiltration in small to medium-sized vessels. Both diseases are classified as autoimmune systemic vasculitis, but the pathogenesis of immune complex-mediated IgAV and that of pauci-immune EGPA are different. **Case:** Here we report a 59-year-old woman presenting concurrent development of IgAV and EGPA with palpable purpura and numbness in a patient with a history of asthma. Histological

examination revealed leukocytoclastic vasculitis with deposition of IgA in the upper dermis and necrotizing vasculitis with eosinophilic infiltration and granulomatous formation in the lower dermis and subcutaneous fat, indicating the existence of IgAV and EGPA. **Discussion:** Our case provides evidence of concurrent development of two different types of vasculitis, which may affect disease-associated complications, therapeutic strategy and prognosis.

MSJR-P2-4

A case of PR3- and MPO-ANCA negative microscopic polyangiitis with dominant lung involvement

Misaki Shoji[1], Yoichiro Akiyama[2], Akiko Miyanaga[2], Hiroi Kusaka[2], Natsuki Shima[2], Katsuya Nagatani[2], Masahiro Iwamoto[2], Seiji Minota[2]
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MSJR-P2-5

A case of granulomatosis with polyangiitis (GPA) with gastrointestinal hemorrhage and perforation, successfully treated with rituximab and plasma exchange

Mei Nomoto, Yutaro Soejima, Takaaki Komiya, Natsuki Sakurai, Yuichiro Sato, Daiga Kishimoto, Reikou Kamiyama, Ryusuke Yoshimi, Yohei Kirino, Hideaki Nakajima
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Thirty-nine years old man was diagnosed with granulomatosis with polyangiitis (GPA) based on fever, serositis, transmission deafness, epistaxis, hematuria, proteinuria, purpura, high titer of PR3-ANCA, and results of skin and nasal biopsies. Although we initiated prednisolone 100 mg/day immediately after the transfer, the patient developed into hemorrhagic shock caused by gastrointestinal (GI) hemorrhage and peritonitis due to GI perforation. Regardless of severe condition, we decided to administer rituximab, and performed plasma exchange. After these treatments, the patient gradually recovered from serious condition, although gastrointestinal perforation persisted. GI involvements in GPA are rare, but severe condition. We suggest that early intensive treatment is necessary for GI involvement in GPA.

MSJR-P2-6

Periodic fever and pleurisy in a MPO-ANCA positive patient with hyperthyroidism

Sorato Segoe[1], Ken-ei Sada[2], Keigo Hayashi[2], Yuriko Yamamura[2], Haruki Watanabe[2], Yoshinori Matsumoto[2], Tomoko Kawabata[2], Jun Wada[2]
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MSJR-P2-7

Simultaneous Development of Aortitis and Phlebitis in Takayasu Arteritis

Mikako Kamogashira[1], Yoshinori Matsumoto[2], Yuriko Yamamura[2], Yosuke Asano[2], Keigo Hayashi[2], Sumie Hiramatsu[2], Michiko Morishita[2], Keiji Ohashi[2], Yoshia Miyawaki[2], Haruki Watanabe[2], Tomoko Kawabata[2], Ken-ei Sada[2], Jun Wada[2]
[1]Okayama University Medical School, [2]Department of Nephrology, Rheumatology, Endocrinology and Metabolism, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences

Background: Takayasu arteritis is a large vessel granulomatous vasculitis with massive intimal fibrosis and vascular narrowing and affects the aorta and its branches, as well as the pulmonary arteries. Patients with Takayasu arteritis show variable symptoms due to obstruction of the affected arteries. Here we report a previously undescribed case of simultaneous development of aortitis and non-thrombotic phlebitis in Takayasu arteritis. **Case:** A 26-year-old man who had been diagnosed as having Takayasu arteritis at the age of 24 and treated with oral prednisolone (25 mg/day) in combination with cyclophosphamide (100 mg/day), was admitted to our hospital due to chest pain. Computed tomography (CT) showed wall thickening of the descending thoracic aorta, indicating relapse of aortitis. Additionally, the patient presented a vascular pain on extensor surfaces of the upper extremities which was diagnosed as median antebrachial non-thrombotic venous phlebitis by vascular ultrasonography. The patient was treated with high-dose prednisolone (50 mg/day), and both aortitis and phlebitis disappeared. **Discussion:** Our case provides evidence of concurrent development of aortitis and phlebitis in Takayasu arteritis, which may affect disease-associated manifestations and complications.

MSJR-P2-8

Two case of intestinal Behcet's disease treated with adalimumab administration resulted in dose reduction of corticosteroids

Kana Higashitani, Ayako Matsuki, Takeshi Umibe
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MSJR-P3-1

Influence of Disease Duration on the Quality of Life in Patients with Behçet's Disease

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[Object] This study aimed to investigate differences in influence of Behçet's disease (BD) duration on the quality of life (QOL) of BD patients. [Methods] The mean scores of subscales in the Short Form-36 (SF-36) (Physical functioning <PF> Role physical <RP>, Bodily pain <BP>, General health <GH>, Vitality <VT>, Social functioning <SF>, Role emotional <RE>, and Mental health <MH> and 2 component summaries (Physical <PCS>, and Mental <MCS>) was used to evaluating 100 patients' QOL. The patients were divided into quartiles. The mean scores of subscales and summaries were statistically investigated regarding whether they were different among the four groups. In addition, the associations between BD duration and SF-36 scores were assessed using correlation analysis. [Results] The mean scores of PF, GH, RE ($P = 0.002$, 0.024, and 0.004, respectively) subscales, and component summery in PCS ($P = 0.008$) were a significant difference. In all subscales, the patients who had BD for 36-60 years were the lowest QOL. As BD duration became longer, the score of subscales significantly got higher except RP, BP, and MH. [Conclusions] We showed that longer BD duration contribute to decrease QOL associated with physical aspect. It is important to focus on QOL associated with physical aspects for BD patients with long duration.

MSJR-P3-2

What Are the Symptoms that Affect QOL of Behçet's Disease Patients?

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[Object] The objective of this study was to investigate differences in influence of the symptoms on quality of life (QOL) of patients with Behçet's disease (BD). [Methods] The Short Form-36 (SF-36) scale was performed to evaluating 100 BD patients. The patients were grouped according to the presence of genital ulcers, skin lesions, eye symptoms, headache, joint involvement, and fatigue for comparisons. The mean scores of subscales in the SF-36 (Physical functioning <PF>, Role-physical <RP>, Bodily pain <BP>, General health perception <GH>, Vitality <VT>, Social functioning <SF>, Role-emotional <RE>, and Mental health <MH>) were statistically investigated by the unpaired t-test regarding whether they were different between the two comparisons. [Results] BD patients with eye symptoms had significant difference than

those without eye symptoms in two subscales of PF ($P < 0.001$) and MH ($P = 0.019$). BD patients with fatigue had significant difference than those without fatigue in four subscales of BP ($P = 0.026$), VT ($P = 0.004$), SF ($P < 0.001$), and MH ($P = 0.004$). The other symptoms did not find any significant difference. [Conclusions] Two symptoms of eye involvement and fatigue in BD patients led to reduced QOL. Particularly fatigue had affected more QOL. It is important to focused approach on fatigue of BD patients.

MSJR-P3-3

Does Gender Influence the Quality of Life (QOL) of Behçet's Disease?

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<Object> This aimed to examine the gender differences in the quality of life (QOL) of Behçet's disease (BD) patients. <Methods> The mean scores of subscales in the Short Form-36 (SF-36) (Physical functioning <PF> Role physical <RP>, Bodily pain <BP>, General health <GH>, Vitality <VT>, Social functioning <SF>, Role emotional <RE>, and Mental health <MH> was used to evaluating 100 BD patients. The patients were divided into male and female. Moreover, the associations between SF-36 scores and severity scores of genital ulcers, skin lesions, eye symptoms, headache, arthralgia, and fatigue were assessed using correlation analysis. <Results> Female patients had significantly lower than male patients in BP subscale ($P = 0.048$). No statistical differences were observed between women and men in the other SF-36 scores. In female patients, as the BP score became lower, the severity score of arthralgia significantly got higher ($P = 0.005$). In male patients, there was no significant correlation between severity scores of each symptom and SF-36 scores. <Conclusions> Female patients with BD were more likely to have low QOL compared with male. In particular, the severity of arthralgia was affecting the decrease in QOL. It is important to focused approach on the effect of arthralgia on their daily life for the female BD patients.

MSJR-P3-4

Investigation of acute non-pyogenic cervical spondylitis without calcification

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MSJR-P3-5

Dose escalation of adalimumab is effective in patients with inflammatory bowel disease-associated arthritis

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Background: Arthritis is the most common extraintestinal manifestation of inflammatory bowel disease (IBD) and associated with morbidity and quality of life. Adalimumab (ADA) is a fully human monoclonal antibody against TNF-α that is efficacious in patients with IBD and IBD-associated arthritis, while dose escalation of ADA for IBD-associated arthritis in case of loss of response has yet to be examined. **Case:** Two patients (a 44-year-old man and a 46-year old woman) with ulcerative colitis-associated arthritis were treated with ADA (40 mg/2 weeks) in combination with methotrexate (MTX) or disease modified anti-rheumatic-drugs (DMARDs) and showed exacerbation of arthritis as a consequence of secondary failure of ADA. We treated these patients with 80 mg/2 weeks of ADA and observed improvement of arthritis with reduction of DAS28-CRP, Clinical Disease Activity Index (CDAI) and CRP level at 8 weeks and 52 weeks after commencement of dose escalation therapy with ADA. Additionally, serious adverse events did not occur during the observation period. **Discussion:** Our observation that dose escalation of adalimumab is effective in case of secondary failure may provide a new therapeutic strategy for the treatment of IBD-associated arthritis.

MSJR-P3-6

Ankle abscess under the tocilizmab therapy in Rheumatoid arthritis; a case report

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MSJR-P3-7

Molecular and functional analysis of HLA-B27 subtypes by a proteomic approach

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MSJR-P4-1

Anti-MDA5 antibody might be a possible biomarker in clinically amyopathic dermatomyositis; a case report

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Sixty-five-year-old woman recognized erythema of palms at the end of March. She developed dyspnea early in May. CT detected multiple pulmonary infiltrations near the pleura and she also felt wrist and shoulder joints' arthralgias and slight myalgias. Creatine kinase was mildly elevated. Fever developed at the middle of the month, then she was admitted to our department. On admission, mechanics hands, Gottron's signes and inverse Gottron's papules were found. Manual muscle testing was normal and anti-MDA5 antibody was detected; therefore, she was diagnosed as clinically amyopathic dermatomyositis. The ferritin level was elevated, then combination therapy with PSL, TAC and intravenous CY was initiated. Referring the ferritin level, PSL was tapered; however, dyspnea was developed in August and her lung disease was revealed to be worsened. Though the ferritin level was decreased at that time, the anti-MDA5 antibody/total IgG ratio was elevated compared to the level at the time of remission. The high ferritin level at baseline is known to be a prognostic factor; however, this case might suggest that the anti-MDA5 antibody/total IgG ratio is a possible biomarker for monitoring lung disease rather than ferritin.

MSJR-P4-2

TAFRO syndrome associated with Sjögren's syndrome: A case report

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MSJR-P4-3

Two cases of ANCA positive vasculitis associated with long-term use of Minocycline

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(case1) A 47-year-old man was diagnosed as palmoplantar pustulosis and then minocycline was started 2 years before. Lower limb pain, livedo

reticularis, and slight fever were appeared 4 months before which made him admit to our hospital. Blood test showed the elevation of inflammatory markers and positivity of MPO-ANCA. CT scan and endoscopy revealed no abnormalities. Skin biopsy was compatible with vasculitis, and we concluded that his symptoms was due to drug-associated ANCA positive vasculitis. Oral administration of prednisolone was started. The symptoms ameliorated smoothly and the laboratory data was improved. Prednisolone was reduced carefully, and no recurrence is occurred. (case2) A 52-year-old woman was diagnosed as palmoplantar pustulosis 10 years before and then minocycline was started 2 years before. Slight fever, edematous erythema, pigmentation and numbness of lower limbs appeared one month before. Blood test showed the elevation of inflammatory markers and positivity of MPO-ANCA. Drug-associated ANCA positive vasculitis was suspected /and minocycline was stopped, the symptoms were improved smoothly. Two weeks after the discontinuation of the drug, the skin biopsy was carried out. However; we couldn't find out features suggestive of vasculitis. We concluded that the symptom was due to minocycline associated ANCA positive vasculitis from the clinical course. (discussion) After Cluver et al. reported cutaneous polyarteritis nodosa (CPN). (Arthritis Care Res 2005:53 (3):468-70), similar cases were reported. Our two cases were compatible with minocycline-induced CPN proposed by them, fulfilling their criteria. It is important to check the medical history if the patient presents the symptoms clinically suggestive of CPN.

MSJR-P4-4

An autopsy case of following a rapid clinical course with double-seropositive for ANCA and anti-GBM antibodies

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MSJR-P4-5

Tocilizumab is effective in a Takayasu arteritis patient complicated with corticosteroid resistant scleritis and sensorineural hearing loss

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A 49-years-old man had suffered from fever and bilateral conjunctival hyperaemia for a month. He was admitted to our department for the further evaluation of scleritis and soft exudate around the optic disc in both eyes. On adimission, his CRP level was elevated at 8.96 mg/dl. Contrast enhanced CT revealed the wall thickening in the aorta and three arteries branching from the aorta. Even though MRI revealed wall thickening of both temporal arteries which is suggestive of GCA, a biopsy showed no evidence of vasculitis. A test for human leucocyte antigen (HLA)-B52 was positive. Based on these findings, we diagnosed with Takayasu arteritis (TA) complicated with scleritis and sensorineural hearing loss. We then initiated oral prednisolone 60 mg/day, but he did not improve his clinical manifestation including scleritis, sensory hearing loss, and CRP level in the serum. We thus introduced tocilizumab (TCZ) and the patient achieved remission in scleritis along with sensory hearing loss. This case suggests that TCZ has a potential for the treatment of severe complications in TA including ophthalmic complications and sensorineural hearing loss.

MSJR-P4-6

A case of mixed connective tissue disease positive for proteinase 3 antineutrophil cytoplasmic antibody in a patient with slowly progressive type 1 diabetes mellitus and chronic thyroiditis

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MSJR-P4-7

Granulomatous epididymis and cavernous transformation in Behçet's disease

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Forty-seven-year-old man was suffered from granulomatous epididymitis when he was 30 years old. He developed uveitis 4 years later and was treated with glucocorticoids. Contrast-enhanced computed tomography revealed a prominent cavernous transformation of the portal vein when he was 40 years old. In January 2017, he experienced a relapse of the uveitis with high fever, and erythema nodosum and genital ulcerations developed. C-reactive protein level elevated and serum angiotensin-converting enzyme levels remained within the normal range. There were no signs of tuberculous infection. Human leukocyte antigen B51 was detected and thus he was diagnosed with Behçet's disease (BD). After admission to our hospital, his fever spontaneously resolved and treatment with colchicine was initiated to prevent relapse. The formation of cavernous portal vein is very rare in BD. Previous reports suggested the relationship between granuloma formation and vascular involvement in erythema nodosum in BD. BD should be listed in differential diagnoses in a case with cavernous transformation even if granulomatous inflammation is detected.

MSJR-P4-8

A case of retroperitoneal fibrosis presented by deep venous thrombosis

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MSJR-P5-1

Efficiency and Safety of Tocilizumab in Treatment of Large Vessel Vasculitis

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[Object] To investigate the efficiency and safety of tocilizumab (TCZ) for large vessel vasculitis (LVV). [Methods] This study comprised 6 LVV patients treated with TCZ in our hospital from April 2015. Clinical findings, treatment, outcome, relapse and adverse events were evaluated. [Results] Male: female were 3: 3, mean age was 69.3 years old, and mean observation period was 16 months. Three patients were GCA, and 3 were TA. TCZ was initiated for induction treatment in 4 patients, and for relapse in 2. Five patients, excluding 1 with glaucoma, were treated with PSL (median: 40mg, IQR: 21 - 45mg). CRP at 2 weeks after TCZ initiation (median: 0.03 mg/dL, IQR: 0.02 - 0.26 mg/dL) was less than before the initiation (median: 1.33 mg/dL, IQR: 0.41 - 3.65 mg/dL) ($P = 0.043$). PSL at 2 weeks after TCZ initiation (median: 30mg, IQR: 16-32 mg) was decreased than before the initiation (median: 1.33 mg/dL, IQR: 0.41 - 3.65 mg/dL) ($P=0.020$). There was no relapse in the observation period. Infections as adverse events were observed in 2 patients/4 events (2 were upper respiratory infections, 1 sinusitis and 1 herpes zoster.), but not severe. [conclusion] It was suggested that TCZ had rapid efficiency for LVV and suppressing the relapse rate, but possibility that infection may occur a little.

MSJR-P5-2

Pharmacological therapy with or without the surgical resection of huge gouty pohus for bilateral forefeet; a case of report

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MSJR-P5-3

Predicting factors of abatacept efficacy in Japanese elderly patients with rheumatoid arthritis

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Background Abatacept (ABA) is known as a relatively safe biologic disease-modifying anti-rheumatic drug with low infection risk. A recent report from the French Orencia and Rheumatoid Arthritis (ORA) registry showed a positive correlation between anti-cyclic citrullinated peptide antibody (ACPA) positivity and a response to ABA. **Objective** This study aimed to identify predicting factors of ABA efficacy in Japanese elderly patients with rheumatoid arthritis (RA). **Methods** ABA was administered intravenously or subcutaneously to 28 Japanese RA patients older than 65 years at our hospital from April 2012 to November 2016. The patients were divided into responders (ΔDAS28-CRP>1.2) and non-responders at week 12. Age, disease duration, levels of rheumatoid factor (RF) and ACPA, concomitant drugs, and initial DAS28-CRP were evaluated by univariate and multivariate analysis. **Results** The average age was 69.6 (older than 58.5 in the ORA registry). No patient discontinued ABA due to any side effects. ACPA levels were associated with a response to ABA ($p<0.01$), but not RF ($p=0.34$). Age, disease duration, concomitant drugs and initial disease activity did not correlate with a response to ABA. **Conclusion** Higher ACPA levels were associated with a better response to ABA in Japanese elderly RA patients.

MSJR-P5-4

An analysis of frequency in referring to clinical guidelines in rheumatic arthritis management

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MSJR-P5-5

Ultrasound findings of arthritis in a patient with multicentric reticulohistiocytosis

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A 62-year-old woman was referred to our hospital because of polyarthritis. At her age of 54, she had a diagnosis of dermatomyositis because of proximal limb muscle weakness and papules overlying the dorsal surface of the hands. She was treated with prednisolone, tacrolimus, and methotrexate. However, arthritis had developed, and X-ray showed massive bone erosions of the DIP joints. She had received infliximab at her age of 59 until the pleuritis developed on her. She stopped all medication when she was referred to us. The pathological findings of the specimen from the papule showed aggregates of mononuclear histiocytes and multinuclear giant cells infiltrating the dermis. Immunohistochemical findings showed positive staining of CD68 and negative staining of S-100 and CD1a, which indicated the diagnosis of multicentric reticulohistiocytosis. Ultrasound on the DIP joints showed marked synovial proliferation with bone erosion, and distribution of hypervascularity from the surface to the depths of the synovium. Treatment with methotrexate and infliximab decreased her pain and swellings of joints, then the papules had disappeared. Ultrasound showed the decreased synovial proliferation and hypervascularity. This is the first case report presenting ultrasound findings of joints before and after treatment of multicentric reticulohistiocytosis.

MSJR-P5-6

Tocilizumab-induced psoriatic lesion resolved by shortening the dosing interval in a patient with rheumatoid arthritis: a case report

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MSJR-P5-7

The expression and pathogenic role of Activin A at the inflamed synovial cells in rheumatoid arthritis –importance of down-regulation of CXCL10 expression-

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MSJR-P6-1

Liver dysfunction and pancytopenia in a patient with systemic lupus erythematosus: is it lupus hepatitis or autoimmune hepatitis?

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MSJR-P6-2

A case of unilateral pleural effusion preceding diagnosis with anti-EJ antibody positive myositis

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[Case] A 75-year-old male who presented with dyspnea, fever and chest pain was admitted to the hospital. He showed elevated inflammatory response, mild interstitial pneumonia (IP), and right sided pleural effusion (PE). Although some antibiotics were used because of his exudative PE, they were ineffective. His neck and proximal muscles strength gradually weakened, and his CK levels were slowly elevated. A slight STIR high signal intensity in the bilateral deltoid muscles was detected by MRI. The muscle biopsy showed a mild inflammatory cell infiltration with MHC class I over-expression on muscle cell surface. Finally, we found his positive result of anti-EJ antibody and made his diagnosis of anti-ARS antibody syndrome. Although the negative results in electrocardiogram, cardiac ultrasound and cardiac MRI, asymptomatic cardiomyopathy was considered, because of his elevation of cardiac enzyme. Abdominal CT detected a bladder cancer, and transurethral resection was performed. Even after the surgery, the CK elevation was prolonged, so we started 0.8 mg/kg/day of PSL followed by tacrolimus. The CK level gradually decreased to a normal range and pleural effusion also decreased and disappeared within a few months. [Discussion] Previously, the relation between this antibody positive myositis and the incidence of malignancy was reported and in another retrospective study, myositis patients with EJ antibody having IP tend to show a mild pleuritis. Our case was also consistent with these previous reports.

MSJR-P6-3

A case of primary Sjögren's syndrome complicated with both protein losing gastroenteropathy and intra-arterial thrombosis

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MSJR-P6-4

A case of ANCA-associated vasculitis with nasal cavity and piriformis

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[Case] A-75-year-old woman with fever, fatigue, arthritis, muscular pain on upper and lower limb was diagnosed as ANCA-associated vasculitis with additionally purple spot of legs, internal pneumonia, elevated CRP and high titer of MPO-ANCA 2 years ago. And she was treated by predonisolone (PSL) 25 mg/day. PSL was decreased to 8 mg/day a year ago. However, exacerbation of vasculitis occurred with fever, arthralgia, elevated MPO-ANCA as 12.4 IU/L, so PSL 45 mg/day and mycophenolate mofetil 1.5 g/day were started. PSL was decreased to 10 mg/day a year ago, but this year she had fever, headache, nose pain, and laboratory showed CRP 5.21 mg/dl. We recognized soft shadow with contrasting effect by contrast-enhanced CT along right sacrotuberous and sacrospinous ligament. PET/CT showed uptake in left nasal cavity and right piriformis. We performed biopsy on them and the result was that they could be the lesion due to vasculitis. Including clinical course, they were diagnosed as exacerbation of vasculitis. After increasing PSL to 25 mg/day and cyclophosphamide pulse, the lesion were reduced by non-contrast CT. [Discussion] There is no report that the lesion of ANCA-related vasculitis was found on piriformis. The treatment with a steroid and cyclophosphamide was succeeded in this case.

MSJR-P6-5

Hypertrophic Pachymenigitis in a Patient Diagnosed as Polyarteritis Nodosa based on Skin Biopsy

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A 69-year old man developed scleritis and livedo reticularis, and a skin biopsy revealed necrotizing vasculitis. He has diagnosed with polyarteritis nodose (PAN) and treated with prednisolone (PSL). His scleritis repeatedly relapsed, and he was referred to our hospital. His scleritis improved with topical steroids, and azathioprine (AZP) was added. Six months later, while taking PSL 14 mg daily and AZP 50mg daily, he developed a headache. MRI revealed hypertrophic pachymeningitis. Although both PR3-ANCA and MPO-ANCA were negative, he had a perforation of the nasal septum, as well as sinusitis and interstitial pneumonia. The diagnosis of granulomatosis with polyangiitis (GPA) was considered, but a biopsy of the sinus did not show granulomatous inflammation. There was abnormal enhancement of the soft tissues around the superficial temporal artery on MRI and abnormal uptake on FDG-PET in the abdominal aorta. The possibility of giant cell aortitis was considered, but superficial temporal artery biopsy did not show signs of vasculitis. Based on the clinical findings and the results of the past skin biopsy, he was presumed to have GPA or PAN and treated with PSL 45mg daily and cyclophosphomide, which resulted in improvement of the headache and the MRI findings.

MSJR-P6-6

Three cases of fever of unknown origin with polyarthralgia and polymyalgia using fluorodeoxyglucose positron emission tomography/computed tomography

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MSJR-P6-7

A case of relapsing polychondritis without auricular chondritis involving arterial lesion

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MSJR-P7-1

Immunoglobulin G4-related disease with a mass in the paravertebral muscle: A case report and review the literature

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IgG4-related disease (IgG4-RD) is characterized by tumor-like swelling of involved organs, IgG4-positive plasma cells infiltration, and fibrosis, and has similar features with lymphoma, and sarcoidosis. We report a case who was diagnosed to be the IgG4-RD with a mass in the paravertebral muscle. A 74-years-old male presented with pitting edema of lower extremities and weight gain on September 201X. CE+CT scan with revealed a para-aortic mass, pulmonary nodules, and left sided pleural effusion. Cancers of unknown primary site was suspected, and he admitted to our hospital on October. PET/CT showed positive uptake in a mass in the paravertebral muscle. Biopsy of the mass was performed, which showed plasmacytic infiltrates enriched in IgG4-positive, and fibrosis. There were more than 10 IgG4-positive plasma cells/HPF and the ratios of IgG4- to IgG-positive cells was 95%. The serum IgG4 was 570 mg/dL, and he was diagnosed as IgG4-RD. PSL 35mg/day was started, and within a week, pitting edema, pleural effusion and pulmonary nodules were resolved and the size of the para-aortic mass reduced. This is the first case report of IgG4-RD with a nodule on muscle as far as we searched. Biopsy is very important to make a diagnosis of IgG4-RD particularly in unusual cases.

MSJR-P7-2

A SLE patient with maculopapular rash induced by hydroxychloroquine: A case report and review of the literature

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Hydroxychloroquine (HCQ) has been used to treat SLE around the world for more than half a century. However, it has been only two years since its approval in Japan, thus we do not know the exact profile of its adverse events in Japanese population, such as retinopathy and drug eruptions. He we report a case of SLE patient who developed maculopapular rash induced by HCQ. A 31-year-old woman with seven-year history of SLE presented with fever, malar rash, and arthralgia, which was accompanied by leukopenia and increased level of anti-ds-DNA antibody. We started PSL 30mg/day and HCQ 300mg/day simultaneously. Nine days later, she noticed erosion on her lips, followed by generalized erythema and papules. We stopped HCQ and increased the PSL dose to 55mg/day. The lesions started to disappear over one week of treatment. The half time elimination of HCQ is up to 40 days, thus the rash might persist or relapse if PSL is tapered too quickly. The post-marketing surveillance of HCQ in our country has already reported 4 severe skin reactions out of 1000patients. We should pay attention to the possibility that the frequency of drug eruptions by HCQ might different between Japanese and oversea patients.

MSJR-P7-3

A case of a patient with systemic sclerosis complicated in its early phase with renal crisis associated thrombotic microangiopathy (TMA)

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MSJR-P7-4

A case of microscopic polyangiitis with refractory otitis media

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MSJR-P7-5

A case of relapse of elderly Takayasu arteritis with bilateral renal arteritis successfully treated with tocilizumab

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MSJR-P7-6

A case of giant cell arteritis without headache complicated with elderly-onset rheumatoid arthritis

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MSJR-P7-7

A case of Behcet's disease with a seizure as an initial symptom

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A 39-year-old woman, she was experienced of first seizure and diagnosed with an epilepsy in 2003. Because she had a recurrence of repeated seizure, treatment with zonisamide was begun in 2013. One month later, symptoms of oral ulcers, arthritis, genital ulceration, folliculitis and erythema nodosum on lower legs appeared. Those symptoms are disappeared in one week. Positivity of HLA-B51 was revealed, but she didn't hope to be added another examination. In October 2017, she had symptoms of multiple oral ulcers, arthritis, erythema nodosum, folliculitis with pyrexia. She was diagnosed with Bechet's disease and admitted to our hospital. Her symptoms improved by quiet rest within a week. There was no abnormalities in MRI and electroencephalography. We examined cerebrospinal fluid, because she complained of headaches from events in 2013. interleukin-6 (IL-6) in her cerebrospinal fluid was 23.7 pg/ml, so we diagnosed neuro-Behcet's disease. In this case, she was treated as epilepsy due to a relapse of seizure. However, in fact, IL-6 level in her cerebrospinal fluid was elevated. It was revealed that chronic inflammation in her nerve systems was continuous. We know that neuro-Bechet's disease diagnosed because of seizure and epilepsy in the course of Behcet's disease. However, this is a rare case with a seizure as initial symptoms of Bechet's disease and we report here.

MSJR-P7-8

Successful treatment of rheumatoid meningitis with prednisolone and cyclophosphamide

Satoshi Hama, Misako Konishi, Masako Tsukamoto, Keisuke Izumi, Mari Ushikubo, Kumiko Akiya, Hisaji Oshima
National Hospital Organization Tokyo Medical Center

MSJR-P8-1

Treatment of a case with anti-MDA5 antibody-positive dermatomyositis with interstitial lung disease

Shunta Miwa[1], Shuhei Shimoyama[2], Nobuya Abe[2], Kohei Karino[2], Yuichiro Fujieda[2], Tatsuya Atsumi[2]
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MSJR-P8-2

FDG-PET was useful tool in diagnosis and evaluating disease severity of TAFRO syndrome in a patient developed with purpura, pleuritis and thymus lesions during the course of Sjögren syndrome

Asako Sato[1], Naohiro Sugitani[2], Ayaka Ino[1], Yuki Mizutani[1,2], Yosuke Hirabayashi[3], Yasuo Suzuki[2], Eiji Ishikawa[3], Ayako Nakajima[2]
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MSJR-P8-3

A case of ANCA-associated vasculitis presenting with retinal vasculitis and rapidly progressive glomevulonephritis

Satoko Kishimoto[1], Takeshi Yoshida[2], Hiroaki Chikazawa[2], Yoshitaka Kumon[2]
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MSJR-P8-4

Myeloperoxidase-antineutrophil Cytoplasmic Antibodies (MPO-ANCA) positivity in a cohort of patients with idiopathic interstitial pneumonia

Jun Matsumoto, Yuta Mori, Yasuhiro Kondo, Tomoki Kimura, Kensuke Kataoka, Toshiaki Matsuda, Toshiki Yokoyama, Yasuhiko Yamano
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MSJR-P8-5

A case of Behcet's disease with atypical vascular involvement and a strong family history, treated with adalimumab

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[Case] The patient was a 74-year-old woman. She had a history of a cerebral aneurysm. Sixteen months ago she presented with intra-oral ulcers, genital ulcers, nodular erythema, thrombophlebitis, and acne, and was diagnosed with Behcet's disease (BD). Her symptoms persisted despite non-steroidal anti-inflammatory drugs and colchicine, but improved with prednisolone (PSL; 15 mg/day). The symptoms repeatedly recurred when the PSL dose was tapered to 10 mg/day. She sought evaluation at our hospital 8 months ago and the addition of cyclosporine (CyA) ameliorated the skin lesions. She developed arthritis 2 months ago, and the PSL dose was increased from 2 to 7 mg/day. CyA was switched to methotrexate (MTX; 6 mg/week). A computed tomography (CT) scan showed an asymptomatic dissection of the abdominal aorta and right fibular varices. These findings led to the diagnosis of vasculo-BD. The same CT, taken before initiation of MTX, also showed asymptomatic interstitial pneumonia (IP). Her older brother had vasculo-BD and died of abdominal aortic dissection. Her older sister was suspected to have BD, and her nephew died due to BD. HLA-B51 and A26 were negative. Adalimumab therapy was initiated. [Clinical significance] We have presented a patient with atypical BD, a strong family history of BD, IP, and atypical vessel lesions (aortic dissection and cerebral aneurysm). The clinical response to adalimumab is discussed with a review of the literature.

MSJR-P8-6

A case of relapsing polychondritis with meningoencephalitis

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MSJR-P8-7

Study of Human Autoimmune Diseases Enabled by Gene Editing in Reporter Cell Lines

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nopathology, World Premier International Research Center, Immunology Frontier Research Center, Osaka University, [3]Department of Respiratory Medicine and Clinical Immunology, Osaka University Graduate School of Medicine

A human monocytic cell line, THP-1, has been widely used to study the innate immune system. THP-1 is activated by various stimuli, including pathogen-associated molecular patterns (PAMPs) and damage-associated molecular patterns (DAMPs), and can be differentiated into macrophage-like cells using phorbol-12-myristate-13-acetate (PMA), providing a useful tool in myriad experimental settings. However, being a suspension cell line, THP-1 has proven a difficult target for transfection using conventional methods, such as lipofection, electroporation, and viral transduction. Thus, gene-engineering of THP-1 has long been desired since it will significantly expand the range of application of THP-1 cells in the study of human immunology. By modifying the method for lentiviral transduction, we were able to effectively introduce genes of interest into THP-1 cells with transduction efficiency over 90%. Using this technique, we transduced CRISPR/Cas9 into THP-1-based reporter system, which allows monitoring of the activation of interferon-stimulated genes (ISGs). Because these cells constitutively express Cas9, knockout cell lines can be generated easily by adding gRNA into the cells. With this gene-editing system, we established THP-1 cells deficient of molecules that are essential in various interferon-inducing signaling pathways, namely STING, MAVS, IRAK1, and IFNAR2. Utilizing these cells, we studied the inflammatogenic factors in sera of human autoimmune diseases.

MSJR-P9-1

Utility of musculoskeletal ultrasonography at central clinical laboratory for daily care in rheumatology clinic

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MSJR-P9-2

The typology of rheumatoid arthritis patients during the transition period of introducing PGA

Rika Nakamura[1,2], Takeshi Hida[2], Masayo Kojima[3], Mina Suematsu[2], Hiroki Yasui[2], Kazumasa Uemura[4], Kentaro Okazaki[2], Noriyuki Takahashi[2], Toshihsa Kojima[5]

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MSJR-P9-3

A case of finger ulnar deviation in psoriatic arthritis successfully corrected by medical treatment

Hiroto Nishimura[1], Ryota Hara[2,3], Tsutomu Kira[2], Naoki Shimmyo[2], Akira Kido[2], Yasuhiro Akai[2], Takashi Fujimoto[2], Takashi Yoshii[3], Yasuhito Tanaka[2]

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MSJR-P9-4

A case of sarcoidosis with anti-cyclic citrullinated protein antibodies presenting as acute cardiac failure and polyarthritis

Kana Bandou, Natsuka Umezawa, Seiya Oba, Hisanori Hasegawa, Hitoshi Kohsaka

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A 51 year-old man with elevated anti-citrullinated protein antibodies (ACPA) and rheumatoid factors had been suffering with recurrent polyarthralgia and lower leg edema for 6 months. He developed progressive dyspnea and fever with worsening polyarthritis of the bilateral wrists, fingers and ankles. No erosion was found with hand and foot X ray. Bilateral ground glass opacity (GGO) and mediastinal and bilateral hilar lymphadenopathies were detected by chest X-ray and CT. Although ECG revealed left ventricular hypertrophy and UCG revealed hypokinesis at antero-septal and inferior walls, coronary angiography described no abnormality. While diuretics improved the GGO, myocardial hypokinesis remained. He underwent transbronchial lymph nodes biopsy and was diagnosed as sarcoidosis according to histological findings of non-caseating granuloma. Corticosteroid ameliorated his cardiac function and arthritis. Whereas specificity of ACPA for rheumatoid arthritis (RA) was over 80 %, 4-8 % of sarcoidosis with/without arthritis was reported ACPA+. We diagnosed him as sarcoidosis and not as co-occurrence of RA and sarcoidosis, based on the simultaneous development of articular and cardiac involvements. Sarcoidosis should be considered as differential diagnosis for arthritis with ACPA.

MSJR-P9-5

A case of showing repaired joint destruction by TNF-α inhibitor for the patient of rheumatoid arthritis with hepatitis B virus

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MSJR-P9-6

A case of rheumatoid arthritis with JAK2V617F mutation

Kosuke Sugihara[1], Tsukasa Sotobori[2], Kenta Watanabe[2], Kozo Kitazawa[1], Yasuhiro Ohashi[1], Akira Idogaki[1], Hirohiko Onoyama[1], Seigo Sya[1], Takashi Matsumoto[2], Takenori Itohara[1], Shoun Tyo[1], Hayato Katayama[1], Tomoyuki Yamaguchi[1], Reiko Takahashi[3]

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MSJR-P9-7

The effect of IL-24 on fibroblast-like synoviocytes from rheumatoid arthritis patients

Shunsuke Tsutsumi[1], Miori Shimizu[1], Haruka Tsuchiya[2], Megumi Ogawa[2], Mineto Ota[2], Hirofumi Shoda[2], Shuji Sumitomo[2], Sakae Tanaka[3], Keishi Fujio[2], Kazuhiko Yamamoto[4]

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